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Complementary and Alternative Medicine: Feed Additives

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PREFACE

Animal nutrition has evolved rapidly, with feed additives playing an essential role in shaping the health, productivity, and well-being of livestock, poultry, pets, and aquatic species. *Complementary and Alternative Medicine: Feed Additives* explores the multifaceted benefits of feed additives, from natural herbs to advanced nano-supplements, and their transformative impact on animal agriculture and sustainable farming practices. In this book, readers will find comprehensive insights into feed additives that promote growth, enhance immunity, and prevent diseases in a variety of animals. It covers the use of natural additives in broiler birds, ruminants, and aquaculture, illustrating how these supplements not only improve production but also contribute to product quality. Herbal additives, for example, have been shown to boost immune responses in livestock, reduce pathogen loads, and improve fillet quality traits in fish. This holistic approach to animal health highlights the potential of nature-based solutions in improving farm practices, ensuring both animal welfare and environmental sustainability. One area of particular interest is the growing use of nanoparticles as feed additives. Nanotechnology in animal feed is at the frontier of animal nutrition science, offering efficient delivery systems and enhanced bioavailability of nutrients. This book examines the preparation, mode of action, and application of nano-feed additives, which have shown promise in boosting health and growth traits in various animals. Furthermore, these additives provide solutions for disease prevention and control, giving farmers and veterinarians powerful tools to mitigate issues such as salmonella in poultry and reproductive disorders in dairy cattle. Alongside technological advancements, traditional feed additives like milk thistle, Prosopis, and tannins have also been highlighted for their therapeutic roles across different species. Each of these offers unique health benefits, from liver protection to mastitis prevention, demonstrating that a balanced approach combining traditional wisdom with modern science yields optimal results. The book further delves into nutraceuticals—natural products that serve as preventive and therapeutic supplements—illustrating their critical role in safeguarding animal and even human health. Functional foods and biotic supplements are examined for their benefits in gut health and disease prevention, reflecting the broader, integrated view of nutrition in veterinary medicine. In addition to livestock applications, this volume addresses feed additives for pets and fish, considering their distinct nutritional needs and the specific additives that enhance their health and longevity. Nutritional strategies such as probiotics, prebiotics, and enzymes are explored for their potential to improve the gut microbiota, resilience, and overall health of these animals. The book also highlights innovative approaches, such as the addition of Bacillus subtilis to aquariums for improved water quality and enhanced fish health, as well as non-conventional mineral sources that support sustainable practices in aquaculture. Regulatory and functional perspectives on feed additives are also presented to guide readers through the complexities of their use in the animal industry. This includes an in-depth look at alternative minerals, flavor additives, and the interactions between diet, microbiota, and health. Such insights underscore the importance of a strategic, science-based approach to nutrition, where each additive plays a distinct role in promoting resilience, productivity, and disease prevention. *Complementary and Alternative Medicine: Feed Additives* is designed for students, researchers, veterinarians, and animal health professionals who are looking to explore cutting-edge advancements in animal nutrition. By bridging traditional and alternative medicine approaches with modern nutritional science, this book offers a valuable resource for improving animal health, supporting sustainable farming, and meeting the complex challenges of today's animal agriculture industry. Through this journey, readers will gain a deeper understanding of how feed additives—natural, herbal, and technological—are reshaping the future of animal health and production.

Editor

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Chapter 01

Understanding Concepts of Feed Additives in Animal Nutrition: their Potential in Improving Livestock Production Performance and Product Quality

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ABSTRACT

Feed additives are the ingredients added to animal feed for improving feed efficacy, nutrients metabolism and animal health and productive performance in addition for enhancing the quality of animal products. The most commonly used additives are vitamins, minerals, amino acids, enzymes, prebiotics, probiotics and natural herbal extracts. Due to more than 60% animal feed utilization, North America and Asia-Pacific are the topmost consumers of additives in the world. The major factors for global market are increasing meat production and consumption, awareness about meat quality and safeguard measures, and disease epidemics. Additives are classified into different categories based on the European commission regulations, holistic practices, originality and functionality. Having no negative interaction with nutritional quality, easy availability with fair prices, composition, modes of actions, recommended levels, storage ability, lack of anti-nutrients and hazards free are factors for selection criteria of additives. Improvement in the animal health and productive performance, animal product quality, reduced environmental impact and animal efficiency come under the scope of feed additives. A new feed additive requires a formal pre-market authorization before it can legally be marketed out. The feed industries, feed dealers and feed business entrepreneurs should make it sure that these materials are safe and register their production facilities.

KEYWORDS		
Classification; Feed additives; Herbal extracts; Recent trends; Scope; Regulatory measures	Received: 16-May-2024 Revised: 02-July-2024 Accepted: 21-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

The application of feed additives to improve palatability and intake of feed has long been practiced when farming community used to add salt to animal feed. With the passage of time, feeding these additives to animals has become more common with developments in animal nutrition. During 20th century, discovery and inclusion of vitamins in the animal diet prevented deficiencies and improved the growth performance. This has brought the development of several other feed additives such as enzymes, amino acids and minerals. To date, feed additives have taken much attention as indispensable components in the animal nutrition. These are substances added to feed to improve the feed efficiency and acceptance, or for enhanced metabolism, and, animal health. They are used to improve nutrients utilization, promote growth, and enhance the health and well-being of animals. Regulation of using additives in the animal feeds is set by government sector to confirm their safety measures and effectiveness.

Proper nutrition is a primary requirement for the optimum animal production. As aquaculture is increasing day by day and new advances are being made in nutrition and feed development, it becomes necessary that the feed manufactured should be consumed readily by the animals with less wastage. In the light of European Commissions commonly accepted definition, "Feed additives are products utilized in the animal nutrition in order to improve the feed or food quality from animal origin and or to improve the animal health and performance like providing enhanced digestibility of the feed materials" (Yadav et al., 2021).

Moreover, feed additives are ingredients or combination of ingredients supplied in routine basal diet to achieve specific goals. Commonly, these are added in minor (micro) quantity with vigilant handling and mixing. Their purpose of inclusion is to enhance gain in the body weight, feed efficacy and mitigation of diseases against environmental factors. Most commonly used feed additives are vitamins, minerals, amino acids, enzymes, prebiotics and probiotics. These also enhance quality of animal products such as meat, milk, and eggs.

As described above that application of feed additives in animal nutrition is attracting more attention on daily basis due to the factors like growth enhancers, transmissible diseases mitigation agents and enhancer of nutrients' digestibility (Rafiq et al., 2022).) . There is an unwavering rising graph in the market of additives and more growth is predicted in the near future, due to increasing demand for meat, milk and their products. The consent of beef and dairy producers has augmented towards feed quality standards and official certifications due to the prevalence of diseases like bird flu, foot-and mouth-disease, and environmental issues. North America and Asia-Pacific are the world topmost utilizers of feed additives by accounting more than 60% of consumption (Makkar, 2018). This region is considered one of the most rising regions in income production. India, China, and Brazil are predominant in emerging economies due to steady increase in the population income because of more industrialization (Chaitanya, 2007). The market of feed additives is mainly covered by poultry and followed by pigs. The major factors considered for marketing of additives are increasing trends of meat consumption globally, awareness about meat quality and safeguards measures, high meat production and disease epidemics in the livestock sector (Henchion et al., 2017).

The market limitations are causing high price of raw materials and amendments in the regulatory set-up. Nevertheless, high prices of feed ingredients of natural origin, is giving importance to feed additives, as a suitable substitutions. This chapter will explore comprehensive classification, importance, selection criteria and potential of feed additives in improving the animal productivity.

Classification of Animal Feed Additives

The comprehensive classification of these additives into various groups in accordance with variable functional parameters is presented in Fig. 1. Some feed additives of herbal origin along with their botanical names, part used as feed additive, composition of active components and functions are summarized in Table 1.

Importance and Selection Criteria of Animal Feed Additives

The significance of feed additives cannot be overlooked as they not only provide vitamins and minerals; but they are also used to increase feed palatability to keep the animals on consumption continuously. They enhance nutrient digestibility to avoid any stress and other digestion issues that usually occur.

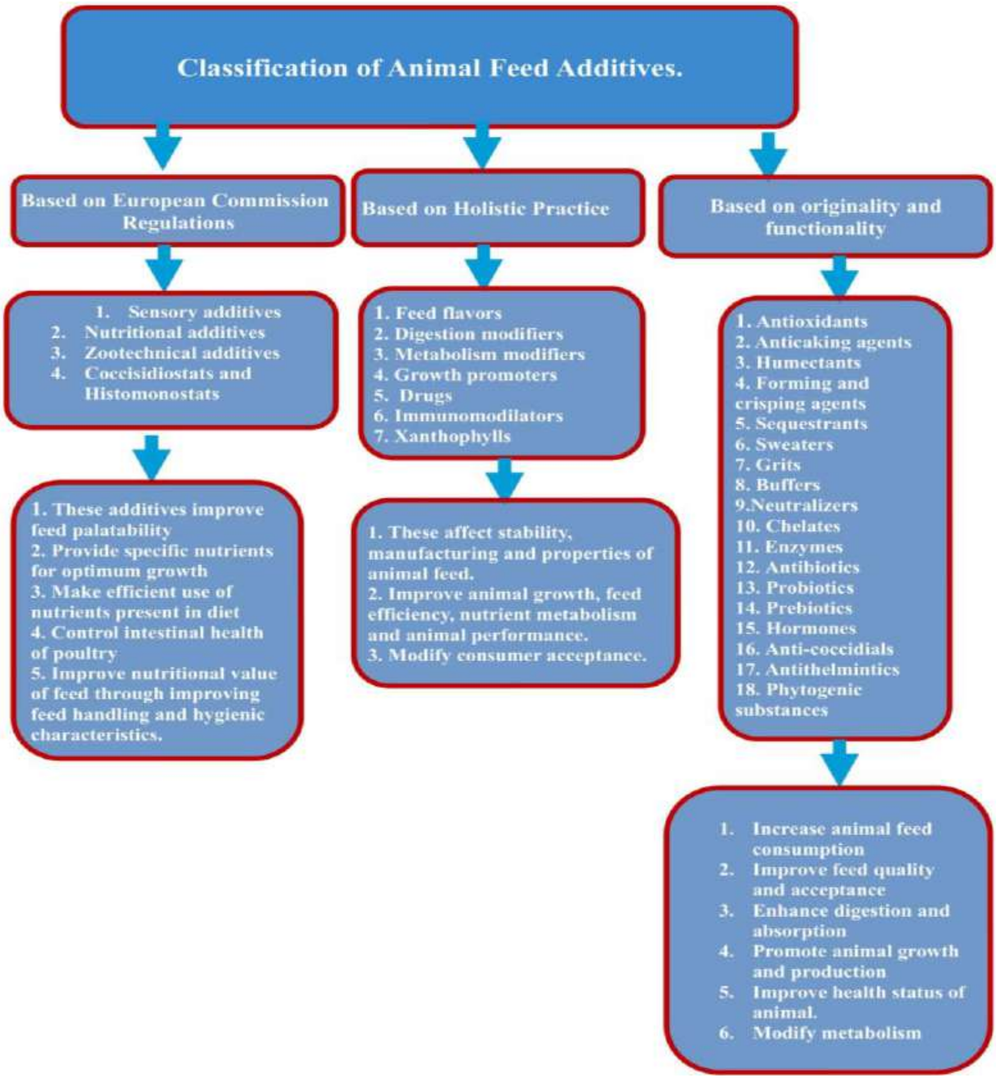

Fig. 1: Classification of Summary of Animal Feed Additives

Table 1: Animal feed additives of herbal nature used for improvement in the animal health and production performance

Botanical name of herb	Herb/part/parts	Significant active components	Applications	Source
Acacia catechu	Stem extract and fruit	Epicatachin, epigallecatechin, cataechin, epicatechinn, , aldebiuronic acid, gallic acid, D-galectose and quercetin	Antioxidant, anti-inflammatory and antidiarrheal	(Duke,1992), (Rastogi and Mehrotra, 2005)
Aloe Barbadensis.	Leaf	Folic acid., choline, barbalion, and amoden	Antibacterial, anti-inflamatory and emmenagogue	(Blumenthal et al., 1998, (Rastogi and Mehrrotra, 2005)
Asparagus racemosus	Root	Asparagamine and steroidal saponins	Galactogogue, antistress, immunostimulant	(Bopana and Saxena, 2007).
Allium sativum	Bulb	Allicin, alliin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, ajoene, and s-allyl-cysteine	Anti-inflammatory , antoprotozoal, hypolipidemic and carminative	Tesfaye, (2021), (Sharma et al., 2000–.2005)
Balanites roxburghii	Fruit, seed and seed oil	Bergapten and marmesin and Balanitisins A-E	Anti-colic, anthelmintic, puragative, spasomolytic and anti-colic,	(Hussian and Virmani 1992)
Cinnamomum verum	Leaves	Caffeic acid, coumaric acid, coumarin, benzoic acid, quercetin, quercetin, cinnamyl alcohol and cinnamaldehyde,	Antibacterial, antioxidant, anti-inflammatory and anticancer	(Kumar e al., 2019)
Cissus quadrangularis	Leaves, stem and root	Pallidol, piceatannol and quadrangularins	Healing of Fracture and beneficial in dyspepsia	(Rastogi and Mehrrotra, 2005)
Cuminum cyminum	Seeds	Cuminaldehyde, Cumin and cumin oil	Stimulant for digestive enzymes and enhancer for microbial growth	(Srinivasan, 2018)
Curecuma longa	Rhiezome	Desmethoxycurcumin, turemerone and curcumin	Anti-inflamatory, caraminative, spasomolytic, anti-oxidant and hepato-protective	Blumenthal et al., 1998 (Duke, 1992), (Hussian and Virmani 1992).
Eucalyptus globulus	Leaves, oils	Eucaglobulin, limonene, cineole and pinene	Carminative, digestive and expectorant antibacterial and anti-inflammatory	Rastogi and Mehrrotra, 2005), (Blumenthal et al., 1998), Hussain and Virmani 1992)
Glyocyrrhiza glaibra	Root	Glabranins liquireitin and glycyrrhizin	Anti-inflamatory, expectorant and antihistaminic	(Duke, 1992), (Blumenthal et al., 1998)
Leptodenia reticiulata	Root	Rutin, stigemasterol and hentriaecontanol	Galactogogue, stimulent and uterine cleaner	Hussain and Virmani, 1992, (Mirzaei, 2011)
Ocimium sanictum	Leave, whole plant and oil	Eugeneol, urusolic acid, carvaccrol, luteoleen and methylochavicol	Immunomodulator, antinflamatory, antittussive and antiprotozeoal	(Sharma et al., 2000–2005), (Rastogi and Mehrrotra, 2005)
Origanum vulgare	Leaves	Carvacrol, p-cymene, limonene, ocimene, caryophyllene, linalool, antibacterial, antifungal, antiparasitic, antimicrobial and antioxidant.	Antibacterial, antioxidant, antiviral, immunomodulatory and antiparasitic	(Bora et al., 2022)
Phyllanithus emblica	Fruit, leaves	Gallic acid, ascorbic acid and embliecanins A and B	Antioxidant, hepato-protective and imunomodulator	(Rastogi and Mehrrotra, 2005)
Solanium nigrum	Whole plant	Solamargine, solanine, solasodine and solasonine	Mycotoxin inhibitor, duiretic, hepato-protective and antioxidant	(Duke, 1992), Hussain and Virmani (1992)
Swertia chirata	Whole plant	Gentianine, swerchirin and Swertiamarin	Anti-helminitc, Hepatoprotective and anti-inflammatory	Hussain and Virmani 1992
Withania Somnifera.	Root	Withferin-A, withianine, somniferine	Adotogenic, anti- stress, immunmodulator and anti-oxident	(Duke, 1992).

Usually there are 8 groups of animal feed additives that are being used to perform different functions Okey, (2023). These include vitamins, minerals, amino acids, binders, enzymes, antibiotics, acidifiers and antioxidants. Vitamins are added in animal feeds to make them more nutritional. The macro minerals are given in higher amounts while micro minerals are required in trace amounts. Minerals are added for the bone and teeth health, body fluid regulation, nerves and muscle support, fluid regulation, blood and hormone synthesis and enzyme activation and immune functions. Amino acids act as the foundation for protein which is imperative for muscles, tissues, skin and hair (Scrimshaw and Young, 1976). They prevent growth of harmful pathogens, assisting with animal's immune system and protect nutrients from degradation. Antioxidants cover nutritional deficiencies occurring through destruction of vitamins and fats. They also play a key role against free radicals that may result in cancers and heart disease. Enzymes are not only used to supplement digestive enzymes in the animal but they also warrant an improvement in meat and egg production. The mold inhibitors and mycotoxin binders prevent mold growth and mitigate them from being absorbed into gut and bloodstream (Tokach et al. 2010). The probiotics and prebiotics are added in feeds for nutrients digestion, absorption and gut health. The antibiotics are used for disease prevention and also aid in rapid growth. The acidifiers are added to animal feeds to support in digestion and also assist in minerals absorption and improvement of immune system. In general, usage of feed additives greatly improves animal health and productive performance. The following factors should be considered while purchasing and applying feed additives to animal feeds.

The feed additives should not be poisonous and interact negatively with feed ingredients or nutritional quality. The quality of feed additive should be tested through laboratory analysis to avoid any negative impact on its application. A typical testing procedure should consist of information regarding its composition, mode of action and recommended levels for different animal species.

The variability can be a significant factor for various alternative feed additives in animal feeds. In addition to have an accurate profile gathered over a long time frame, it is of greater importance to have information about source and supplier. With greater variability, there should be lower inclusions as a precautionary measure.

The nutrient digestibility and availability are extents of the animal's digesting and absorbing the nutrients within feeds. The animal feed additives should have a considerable potential to enhance nutrients availability from the feed and availability to animal. The digestibility studies, chemical analysis in laboratory, available literature, and databases are important informative sources of feed additives (NRC, 1996)

Some natural phytogenic feed additives can impair digestibility, metabolic process, or animal health status through presence of anti-nutritional factors such as mold and mycotoxins produced under unfavorable storage conditions (Steiner and Syed, 2010). Therefore, prior to their usage, they should be investigated for presence of anti-nutritional properties via analysis and then recommendations should be made regarding their application and adjustment of inclusion level.

Depending upon the source and type of processing, some feed additives may contain contamination that can be considered hazardous to animal. So feed additives used in animal feeds should be free of hazards and should be handled and stored properly.

Prior to the cost evaluation, there should be enough supply of these feed additives. It should be determined by considering animal breed, diet, supplementation level and quantity for calculating the potential volumes needed over time period.

Storing ability and long term quality feed additives are of greater significance to ensure proper preservation of the product to avoid spoilage under storage conditions.

Inclusion level of the feed additive in diet of animal and conditions involved are greatly interpretable. Vast experience in setting the boundaries and then inimitable set of methods and school of thoughts of nutritionist or company regarding incorporation of unusual feed additive in the feed are accountable. In addition, some specific guidelines of feed industry, research articles and other sources of literature are also significant contributors towards developing base line for inclusion level of the feed additives.

Economic impact is the biggest factor in application of feed additive in the animal feeds. It must not adversely affect the eating quality and consumer's appeal of the meat, milk and eggs of the animal that it is fed. The material must be available in sufficient quantities at a fair price

Scope of Animal Feed Additives

The scope of feed additives is immense, as they can be used to improve animal health, increase growth rates, and enhance the quality of animal products. Furthermore, feed additives can be used to reduce environmental impact of animal production by reducing the amount of waste produced. Overall, application of feed additives in livestock sector is an important aspect of modern animal agriculture and plays a vital role in ensuring the sustainability and efficiency of animal production (Athithan and Felix, 2012). These also enhance flavor, texture and shelf-life of animal products. Additionally they improve nutrients digestibility and absorption. However, as concerns like food safety, environmental impacts and animal welfare, feed additives that farmers feed their animals are marketed out under closer scrutiny. Therefore, they play a vital role in addressing these concerns by supporting animal health, improving productivity and ensuring food quality.

Application of the feed additives has higher impact on animal welfare, productivity and food safety, i.e. animals grow at normal rates, need little medication, present rigorous outlook, extend product quality and shelf-life, utilization of the feed more effectively with no or less toxic runoff. To cover the concerns, following considerations should be taken into account:

1. Feed additives should be from reputable companies with research back, an authentic track record of security and efficacy.
2. They should evade toxic residues, drug interactions or dubious origins.
3. Declaration of right feed additive with its dose based ethical value, life stage, species, health conditions and performance achievements by nutritionists and research.
4. Following scientific guidance properly, maintaining consistency and avoiding over/under supplementation level for optimum animal health, welfare and food safety.
5. After transitioning to or from feed additives, animals should be closely monitored for any changes in behavior, appetite, feces and productivity for needful adjustment.

6. Keeping records on composition of the feed additives, animal health metrics, productive performance and product quality.

Recent Trends in Animal Feed Additives

There is a growing trend using different products as feed additives in animal nutrition. Application of the medicinal plants and their extracts for production purpose in livestock is attaining more attention due to public health reservations caused from antibiotics resistance against bacterial diseases and residues in foods and food by-products (Ekunseitan et al., 2016). Due to ban on using antibiotics in the animal diets by EU in 2006, medicinal plants and their extracts are conversely used as botanical alternative in livestock sector. The globe interest on using herbal products has grown significantly by 70% in cattle, goat, sheep, horses and pigs followed by poultry (9.1%), dogs (5.3%) and rabbits (4.3%). In rural areas, these are used by small livestock holders because of low price, easy availability and their effectiveness (Kuralkar and Kuralkar, 2021).

The latest studies have proposed the application of herbal extracts and essential oils, probiotics, prebiotics and organic acids as natural alternatives because of antifungal, antioxidants, antimicrobial, antiviral, anti-parasitic and anti-helminthic activities due to the presence of phytogenic and bioactive components (Joshi et al., 2020). Concentration of active components present in these plants and their parts vary widely depending on leaf and seed parts, extraction procedure, stage and age of plant maturity, geographical origin, storage conditions and harvesting seasons (Burt, 2004). These plants and their extracts have been shown to perform different physiological activities such as animal productive performance, nutrient digestibility and availability. They are non-toxic and free of undesirable residues.

Inclusion of natural identical compounds like phytochemicals, and secondary plant metabolites to the fish diet might be a promising alternative for promoting growth performance, manipulating gut-microflora and improving immune and oxidative status against bacterial infections in aquatic sector (Beltrán and Esteban, 2022).

Some of the agro-food sector byproducts compose functional and bioactive components, containing valuable molecules with high functionality and/or bioactivity. Typically secondary products from the primary agro-food industry support idea of a circular economy by serving as a fascinating and less expensive source of ingredients that may be useful, such as peptides, carotenoids, and phenolic compounds (Faustino et al., 2019).

Many plants extracts contain amino acids, carbohydrates, lipids, vitamins, inorganic materials and isoprene derivatives and flavonoids having antioxidant (Golestan, 2010) and antimicrobial activity (Hammer et al., 1999) as well as enhance overall performance and improve nutrients digestibility (Oluwafemi et al., 2020). These also exhibit anti-inflammatory, anticoccidial (Arab et al., 2006) and anthelmintic properties (Hoste et al., 2006). The main factors affecting concentration and bio-diversity of active components in herbs are area of cultivation, climatic conditions, vegetation phase and genetic alterations (Miliauskas et al., 2004). Moreover, the properties undoubtedly are the major mode of actions of plant extracts responsible for the growth performance and animal health (Hashemi and Davoodi, 2011).

Potentiality of Feed Additives in Improving Livestock Performance

Currently application of feed additives in the form of natural products has attained great importance as growth promoters in the animal diet. Livestock industry is facing a pressure by society to enhance animal production, diminish economic losses, and ensure utilization of products for the public sector (Kostadinović and Lević, 2018). The potential uses of these products not only reduce prevalence of bacterial infections but also improve the product quality and livestock production performance, through healthy gut. Actually, gut health denotes interaction among micro-biome, intestinal wall barrier, and physiology and immunity, responsible for coping with different internal and external stressors in animals (Artuso-Ponte et al., 2020).

Supplementation of feed additives of the natural origin in animal feeds improves animal productivity, enhance nutrients digestibility and stabilize beneficial gut micro-flora which in turn improves the animal product quality (Franz et al., 2010). These natural feed additives like phytogenic substances and beneficial microorganisms have greater impact on human, livestock nutrition and health and therefore, can satisfy demands of public sector for natural products (Placha et al., 2022).

In the following paragraphs, how livestock productive performance is potentially improved using feed additives is described.

The dietary supplementation with *Elephantopus scaber* (*E. scaber*) in duck production, which is also known as a traditional herbal medicine has disseminated primary knowledge on *E. scaber* inclusion, to produce high-quality duck meat, for human consumption. This study highlighted better understanding on potential of *E. scaber* as a feed additive in ducks and recommended that *E. scaber* can be an effective supplement with beneficial impact on the meat quality and intestinal development (Hu et al., 2021). Furthermore, mangosteen peel liquid protected soybean meal as feed additive as dietary supplement in dairy cattle was investigated. It was concluded that dietary inclusion reduced rumen protein degradation and made it available to intestine to enhance milk yield and milk composition in dairy cows.

Application of the natural polyphenol, (chlorogenic acid) as feed additive in pigs can be a better alternative against, oxidative stress-induced growth retardation and intestinal mucosa disruption by increasing antioxidant capacity, and improving intestinal barrier integrity, in weaned pigs (Chen et al., 2022).

Dietary feeding of the Licorice (*Glycyrrhiza glabra*) to rainbow trout fingerlings increased resistance in these fish against *Yersinis ruckeri* infection via *E. coli* through production of microcline C7 antimicrobial peptide and enhanced immune system. Impact of microcine C7 as a feed additive was evaluated as important agent for the growth parameters, immunology, gut barrier and intestinal microbiota count of broilers. It was found that M- C7 has potential as a promising alternative in regulation of intestinal immune status, antimicrobial property against pathogen invasion and enhanced gut health, and improved serum index of broilers (Dai et al., 2022).

The Goji berries are fruit of *Lycium barbarum* and its dietary supplementation in rabbits boosted reproductive and productive performances, immune system, metabolic homeostasis, and meat quality of rabbit (Agradi et al., 2022).

Currently using of soy lecithin has attained great attention in poultry production. Its application in hydroxylated form promoted growth efficiency, blood serum enzymatic action and hormones responsible for the lipid metabolism, and carcass quality of Jiangan white goslings (Wu et al., 2022).

Based on the available literature described by Wang et al. (2022), it was reported that information on inclusion of Pommended aeoniae radix alba extract as a feed additive in diet of the raccoon dog is scarce and it was recommended that its extract might be applied with 1–2 g/kg level for ideal activity of raccoon dogs.

For improving stability and bio-availability, of essential oils and their compounds, nano-emulsion as a novel strategy is recommended. Using nano-emulsions of oils effectively mitigated their release in GIT and hence made available immunity in broilers against avian pathogenic *Escherichia coli* (APEC) strains, particularly O78 causing agent for big economic losses via colibacillosis (Ibrahim et al., 2022).

The dietary supplementation of yuicca powder has potential to lessen heat stress and, increase productive performance in broiler birds. Its addition in diet can also reduce heat stress, and recover antioxidant status (Luo et al., 2022)

A comparative study was conducted by Chang et al. (2022) on impact of oligosaccharides predominantly isomaltoligosaccharide, rafinose oligosaccharide, and chitoligosaccharide on the performance, immunity and antioxidative physiology and intestinal microbial count in the broiler birds. The results concluded that application of carbohydrates might be a resilient substitute for antibiotic residues.

Possibility of clay inclusion in diet of animals should be an important consideration with an emphasis that inorganic materials are not entirely inactive agents and can interrupt intestino- rumen digestion with effects on animal health. However, more investigation needs to be carried out with an emphasis on four stomach animals to validate expected interventions of these agents with rumen degradation and absorption of metabolic products, which likely influence animals' metabolism and most probably milk yield and milk composition of dairy animals (Damato et al., 2022).

Research studies and reviews mentioned in above section present original data information on supplementation and effects of additives in the livestock. Despite all existing literature available, attained information presents that dose level of natural feed additives for bioavailability and beneficial effects should be elucidated.

Feed Additives and Quality of Animal Products

Over the last several years, world population has been growing rapidly and further growth is expected in near future. This will cause an increase in the food consumption and demand for animal protein across the globe.

Consumers have an increasing demand for a healthy diet, in which nutritional quality of products, such as level of unsaturated fatty acids or certain minerals is of great importance. The nutritional quality and bio-fortification with certain elements can contribute to a healthier diet and can allow for more efficient consumption of animal protein.

Sustainability of livestock products can be improved by increasing the productivity, reducing waste and spoilage. Major portion of food produced for human consumption goes to waste, which is of greater consideration for an increase in the food availability. Improving the quality of animal products is one of the most important strategies to lessen the food wastage. The most important parameters responsible for quality of animal products are a longer shelf life, appearance, drip loss, pH, and meat color and haugh unit for eggs. With improvement of people's living standards, consumers have increasingly higher requirements for quality of livestock products. Through feed additives, appearance, color, and intrinsic quality of livestock products can be improved, and shelf life and sales price of livestock products such as meat, fish, milk and eggs can be extended.

Regulatory Aspects of Animal Feed Additives

From regulatory point of view, in order to manage any unpleasant occurrence, a new feed material and feed additive require a formal pre-market authorization/ an official registration with authorized body before it can be legally marketed out. In some parts of world like USA and EU, feed materials as well as feed additives need to pass evaluation by Association of American Feed Control Officials (AAFCO) and/or by US Food and Drug Administration (US FDA). In any case, feed industries, feed dealers and feed business entrepreneurs should make it sure that new feed material and or feed additives are safe as an animal feed. They have also to register their production facility in national register before marketing. In addition, decent feed manufacturing practices should be followed regarding feed production and quality control. All these rudiments are equally valid for them to farm animal feeds including pet foods. It is also considerable that feed labeling has its prudently regulatory rules.

Conclusions

The major goal of feed additives is to enhance animal production by making feed more palatable and enhancing resistance to infectious diseases, which would ultimately lead to sustainable aquaculture. These materials are eco-friendly and include mostly natural products. They don't result in a negative impact on animal, aquaculture and environment when used properly. Their application is set and regulated by government authority to sanction their safety measures and effectiveness. Most commonly used animal feed additives are vitamins, minerals, amino acids, buffers, enzymes, prebiotics, probiotics and natural herbal extracts. Their application is higher in poultry as compared to other animal species. Their use in animal feeds needs official approval from authorized body. Some sectors like feed industries, feed dealers and feed business entrepreneurs should make it sure that these materials are safe and register their production facilities. Good feed manufacturing practices should be followed for the feed production and quality control. The phytogenic substances which are natural herbal substances and are being used as animal feed additives need to be researched out frequently in future.

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Chapter 02

Use of Natural Feed Additives in Broiler Birds: Updated Knowledge

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ABSTRACT

The Poultry industry has experienced significant growth in recent years, due to increasing poultry meat demand globally. Enhancing poultry performance and health through improved feed is a primary focus for the industry. Antibiotics are used as one the major growth promoters in poultry industry but due to antibiotic resistance the researchers are exploring the alternative growth promoters. Therefore, feed components like essential oils, herbal extracts, electrolytes, prebiotics, probiotics and organic acids improve the gut health and productivity of birds. Essential oils derived form plants exhibit antimicrobial, antioxidant, anti-inflammatory properties, also improving broiler performance and carcass yield. Similarly, herbal extract used for growth promoting and health benefit purpose. Electrolytes manage heat stress and replenishing lost minerals, optimize feed intake and growth rates. Organic acids lower the gut pH and suppressing pathogenic bacteria improve nutrient absorption and growth performance. They also boost the immune system, aiding in disease prevention. So, feed additives such as prebiotics, essential oil, herbal extracts, electrolytes and organic acids are promising alternative to the antibiotics in poultry feed. Hower, further reach required to understand their mechanism and synergistic effects ensuring sustainable growth and productivity in the poultry industry.

KEYWORDS
Natural feed additives, Broiler birds**,** Essential Oils, Herbal Extracts, Electrolytes, Prebiotics, Probiotics and Organic Acids

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INTRODUCTION

The poultry industry has been growing very productively in the recent decades. The demands of poultry meat and meat products are enhancing due to increasing consumption of meat. The world poultry meat production reached about 137 million tons in 2020, making poultry the most consumed meat in the world (Nawaz et al., 2021). Therefore, broiler meat plays a significant role in meeting the demand of the world. In the modern era, improvement of the poultry industry by improving poultry performance and health is the main target to focus. Feed is the main concern of the poultry birds as various feed component effect the gut health severely, some have positive effects like essential oils, herbs extracts, electrolyte, prebiotics, probiotics and organic acids while other having adverse effects like toxic chemicals, aflatoxin etc. effect the health of birds and their productivity (Ali et al., 2021). The feed components that enhance the digest and absorb the nutrients are encouraged now a days.

The researchers are encouraging the alternative are encourages as alternative to the antibiotic growth promoters. We came to know after exploring various research and found that different feed additives in the market have potential to optimize the poultry production and reduce the load of antibiotics. Essential oils, herbs extracts, electrolytes, prebiotics, probiotics and organic acids have great potential in poultry industry. The stress condition these feed additives not only relax birds form stress but also improve the immunity, improve growth and reduce harmful stress conditions (Gupta and Mishra, 2021).

The poultry production is increasing day by day due to small and large level organized poultry industry. This growth in poultry is achieved due to discovery of modern growth promoting strategies that not only control disease in flock but also improve the growth and health of birds (Constance et al., 2013). In developing countries like the small scale and unorganized sector also play an important role, but due to lack of scientific approach, they also face many problems like threats to pathogens due to higher exposure to dirt. The cost of birds increased due to use of antibiotics as treatment that also decrease the profitability of small-scale poultry industry. Hence, researchers are willing to introduce new trends to maximize the profitability (Bao et al., 2024). For this purpose, the genetic improvement, immune stimulators and growth promoting agents are best option. This trend makes sure the good, cheap and safe poultry meat for the world's growing population.

Feed additives are the substances that are added in the diet to maximize the utilization of feed, increase feed conversion efficiency and ultimately improve growth and health of birds. Different types of feed additives increases the broiler production like antibiotics, exogenous enzymes, antioxidants and coccidiostats, etc. Among all of them, antibiotics growth promoters are widely used due to their high potential and industrial trends. The reduction or withdrawal of these antibiotics' growth promoted not only reduce the production but also increases the morbidity and mortality of birds (Rahman et al., 2022). So, researchers are developing antibiotics free alternatives to maintain birds' health and production. Plant extract, essential oil, nutraceuticals like copper and zinc are best alternative to the antibiotics. Due to their low-cost increase demand for such alternative. So, in this chapter we will focus on the alternatives in deeply that how they may be productive to the industry and how they replace the antibiotics. The chapter also highlights the research gap to attract the researcher to explore more on this important aspect regarding poultry industry.

Essential Oils

Essential oils are called volatile oils that contain chemical compounds in volatile form that are extracted from different plants. The best oil contains aromatic compounds, they are chemical free, without additives and plant compounds. They are basically extracted mostly from flowers, leaves, herbs, fruits and roots (Voon et al., 2012). Most of essential oils are known to have therapeutic and health benefits like they have effect against pathogenic microbes, regulate the lipid metabolism, healthy effects on the gastrointestinal tract, antioxidant and anti-inflammatory effect (Dar et al., 2023). As a dietary supplementation of essential oils like garlic powder, carvacrol, capsaicin and thymol powder etc. positive effect on the carcass yield and performance of broiler (Gholami-Ahangaran et al., 2022). (Peng et al., 2016) found that feed conversion ratio was positively improved when supplementation of oregano leaves. The oil extracted from *Euphorbia hirta* inhibited the *Clostridium perfringens* growth in the intestine of broiler birds (Hashemi et al., 2012). Different *invitro* and *in-vivo* trails proved that essential oils have antioxidant effects that help to reduce stress and decrease the antibiotic load in poultry (Oladokun et al., 2021).

Herbs Extracts

Since the old ages, the herbal plant their products like leaves extract been used for medical purpose as well as flavors and aroma to the food. From Centuries, practitioners utilized aromatic plants for medicinal purpose in both human and veterinary for the treatment of various diseases (Giannenas et al., 2020). In the modern world, the products obtained from plants and fungi are also being used as natural feed additives are getting importance among the consumers. The natural herbal extracts and essential oil have been used as feed additives in the poultry industry (Stevanović et al., 2018). (Gungor et al., 2021) found that *Ginkgo biloba* leaves which were fermented with *Aspergillus niger* mixed in det of broiler birds improve the growth performance. In contrast with antibiotic growth promoters the natural additives like herbal extracts are less toxic, environmentally safe and are economical (Seidavi et al., 2021).

Some plants like ginger, garlic, turmeric and noni etc. are most common plants additives are extensively used in poultry feed and enhance the growth in case of broiler and egg in layer birds (Krysiak et al., 2021). This positive effect is due to active components in plants that show therapeutic effects, like phenols, alkaloids, flavonoids, minerals, vitamins, fiber, protein and carbohydrates. The mechanism behind growth enhancement in broiler is to increase gut microflora, which produce a positive effect on better utilization of nutrition (Jha and Mishra, 2021). It is well documented that curcumin in the turmeric increase the activity of digestive enzymes like chymotrypsin, trypsin, amylase and lipase (Xavier et al., 2021). (Alagawany et al., 2021a) reported that dietary supplementation of extracted oil, leaves increase the secretion of digestive enzymes that increase the digestibility of feed and improve the performance of broiler. Similarly, ginger increase the digestion, absorption and positive effect on gastric secretion, digestive enzymes in broiler birds (Al-Khalaifah et al., 2022).

Electrolyte

In broiler birds due to high metabolic activity, heat stress is common when exposed above normal temperature, the birds start rapid and shallow breathing (McKechnie, 2022) to compensate the body temperature due to absence of sweat glands (McKechnie, 2022). Due to painting high amount of carbon dioxide, bicarbonate ions, mineral like sodium (Na) and potassium (K) from the body ultimately lead to respiratory alkalosis. Due to lost of these minerals, the feed intake reduces, down in growth rate and disturbs the bird's metabolism. To address this issue, sufficient amount of minerals and vitamins, along with supplementation of energy and protein, regulate the feed intake and reduce the stress (Alagawany et al., 2021b). Loss of electrolyte during panting can be regularized by adding a sufficient number of cations and anions in the diet, for example sodium bicarbonate, potassium chloride, calcium chloride, ammonium chloride in diet and water. The researcher found that sodium salt improves the food conversion ratio in broiler birds and also increases the water intake (Martínez et al., 2021).

Prebiotics

As the poultry industry is growing day by day due to increase demand of human food like meat and eggs. As industry is growing faster, the problems facing are also increasing parallel i.e. outbreaks in flock, environmental stress, antibiotic residues and antibiotic resistance are major challenges. To address these challenges, researchers are finding way to develop new techniques to optimize the growth and production of industry. For that, prebiotics are one of the advance techniques in which diet with a small amount of carbohydrates are added to modify the gut ecosystem. Like carbohydrates, fatty acids are also effective in lowering the gut pH by producing lactic acid and inhibiting the growth of pathogenic bacteria. Similarly, the structural carbohydrate stimulates absorption of essential minerals like zinc, iron, calcium and magnesium (Ogbuewu and Mbajiorgu, 2023).

In broiler birds, the prebiotics are commonly added in diet as they improved the immunity of birds. Several deadly diseases to the birds like new castle disease, Infectious bursal disease, can be controlled successfully by prebiotics. So, the mortality and morbidity rate in the flock reduce significantly (Khomayezi and Adewole, 2022). The incidence of immunosuppressive diseases like Marek's disease, mycotoxicosis and reoviral infection can be significantly reduced with the help of prebiotics in diet.

The growing chicks are more vulnerable to the stress and more disease attack on them and results a high morbidity and mortality in early ages. So, probiotics are strongly recommended with antibiotics as they produce a synergetic effect and improve the intestinal balance that was the effective results of antibiotics. Similarly, the antibiotic load and resistance lower in bacteria as prebiotic serve as inhibiting the growth of pathogenic bacteria (Ahiwe et al., 2021).

Probiotics

The excessive use of antibiotics dis-balance the normal bacterial population as well as pathogens in the intestine of birds. As a result, the pathogenic resistant strains of bacteria predominate. So, the researchers are trying to find such alternatives for poultry that show less side effect and optimize the production. In this scenario, the probiotics found to be one of the alternatives have a quality to minimize the diseases and increase the growth (Tarradas et al., 2020). The prebiotics are the live micro-organism that are incorporated in the fed of the animal to balance the microbial production of essential products and inhibit the pathogenic bacteria in the intestine. They also regularized the pH of the gut, increase the immunity of birds as a result increase the productivity. The regular and optimal utilization ensures the health and anti-biotic residues free meat (Adel and Dawood, 2021).

These beneficial microbes in the diet produce certain antimicrobial properties in several ways i) chemicals like lactoperoxidase, hydrogen peroxidase, lactoferrin and bacteriocin etc. ii) consume the nutrients and depleted them for pathogenic bacteria iii) increase the immune responses and iv) occupied the receptor in intestinal epithelium (Tarradas et al., 2020). The commonly used probiotics are beneficial and harmless microbes, the commonly developing probiotics as growth promoters are A*. oryzae, E. faecium, B. bifidum, B coagulans, L. salivarus*, *L. acidophilus* and *L. sporogenes* etc. (Adel and Dawood, 2021). Among this, *L. acidophilus* in the poultry diet decreases the triglyceride level, results in the reduction of lipid profile that changes the acid production in gallbladder and alters the fat digestion. Mixing *Lactobacillus,* a commonly used probiotic in the poultry diet, results in protective effect in meat against pathogenic bacteria (*S. enteriditis* and *L. monocytogens*). Similarly, the poultry diet with *L. johnsonni* decreases the incidence of enteritis (Yang et al., 2022).

The main advantages are summarized here i) they inhibit the growth of disease producing organisms, ii) Decrease the digestion problems like diarrhea, iii) no harmful residues will come in meat and eggs, iv) they are cost effective v) improve the meat and egg production vi) morbidity and mortality rate reduce effectively.

Organic Acids

The organic acids (OA) are the compounds having more than one carboxyl group are now a days used in the poultry feed. Due to diverse properties like lowering the gut pH, they suppress the pathogenic bacterial growth. They also have the ability to balance the gut health and increase the absorption of nutrient in intestine (Du et al., 2024).

The organic acid like benzoic acid in cockerels at a dose of 0.1 or 0.2% increase the growth rate, lower the digestive tract, decrease the bacterial population and decrease the coliform bacterial population in caeca contents while the nutrient digestibility enhances (Ebeid and Al-Homidan, 2022). Another study by (Gong et al., 2021) in laying hen improve productive performance and health status of birds when benzoic acid in 1000 to 2000mg/kg is intake. Similarly, when mixed organic acid in 3000 mg/kg taken in fed of broiler improve the productivity and meat quality (Ma et al., 2021).

Aside from the general benefits of organic acid specific impacts like effect on the digestibility of nutrient, birds' growth performance enhancing the immunity of birds while also improving the egg production. In the broiler birds, the basic attention to be noted is growth and feed intake, it is reported that OA in diet improve the body weight gain and positively improve the feed conversion ratio. Study conducted by (Montironi et al., 2024) found that mixture of acids like lactic acid, fumaric acid and butyric acid improve the weight gain in broiler birds and also improve the average daily feed intake.

As the effect of OA on the immunity to protect against infection via regulation in respect of immune system to pathogens and abnormal cell growth (Altun et al., 2022). The immune regulatory organs like spleen, thymus a bursa of Fabricius for the regulation and maturation of B cells, T cells and natural killer cells. The OA regulates the boosting like IgA, IgG, IgM and TNF-gamma while the downregulate IL-10 in infected birds (Bondar et al., 2023). The effect of stress faced by birds and successfully overcome by feed-additives is overviewed in Fig. 1.

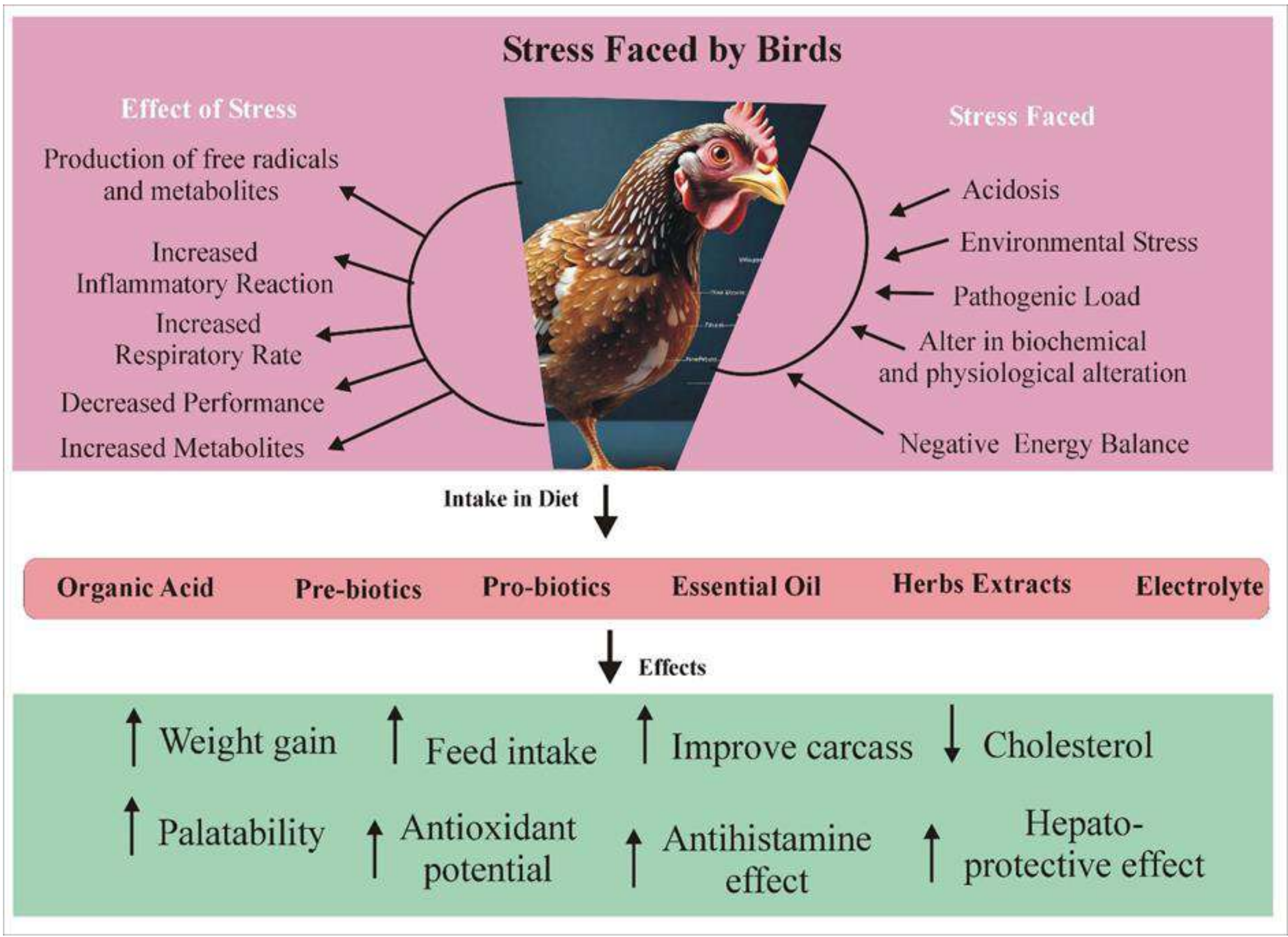

Fig. 1: Overview of the stress faced by bird and can be reduced by intake of different feed additives in the diet

Research Trend and Future Direction

The poultry industry is demanding the alternative growth promoter, like natural feed additives in broiler birds composed for continued growth and exploration. The optimizing formulations and combination of additives to maximize their efficacy with minimum negative effect will be a focus in the future. After the proper understanding of the mechanism of action, these additives in definite dose improve the gut health, immune modulation and performance of bird. Researcher may delve deeper into the synergistic effects of combining different additives to enhance their overall impact. The increasing concerns about antibiotic resistance and consumer demand for antibiotic free product, studies assessing in the long-term effects of natural feed additives on bird health, productivity and the environment (Stevanović et al., 2018).

Conclusion

The feed additives like prebiotics, probiotics, essential oil, herbal extract, electrolyte and organic acid are promising alternative to antibiotics in poultry feed with demonstrated potential by improving growth performance, gut health, nutrient utilization and disease control in birds. Despite this conflict finding regarding their growth promoting effect, these feed additives shown efficacy in curtailing pathogenic bacteria without posing significant public health hazards. However, further research may elucidate the synergetic effect with encapsulation and nano particles formulation is waiting and under process for future researchers.

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Chapter 03

Herbal Feed Additives for Ruminant Nutrition

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ABSTRACT

The livestock industry has been shifted towards the herbal products after the prohibition on the use of antibiotic feed additives which not only harmful for the health of animal but also not cost friendly. Due to the resistance developed in microorganisms against many antibiotics, it is prohibited to use antibiotics as a feed additive in the ruminants. Different plant based feed additives such as herbs and plant extract and many other additives including probiotics, probiotics and different organic acids have been used on a large scale in ruminants due to the wonderful effects of them on animal health and production. These medicinal plants have performed various functions such as improving the feed digestibility, antimicrobial activities, anti-inflammatory activities, antioxidant activities, and immune activities. Due to these activities, medicinal plants are considered the best source of feed additives for animals and also help in safe development of products of human use.

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INTRODUCTION

Feed additives such as antibiotics have been used for many years in ruminants especially in production systems. Antibiotics feed additives for example ionophore antibiotic monencin are used in ruminants to enhance daily gain and feed conversion ratio. In 2006, the antibiotic feed additives were banned in the European Union because of the risk of antibiotic resistance in animals as the residual amount of antibiotic present in the milk and meat products. As a result of increased risk of antibiotic resistance, alternative ways have been discovered and efforts have been made. Plants were considered as an excellent option (Wallace, 2004) instead of antibiotics as plants made secondary metabolites showing antimicrobial activities such as saponins and tannins. These metabolic compounds produced by plants have been studied and results show that these compounds modulate ruminal fermentation in ruminants which ultimately enhance the utilization of the nutrients (Wang et al., 1998; Hristov et al., 1999). The secondary metabolites are limited as compared to the primary metabolites such as carbohydrates, proteins, fats and nucleic acids. The secondary metabolites produced by the plants are a greater source and used in animal production systems. Another complex mixture of secondary metabolites is essential oils (EO) which extract from herbs and spices having low boiling points are phenylpropene and terpenes (Greathead, 2003). The most important function of plant extracts on animals is their role in microbial fermentation, especially the binding of amino to saponins. Plants have many benefits including fulfilling nutrient requirements, endocrine stimulation and action in nutrients metabolism (Wang et al., 1998; Wenk, 2000).

Herbal Feed Additives

Aromatic Plants

Herbs and spices are also called aromatic plants (Ölmez and Yörük, 2022). They have seen use in past as long as 5000

BC. They were majorly used in Middle East regions due to their quality of being food preservative substances and their addition to food also increased its flavor and aroma. Furthermore, they also had medical applications (Li, 2006). Since that time they have been used continuously today with their use frequency increasing over time. This fact became more pronounced when world health organization (WHO) declared that around 80% of the people, especially the ones living in under developed regions continue to rely upon plant based medicinal compounds regarding their health care efforts (Gurib-Fakim, 2006).

The, feed additives sourced from plants, are also termed as phytogenic or phytobiotic chemicals. These plant-derived botanicals can be added to the dietary rations of animal for the purpose of enhancing their production. Besides animals it also affects feed and improves the quality of consequently produced feed and animal products (Ölmez et al., 2022). Out of various types of naturally occurring feed additives, aromatic plants, their products extracted from these plants and like their essential oils, have been under consideration and being examined for their advantages as an alternative to the antibiotics as growth promoters. These compounds obtained from plants are considered better alternatives as they are residue free and mostly identified as safe for consumption (Brenes and Roura, 2010). Various herbs and spices have been discovered all across the globe, with many of them being obtained from the cultivated or wild growth regions of Mediterranean area. These plants include rosemary, oregano, sage, thymus (Negi, 2012).

These naturally present bioactive substance also possessed some therapeutic benefits such as they act as an antioxidant and also work as an antiseptic agents (Li, 2006). Another marvelous property of this natural source is that they have seen to lessen the threat of cancer development and decrease the cardiovascular diseases (Figure 1). All these qualities of these plants made them the best source for therapeutic use against many infections including respiratory infections, intestinal problems and inflammatory issues (Kadri et al., 2011). The chemically active compounds of aromatic plant protect the body of host from deterioration of cells due to free radical activities and stress due to oxidative reactions (Couladis et al., 2003). The natural herb and spices also used to enhance the shelf life of various products of human use as they delay the process of oxidative rancidity. These herbs and spices act as antimicrobial agent and prohibit the growth of bacteria on meat and snacks products (Elgayyar et al., 2001; Li, 2006).

Essential oil

Plant extracted volatile or ethereal pils are alsp know as Essential oils. These oils can be found in various types of plants belonging to edible, medicinal, and herbal plant groups. These are mainly volatile aromatic compounds that can be easily extracted by performing steam distillation or solvent extraction procedures (Greathead, 2003). A large number of plant parts can be used for sourcing essential oils, the number of these plats is estimated to go beyond 3000 plants, out of these around 300 are being used at commercial level as flavoring agents and fragrances. Essential oils extraction can be performed on many portions of a plant. The plant parts usually utilized for essential oil extraction are leaves, flowers, stem, seeds, roots and bark. The ingredients of essential oils may vary in terms of concentration depending upon the part of plat they are being extracted from (Dorman and Deans, 2000). For example, if the seeds of coriander (*Coriandrum sativum*) are used to source essential oil it will have a different composition as compared to the essential oil obtained from immature leaves (*cilantro*) of the same plant (Delaquis et al., 2002). Chemically the essential oils obtained from individual or different types of plants are also observed. These differences on composition occur due to the genetic makeup, age of the plant, and its surrounding environment in which it grew (Cosentino et al., 1999). Martinez et al. (Martinez et al., 2006), explains in his work that the amount of different chemical compounds such as carvacrol in the essential oils of thymol varies from the other species of the thyme plants use to extract oils. Looking for the chemical configuration of essential oils the major part is composed of terpenoids with different chemical structure. Chemical compounds present in terpenoids include monoterpenes (C10), with sesquiterpenes (C15), in some arrangements diterpenes (C20) may also be present, and a mixture of aliphatic hydrocarbons with low molecular weight, acids, different types of alcohols, aldehydes, acyclic esters or lactones and exceptionally N- and S-containing substances, coumarins and homologues of phenylpropanoids (Dorman and Deans, 2000). All these compounds which makes chemical configuration of terpenoids are biologically active and perform different functions such as antioxidation, antifungal and antibacterial activity (Figure 1). Essential oils are the densest mixture of phytogenic chemical and due to their beneficial effects, the use of these oils have been increased in poultry industry to enhance the production rate especially.

Saponins

As a plant extract, saponins are considered as one of the most active substances present in plants. Attributed to the detergent action of the saponins, they kill ruminal protozoa. The eukaryotic ruminal protozoa are more susceptible to the saponins as compared to the prokaryotic bacterial cells due to the presence of cholesterol in their cell membranes and saponins attracted towards the cholesterol (Klita et al., 1996). A major function performed by saponins is the elimination of harmful protozoa which locates in the rumen to enhance the flow of microbial proteins from the rumen, enhance the utilization of feed for the animal, increased availability of nutrients to the animal and make sure that the decrease in number of protozoa does not slow down the breakdown of fiber (Newbold et al., 1997). It has been observed that the feeding of saponins containing plants to the animals increased their production as compared to those animals feeding with antibiotics or any other synthetic chemical compounds (Sultana et al., 2012). Much research work has been done to confirm the effectiveness of saponin-rich plants to the animals (Makkar et al., 1998; Wang et al., 2000; Sultana et al., 2012).

The results of these research works shows that saponins have excellent properties to be used in ruminants for their antiprotozoal activities as an alternative to growth hormones or antibiotics (Figure 1). As a natural group of compounds, saponins have resembling action as detergents or soaps. Saponins are a complex group of compounds having diverse physiological effects present mainly in plants and rarely in marine animals. Common properties of saponins include bitter taste, form stable foams in aqueous solution, hemolysis of red blood cells, and cause toxicity in cold-blooded animals including fish, snails, insects. Saponins also have the ability to interact with bile acids, cholesterol and steroids in aqueous solution as a result of which they form mixed micelles and co-precipitates (Cheeke, 1989).

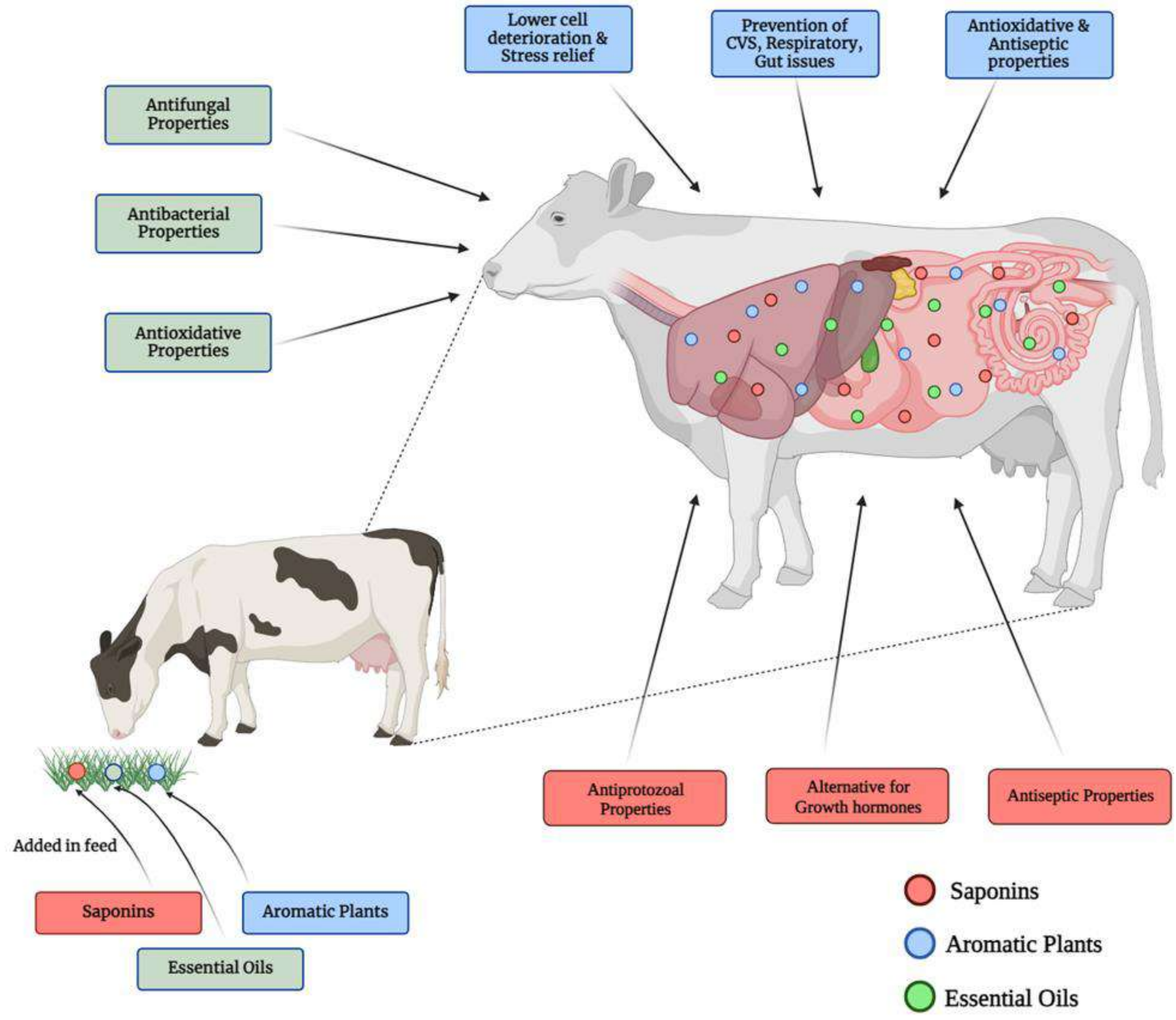

Fig. 1: Impact of herbal feed additives in ruminants.

Impact of Herbal Feed Additives

Herbal feed additives have been very beneficial to the ruminants as they enhance the absorption and utilization of nutrients and help in the stimulation of the immune system. To improve the growth rate of animals, the actions performed by the herbal additives are changes developed in the microbiota of intestine, increased absorption of nitrogen, improved morphological immune responses, modify the histology of gastrointestinal tract, and improved antioxidants activities. In the end, the contribution of herbs in improving the nutrients requirements of animals, endocrine stimulation and nutrient metabolism is of great importance (Li, 2006). Herbs and botanicals have beneficial effects in farm animals as they help in activation feed intake and digestive secretions, stimulation of immune responses anti-bacterial, coccidiostat, anthelmintic, antiviral, anti-inflammatory activities. Following are the ways in which herbal additives perform their function in the animal body (Elgayyar et al., 2001; Kadri et al., 2011).

Effects of use of Herbal Feed Additives on Feed Intake, Digestibility of Nutrients and Animal Performance

The use of herbal additives for better growth of ruminants has become of greater importance after the restriction of use of antibiotics. In herbs and spices different types of active compounds are present which stimulate the process of digestion in different ways. Most of these compounds triggered the secretion of saliva. Many herbs and spices increased the production of bile acids in the liver for example curcuma, cayenne pepper, ginger, anis, mint, onions, fenugreek, and cumin. The secretion of these bile acids in bile have helped in digestion and absorption of the lipids, triggered the pancreatic enzymes such as lipases, amylases and proteases and enhanced the activity of enzymes released from gastric mucosa. Another important function performed by herbal extract is that they accelerate the process of digestion which results in the short stay of feed in the gastrointestinal tract (Frankic et al., 2009). Some plant herbs for example garlic (*Allium sativum*), lemongrass (*Cymbopogon citratus*, DC. Stapf.) and peppermint (*Mentha piperita*) have been used as antibacterial agents and in tropical regions these herbs used for the maintenance of gut microbiota (Shin and Kim, 2004). In livestock production systems garlic is used to improve the growth rate of ruminants and also enhance the carcass traits (Kongmun et al., 2011). In beef and dairy cattle, lemongrass and peppermint have been shown to enhance the production rates (Yang et al., 2007). In recent research it has been seen that methanol (*Mentha arvensis*) enhance the proteins and amino acids digestibility in piglets and increase the feed efficiency (Maenner et al., 2011) and black pepper used to enhance the performance of broiler chicken (El Tazi et al., 2014).

Herbal Feed Additives as Antimicrobial Supplements

Various researches have shown that the plant extract compounds show significant anti-bacterial activity when obtained from specific plants. They act effectively against both gram negative and gram positive bacterial populations. The extracts are actually manufactured by plants for their own protection against various types of diseases, insect attacks, herbivorous grazing, and bacteria. Furthermore, these plants may also synthesize secondary antibacterial metabolites as during their process of normal growth and development or it may be induced for production as a response to stress. Various studies have shown the antibacterial impact of oriental herbs that include *Allium sativum, Angelica dahurica,* and *Sophora flavesens*. These herbs contain major flavonoid components, baicalin, baicalein, limonene, cinnamaldehyde, carvacrol or eugenol which imparts antibacterial effect along with other types of supplemental herbs. These herbs have antimicrobial activity against *Salmonella spp*. or *E. coli* and gram positive bacteria *Staphylococcus spp.* and *Streptococcus spp.* Active component of additional ingredients added to herbal feed can change composition fatty acid which in turn affects the viability of micro-organic life by improving its hydrophobic capacity. This re-affirm the claim that herbs and spices play a key role as antibacterial agents by modifying the qualities of cell membrane, and leading to leakage of ions, hence reducing the virulence of microbes. Phytobiotics are plant extracts that have been under use and consideration for their antibacterial, anti-inflammation, anti-oxidation, and anti-parasite qualities. A large number of variations has been observed in the ingredient make up of phytobiotics. These variations may be developing due to different biological factors of the plant used as an additive (specie of the plant, geographical location of the plant, at the conditions at which plant has been harvested), production practices (such as extraction/distillation and stabilization), and the storage conditions (light, temperature, oxygen tension, and time elapsed (Huyghebaert et al., 2011).

Anti-inflammatory Activity of Herbal Feed Additives

The root of ginger, nutmeg, cloves, red pepper, black pepper, cumin, cloves, cinnamon, and mint products all demonstrated inflammation reducing properties. The main functional substances that have an inflammation reducing effect include flavonoids, terpenoids, and phenols. These compounds prevent inflammatory prostaglandins from being metabolized. Phenolic compounds of plants are the hydroxylated analogues of cinnamic and benzoic acids and they have been shown to have inflammation reducing properties. The flavonoids have known for a longer period of time due to their inflammation reducing, allergic reducing, against viral, and anti-proliferative properties (Muanda et al., 2011). Anise, marigold, chamomile, and liquorice are well-known herbs and spices with inflammation reducing properties (Frankic et al., 2009). The antioxidant properties of *Labiatae* families including mint are because of the phenolic terpenes (Habib et al., 2017). A considerable quantity of monoterpenes, thymol and carvacrol are present in thyme and oregano (Abdulkarimi et al., 2011). Flavonoids-rich plants including green tea and other Chinese herbs have been explained as naturally occurring antioxidant (Wei and Shibamoto, 2007). Black pepper (*Piper nigrum*), red pepper (*Capsicum annuum L*) and chili (*Capsicum fretuscene*) have a lot of anti-oxidative compounds (Nakatani, 1997). However, the active ingredient-containing sections of many of these plants have intensely spicy or aromatic tastes, which makes it illegal to utilize them in animal feed. Aloe-vera's benefits for chickens have recently been studied, including its antibacterial, virostatic, anti-mycotic, anti-cancerous, inflammation reducing, anti-angiogenic, injury-recovery, free-radical scavengers, and diabetes reducing qualities (Babak and Nahashon, 2014).

Antioxidant Activity of Herbal Feed Additives

When antioxidants are added to food they tend to limit rotting, postpone the generation of hazardous aging products, and preserve the nutrient content. Antioxidants are chemicals that assist postpone and prevent the oxidation of lipids (Muanda et al., 2011). It is believed that the shielding properties of free-radical scavengers derived from plants stem have their ability to neutralize oxygen species that are reactive. Numerous studies revealed that eating plants high in free-radical scavengers reduced the incidence of cerebrovascular accident, coronary disease, tumor production, and high blood pressure. These plants also appeared to perform a preventive function in health and fighting illnesses. The content of certain vitamins (E, C, and A) and phenolic compounds (phenolic terpenes) may be associated with the free radical scavenger activity of herbal products. The natural metabolic products of onions and garlic are attributed to their sulfur-containing effective concept, which has been shown to have lipid-lowering properties and to prevent lipoproteins with a low density from oxidizing (Ahmed et al., 2009). Herbs high in phenolics that are frequently utilized include dandelion, marigold, chamomile, ginko, rosemary, thyme, and oregano. Spices and herbs can guard the feed from oxidative degradation while it's being stored.

Herbal Feed Additives as Immunostimulant

Herbs and spices that have a large quantity of flavonoids, citric acid and anti-oxidants are typically good for the proper functioning of immune system. *Purple coneflower, Glycyrrhiza glabra, Acacia greggii* are the plants that have immunomodulatory properties. They also have ability to enhance the performance of white blood cells, macrophagic activity and increase the synthesis of interferon (Frankic et al., 2009).Studies have shown that the oils withdrawn from plants which can be used as a curative agent have the ability to enhance the functioning of immune response and are also capable of changes in the upper part of large intestine (Stef et al., 2009). In broiler chicken the results of the β-glucan and urine of the cow have been found of great importance (Ganguly, 2013).

Herbal Feed Additives as Coccidiostat

Coccidian in particular and some other parasites of chicken are believed to be treated by some of the by-products of the plants (Naidoo et al., 2008; Arczewska-Wlosek and Swiatkiewicz, 2012). Betaine has been effectively controlling coccidiosis and is produced by the sugar beet industry. It allows the cells to perform its normal metabolic activity and prevents dehydration. In addition, the defensive activity of betaine is also acted on the parasitic cells of intestinal mucosa. Curcumin is an active ingredient obtained from the phenolic compounds have its recovery effect on the coccidiosis in association with the free radical scavengers on the immune system (Allen et al., 1998). *Galla rhois* and *Nectaroscordum tripedale* extracts have been used against coccidial infection and the outcomes are very satisfying (Lee et al., 2000; Habibi et al., 2016).

Benefits of Plants as Feed Additives

The reason to choose and feeding the animal with natural plant products instead of other food enhancers are because of the following reasons:

- Natural ingredient of feed
- No presence of the waste materials in the feed
- Have no hazardous effect on the ecosystem
- Reduced problem of drug resistance

Constraints of Herbal Feed Additives

1. Due to their ambiguous composition they are difficult to quantify and standardize
2. The composition of plants is greatly affected by the place where it is grown, the technique used to harvest the crops, climate conditions, the heights from the sea level and the conditions where the plants products are being saved.
3. Where most of the natural products of plants are stable there are few products that are not stable to heat and light.
4. The herbals that limits their addition to the food include contamination of the products by parasites, techniques used to harvest the plants, enhancing and working opposite effects, environmental conditions, the duration of time for which it is stored and many more factors (Habibi et al., 2016).

Conclusion

The good health of farm animals is very important in order to get the best production rate from them. For the last few decades, the products of natural origin have gained importance to be used as additives in animal's feed as well as in humans. These herbal feed additives help in maintaining the health of the gut by keeping check on the normal flora of the intestinal tract which in turn give better production in terms of milk and meat. The entry of herbal products in feed additives help in not only improving the health of animals but also very cost effective. Now the studies have been focused on getting more knowledge about the chemistry of the natural compounds and the functions of these natural feed additives including plant extracts and organic acids. To get the best advantage of these natural products, they have been added in the feed of animals as extras of plants or dried plants. Some properties of these plant additives are still under research which mainly include the dosage rate to get best outcomes, the antimicrobial activities and antioxidant activities of these herbal products.

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Chapter 04

Role of Natural Feed Additives in Poultry

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ABSTRACT

Poultry is one of the primary sources of animal protein and is an important pillar to fulfil the nutritional requirements of humans. Poultry birds fulfil our great need for eggs and meat, so the introduction of natural feed additives to their diets results in an increase in quantity and quality of the products gained from them. Different medicinal plants and herbs, prebiotic, probiotic, organic acids, phytogenics, essential oils, minerals, enzymes, metabolites etc. are used as feed additives in poultry birds to increase production efficiency, improve health and decrease the chances of disease. Use of natural feed additives in poultry results in more production of meat and eggs for worldwide consumption. Some natural feed additives include essential oils, plant extracts, phytogenic compounds, organic acids, organic salts, vitamins, minerals, probiotics, prebiotics, and different enzymes, etc. These natural feed additives have beneficial effects on birds like antiviral, anti-parasitic, insecticide, antimicrobial, antioxidant, improve digestion, remove pathogens, increase nutrients absorption, and enhance birds' production and performance. Natural Feed Additives (NFAs) are beneficial and in demand because of their less toxicity, safety, cost effective and environment friendly properties.

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INTRODUCTION

To fulfill the dietary needs of an increasing population of the world, it now become very essential to increase production of food-producing animals (Bradford, 1999; Weber and Windisch, 2017). This is achieved by improving animals' health, by prevention of infectious diseases to them and by increasing growth rate. Poultry is a major source to get proteins and important to fulfil the nutritional requirements of humans (Chadd, 2007). Poultry birds fulfil our great need for eggs and meat, so introduction of natural feed additives to their diets results in an increase in quantity and quality of the products gained from them (Alagawany and Abd El-Hack, 2020; Upadhayay and Vishwa, 2014). Different medicinal plants and herbs, prebiotic, probiotic, organic acids, phytogenic, essential oils, minerals, enzymes, metabolites, etc. are used as feed additives in poultry birds to increase production efficiency, improve health and decrease the chances of disease (Upadhayay and Vishwa, 2014; Yadav et al., 2016). The use of natural feed additives in poultry outcome in raises production of meat and eggs (Abaza et al., 2008; Alloui et al., 2014; Windisch et al., 2008). After the scientific evaluation and confirmation of no harmful effect of feed additives on the environment, animal and human health, the authorization given to the feed additives and put on the market (Additives and Nutrient Sources added to, 2012; Anadon and Martınez-Larranaga, 1999). By use of synthesized growth promoter antibiotics, residues of antibiotics remain in meat and eggs results in different pathological abnormalities in humans like imbalance intestinal microbiota, bacterial resistance to antibiotics and cell mutations (Biswas et al., 2019; Mia, 2020). Most popular plants that are nutritious for animals are oregano, cinnamon, cumin, sumac, garlic, anise, cloves, mint, ginger and coriander and also the best anthelmintics and immune stimulators (Maqbool et al., 2024).

Phytogenic Feed Additives in Poultry

Growth promoting antibiotics (GPAs) were commonly used to improve egg and meat production (Ahmad et al., 2022; Castillo-López et al., 2017), but these have a harmful effect like antibiotic residues in animal products and accumulation of antimicrobial resistant bacteria and their transfer to humans by such animals' products consumption (Muhammad et al., 2020; Ur Rahman and Mohsin, 2019). Health authorities of the European Union banned the use of GPAs in egg and meat production animals in 2006 to control this problem (Anadón et al., 2018; Guyomard et al., 2021). To replace GPAs, some new natural growth promoters (NGPs) like phytogenic additives were introduced that improve performance and health of animals without any harmful residues in animal products (Yitbarek, 2015). These are gained from plants, herbs and spices (garlic, thyme, oregano, cinnamon, coriander and rosemary) and added to animal feed or water (Alloui et al., 2014). These have beneficial effects on birds like antiviral, antiparasitic, insecticide, antimicrobial, antioxidant, improve digestion, remove pathogens and increase nutrient absorption (Wallace et al., 2010). Different forms of phytogenic feed additives are available like solid, ground and dried form and also as extracts or in the form of essential oils (Steiner and Syed, 2015). Active ingredient of phytogenic feed additives vary depends on the part of plant used, geographical location and season during harvesting (Windisch et al., 2008). Table 1 shows the commonly used plants, herbs and their active ingredients and functions.

Table 1: Commonly used plants, herbs and their active ingredients and functions:

Plants (aromatic spices)	Active ingredients	Plant part	Uses	References
Celery	Phthalides	Leaves, fruits	Anti-diarrheal, digestion stimulant	(Salehi et al., 2019)
Cloves	Eugenol	Cloves	Antiseptic, appetizer, digestion stimulator	(Badnale et al., 2022)
Nutmeg	Sabinene	Seeds	Anti diarrhetic, stimulate digestion	(Kumar et al., 2014)
Cardamom	Cineol	Seed	Stimulate digestion, appetizer	(Paswan et al., 2021)
Cinnamon	Cimetaldehyde	Bark	Antiseptic, stimulate digestion, appetite	(Saeed et al., 2018)
Cumin	Cumin aldehyde	Seed	Galactagogue, carminative, digestion	(Singh et al., 2017)
Fenugreek	Trigonelline	Seed	Appetizer	(Wani and Kumar, 2018)
Anise	Anethol	Fruit	Galactagogue, digestion	(Kalra et al., 2018)
Parsley	Apiol	Leaves	Digestion, appetizer, antiseptic	(Nasrallah, 2021)
Plants (pungent spices)				
Garlic	Allicin	Bulb	Antiseptic and digestion	(Papu et al., 2014)
Horseradish	Allyl izotiocianat	Root	Appetizer	(Doll, 1973)
Ginger	Zingerone	Rizom	Gastric stimulation	(Ghayur and Gilani, 2005)
Pepper	Piperine	Fruit	Stimulate digestion	(Platel and Srinivasan, 2004)
Mustard	Ally izotiocianat	Seed	Stimulate digestion	(Salem et al., 2022)
Capsicum	Capsaicin	Fruit	Stimulate digestion	(Maji and Banerji, 2016)
Herbs				
Thyme	Thymol	Whole plant	Digestion, antioxidant, antiseptic	(Lorenzo et al., 2019)
Mint	Menthol	Leaves	Appetizer, antiseptic, digestion	(Sidhu et al., 2007)
Sage	Cineol	Leaves	Carminative, antiseptic, digestion	(Sharma et al., 2019)
Rosemary	Cineol	Leaves	Antiseptic, appetizer, and digestion	(Sharangi and Guha, 2013)
Laurel	Cineol	Leaves	Appetizer, antiseptic, digestion	(Nasrallah, 2021)

Essential Oils (Plant Extracts) use in Broilers and Layers

Essential oils are secondary metabolites from different plants (buds, flowers, seeds, barks, herbs, wood, leaves, fruits and roots) and are a mixture of aromatic oily liquids (Figueiredo et al., 2008). These are volatile and have fragrance. There are many methods, but steam distillation is the commercial method used to obtain essential oils. They are used in feed of birds because of their properties like antioxidant, antifungal, antibacterial, antiviral, immunomodulator, digestive stimulants, dietary antibiotic, free radical scavengers and increases the shelf life of feed and the meat gain from such birds. The meat obtained from birds fed with essential oil as additive reduces the risk of elevating of lipids level (hyperlipidemia) and provides protection from cancer in consumers. Essential oils also add flavor to feed. Some examples of essential oils are lavandin oil, olive oil, cinnamon oil, oregano, thyme oil, peppermint oil, carvacrol oil, juniper, terpenoids and phenylpropanoids etc. (Herman et al., 2019). EOs act as growth promoters in broilers and help in their weight gain (Attia et al., 2019). In broilers, EOs enhance digestibility and improve digestive enzymes secretion and improve gut microbial ecosystem. EOs (24-48 mg/kg diet) in broilers enhance FCR (feed conversion ratio) and reduces mortality rates. Growth performance of live broilers can be enhanced by using EOs mixture (200 ppm) of anise oil, oregano, clove, turmeric oil and rosmarin. In layers, EOs increase the egg production and quality of eggs and decrease the production of cracked or broken eggs. EOs as single or mixture also upgrade feed efficiency of laying hens and maintain their performance during summer season because in summer egg production usually decreases, egg breakage increases and mortality also rises. EOs consumption shows anti-heat stress effect in summer. In layers, EOs were given at the rate of 24 mg/kg diet to improve egg quality and quantity (Cheng et al., 2022).

Plant extracts mostly contain oligosaccharides, proteins, peptides, fatty acids, micro minerals, and vitamins. They have anticoccidial, anti-inflammatory, antioxidant, anthelmintic and antimicrobial properties, so improve the growth, weight gain, feed intake and health of birds (Idris et al., 2017). These enhance the ecosystem of gastrointestinal microbiota by managing potential pathogens. These also invigorate the endocrine system and improve performance and survivability (Panossian et al., 2021). Table 2 shows list of some plant extracts and their effects on the performance of animals.

Probiotics, Prebiotics, and Synbiotics use in Poultry

Probiotics are live bacteria and yeasts (microorganisms) given to animals by adding in diet that contribute live, beneficial microbes to the populations in their gut microflora and help to improve their intestinal microbial balance (Anee et al., 2021). It would stimulate digestion and metabolism of minerals and synthesis of vitamins like Vit-B1, B2, B12 and K,

Table 2: Some Plant extracts and their effects on the performance of the animal:

Plant Extracts	Dosage	Effect on performance	References
Cinnamon	0.2%	Growth increases	(Habiba et al., 2021)
Thyme extracts	3 and 6%	No improvement on performance and carcass traits	(Amouzmehr et al., 2012)
Chinese herbal medicine	0.5-1%	Growth betters from 7 to 21 days	(Zhu et al., 2021)
Red pepper extract	0.1%	No increase in performance or organ morphometrics	(Yigit et al., 2021)
Thyme essential oil	0.2%	Growth performance increases	(Abdel-Wareth and Metwally, 2020)
Capsaicin plant extract	0.1%	No effect on body weight but 4.2% improvement in feed efficiency	(Zanotto et al., 2023)
Black cumin seeds	1%	Improve feed efficiency and increase body weight	(Mahmood et al., 2021)

which results in growth enhancement and improve metabolism. Probiotics consist of single or multiple strains combination and are mostly active in small intestine. Probiotic preparations which are being used to improve animal nutrition in the European Union consist of different strains of *Enterococcus, Lactobacillus, Saccharomyces, Pediococcus* and *Bacillus* (Muzaffar et al., 2021). Competitive prohibition, bacterial antagonism and immune regulation are the principles on which probiotics act. Some popular probiotics are *Lactobacillus (L.) acidophilus L. bulgaricus, L. sporogenes, L. plantarum, L. case, L. salivarius, L. cellobiosus, Streptococcus (S.) thermophilus, S. faecium, Bifidobacterium bifidum, Enterococcus faecium, Bacillus (B.) licheniformis, B. coagulans, Saccharomyces cerevisiae, Torulopsis spp.* and *Aspergillus oryzae* (Minj et al., 2021). Probiotics play vital role in prevention of enteric infections by hindering pathogens like *Clostridium perfringes, Campylobacter jejuni, Candida albicans, Eimeria spp. Listeria monocytogenes, Salmonella (S.) enteritidis, S. typhimurium*, *Escherichia coli, Staphylococcus aureus, Yersinia enterocolitica* and coccidian parasites. Probiotics improves fertility, prevents diarrhea, improves egg quality, caused by vaccination, feed change, overcrowding and transportation (Feng and Liu, 2022).

Prebiotics are indigestible ingredients added to the feed like fermentable sugars which works by fostering the activity and growth of one or restricted number of beneficial microorganisms like bacteria and fungi in large intestine (Panwar et al., 2022). Gibson and Roberfroid in 1955 introduce the term 'prebiotics. Examples of poultry used prebiotics are nondigestible oligosaccharides including fructooligosaccharides (FOS), mannan oligosaccharides (MOS), xylooligosaccharides (XOS), galacto-oligosaccharides (GOS), and iso-malto-oligosaccharides (IMO) which stimulates absorption of minerals like zinc, magnesium, calcium and iron. Prebiotics increase colonization of *Lactobacillus* and increase density of lactic acid, which results in a change of acidity of intestine and improves activities. Prebiotics improve the activity of harmless bacteria, which synergistically work with probiotics. Prebiotics provide energy and nutrients to the mucosa of intestine and stop the colonization of pathogenic bacteria (Peng et al., 2020).

Synbiotics are a combination of both pre and probiotics (Wang et al., 2021). To maintain microflora of intestine, enhance immunity and liver functioning, these synbiotics are beneficial. It also helps to increase the FCR of feed and increase the body weight of birds. Examples of some probiotics like *Bifidobacteria spp, B. coagulans, S. boulardii, Lactobacilli* etc. added with some prebiotics like oligosaccharides (fructooligosaccharides, inulin and xylooligosaccharides) (Palai et al., 2020).

Betaine and Turmeric use in Poultry

It is a byproduct obtained from the sugar beet industry (Reguengo et al., 2022). It seems to be effective against coccidiosis and prevent weight loss during cocccidial infection whose causative agent are different *Emeria* spp. It promotes normal metabolic activity of cells and prevent dehydration (osmotic stress). It also has a beneficial effect on intestinal cells and damage parasitic cells (Arumugam et al., 2021).

Turmeric obtained from rhizome of plant *Curcuma longa* contains active ingredient curcumin. Turmeric has medicinal benefits, anti-inflammatory, immune modulator and antioxidant, anti-cocccidial effects and also used as a coloring agent in food (Geevarghese et al., 2023).

External Enzymes as Feed Additives

Enzymes are biological analyzers that are essential and plays very important role in living organisms (Copeland, 2023). These are produced naturally in the body, but some are also produced by culturing in aerobic and anaerobic conditions and in fungi. In poultry, broilers lack enzymes that require for the digestion of grains fibers so for digestion of such fibers external enzymes administered through diet of birds. Digestion and absorption of nutrients stop due to the attachment of these grain fibers to internal enzymes so stops the process of digestion, metabolism and increases the number of microbiotas that are not beneficial for birds (Medjekal and Ghadbane, 2021). It also reduces the quality of meat and stops birds' growth. External enzymes are added in feed of birds to hinder harmful effects cause by grain fibers. The role of enzymes are the digestion of feed and availability of nutrients to birds, so some plants used as feed stuff contain anti-nutritional agents in their cell wall. It stops the digestion of essential nutrients present in such plants, to overcome these enzymes' action and make a hole in cell wall of such plants and enter in it. It helps in digestion of proteins and starch. Enzymes break up the non-starch polysaccharides in diet and result in decrease viscosity of digested material and increase energy level of broilers. Commonly used poultry enzymes are hemicellulase, xylanaze, glucanase, phytase, pectinase and mannanase etc. (Velázquez-De Lucio et al., 2021).

Vitamins and Minerals as Feed Additives

These are essential for maximizing good production of eggs and meat in poultry industry and necessary for proper growth, weight gain, immunity, and reduced mortalities (Alagawany et al., 2021).

Minerals are classified as macrominerals (sodium, potassium, phosphorus, calcium, and magnesium), microminerals (zinc, iron, copper, manganese, iodine), trace minerals (cobalt, selenium) (Saha et al., 2021). Minerals play a vital role in the growth and development of poultry birds. They improve egg production, metabolic functions, blood pigment formation, bone development, and activation of many enzymes' activity. While deficiency of the minerals from the body can cause loss in the production, poor growth, low quality of egg shells, poor hatchability, anemia, rickets, and many more problems (Alagawany et al., 2021).

Vitamins are classified as fat soluble and water soluble like Vit A, D, K, E and Vit B complex, C, and folic acid (Rafeeq et al., 2020). Vitamins are essential for the normal functioning of the body. Although vitamins are needed in the trace amount, they have significant role in the development of bone and eggshell formation, growth of the bird, maintaining health of eyes, promotion of feathering, skin health and maintenance of the brain health. While deficiencies of these trace vitamins in the body of the bird can cause severe problems some of them are thinned eggshells, retarded growth, rickets, lowered egg production, anemia, dermatitis, and lesions of mouth and feet (Fulton, 2020).

Organic Acids and Organic Salts use

These are weak acids and used in metabolic processes and have acidifying properties which help in combating microbial populations (Lund et al., 2020). These can be used individually or in combinations. Organic acids consist of amino acids and fatty acids. These acids' function is the same as antibiotics, but it is safer to use, and no residue and resistance occur. Organic acids like propionic, lactic, citric, fumaric, sorbic and formic acids and their salts like calcium propionate and formate are used as feed preservatives. Organic salts like calcium, sodium and potassium salts are preferred over acids because of no odor and ease to handle them due to their solid, water soluble, less toxic, and less volatile nature. These acids help birds by improving nutrients utilization, feed conversion and improve their growth, immunity, and health. Organic acids have positive effects on birds with gastrointestinal and enteric diseases and enhance performance of broilers and layers. Most popular bacteria that harm poultry by interfering with intestinal health are *E. coli, Campylobacter* and *Salmonella* and can be excluded by use of organic acids (Ricke et al., 2020).

Benefits and Limitations of Natural Feed Additives

Natural feed additives are obtained from plant sources, so they have less harmful effects, and they are natural, residue free, less toxic, favorable, and ideal feed additives in comparison to synthesized additives and inorganic chemicals (Mahfuz et al., 2021). They are added to the feed of birds for rapid weight gain, higher production, enhanced feed efficiency, improve digestibility, improve immunity, and improve nutrition of animal. It also decreases the harm of antibiotic residues for consumers. NFAs increase the flavor, palatability, shelf life of feed and shelf life of animal products. Natural feed additives improve the performance of broilers and layers and have antioxidant, antifungal, antibacterial, antiviral, antiparasitic, anti-inflammatory, anticoccidial and insecticidal properties (Mahfuz et al., 2021). NFAs are environment friendly, cost effective, safe and with no side effects. These are helpful for birds to bear different environmental, deworming, overcrowding, vaccination, heat, and cold stress. The composition of phytogenic feed additives depends on the location, soil type, part of plant used, season, weather conditions, altitude, harvesting method and storage conditions so these may affect composition of plants used. Overdose of natural feed additives may cause harm to the birds (Alagawany and Abd El-Hack, 2020).

Conclusion

It is proved that the addition of natural feed additives in the diet of poultry improves digestibility, performance, weight gain, egg quality and quantity, disease resistance and economic efficiency. Different feed additives have different benefits to birds' health, growth and production of meat and eggs. Furthermore, advancements and research are required to use these additives and their combinations to enhance poultry performance and production. These feed additives consumption by birds also have beneficial or positive impact on humans' health by production of healthy, nutritious, safe and nontoxic meat and eggs.

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Chapter 05

Natural Feed Additives for Animals' Growth and Production

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ABSTRACT

In 2006, antibiotics growth promoters were banned by the European Union due to harmful effects like bacterial resistance, residual effects in the products obtained and increased chances of harm for consumers. These reasons increased the demand for use of natural feed additives in animals' diet to overcome the deleterious effects. To fulfill the increasing demand of animal products by worldwide population, farmers improved the quality and quantity of meat, milk and eggs by using botanical or herbal feed additives in animals' diets. These additives have many beneficial effects on animals and as well as on the consumers. The natural feed additives like phytogenic or herbal feed additives, probiotics, prebiotics, synbiotics, fermented feed and byproducts from plants industry etc. enhances the quality and quantity of desired animals' products, reduces impacts on the environment and also improve the health status of animals. Natural feed additives improve digestibility and have antimicrobial, anti-inflammatory, antioxidant, antiparasitic, immunostimulant and insecticidal effects.

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INTRODUCTION

The population of humans is increasing day by day and their requirements for nutrition are also increasing, to fulfill these requirements we have to improve the quality and quantity of animal products (Prado et al., 2020). Nowadays, the natural feed additives are added to animal feed to increase growth, digestibility, productivity and stabilize beneficial microflora in the gut (Adetunji et al., 2022). These feed additives also aim to provide quality animal products for human consumption (Silveira et al., 2021). Due to the use of antibiotics as feed additives in the animals results in an increase in the antibiotic resistant bacteria and the presence of residues in animals' products and make it unhealthy and harmful for the human intake (Van et al., 2020). To overcome this problem natural feed additives like plant feed additives (essential oils, organic acids, plants extract, byproducts of plants food industry) are now added in animal feed. The use of byproducts of the plant food industry as additives in animals' diet also helps to reduce such industrial wastes and convert these useless byproducts into very valuable food products (milk, meat) (Gómez-García et al., 2021). PFAs act as good antioxidants and in ruminants' essential oils act more as rumen modifiers. Feed additives like probiotics, prebiotics, synbiotics, fermented feed and byproducts from plants industry enhances the quality and quantity of desired animals' products, reduce impacts on the environment and also improve the health status of animals (Michalak et al., 2021). The natural feed additives improve digestibility and have antimicrobial, anti-inflammatory, antioxidant, antiparasitic, immunostimulant and insecticidal effects (Mandey and Sompie, 2021).

Botanical and Herbal Feed Additives use in Animals

The herbal and botanical feed additives are the leaves, roots, stems, fruits, barks and flowers of the plants which have medicinal and beneficial effects and added to animals feed to improve the nutritional requirements, health and performance of animals and have no harmful effects to their health (Rafeeq et al., 2022). These additives enhance the appearance, color and flavor of the feed and make it more attractive and palatable for animals and as a result there is improvement in the animals eating pattern, total feed intake and increase in the secretions of digestive juices. These additives also have antioxidant property and act as antibiotics and improve the animals' metabolism (Seidavi et al., 2021). The herbal feed additives enhance the immune system and endocrine system and increases the absorption and utilization of nutrients (Ahmadifar et al., 2021). The herbal additives also have anthelmintics, anti-inflammatory, antiviral and antibiotics capabilities (Table 1).

Table 1: Botanical and Herbal feed additives, their active ingredients and functions

Plants (local and botanical names)	Active Ingredients	Parts involved	Purpose of use	References
Cinnamon (Cinnamomum zeylanicum)	Cinnamaldehyde	Bark	Antiseptic, increase appetite, improve digestibility	(Moncada et al., 2022)
Cardmom (Amomum subulatum)	Cineol	Seed	Increase appetite and digestibility	(Mackonochie et al., 2023)
Cumin (Cuminum cyminum)	Cuminaldehyde	Seed	Improve digestion, galactagogue, act as carminative	(Joshi and Soulimani, 2020)
Celery (Apium graveolens)	Phthalides	Fruit, leaves	Stimulate digestion and appetite	(Khairullah et al., 2021)
Fenugreek (Trigonella foenum-graecum)	Trigonelline	Seed	Improve appetite	(Sun et al., 2021)
Pepper (piper nigrum)	Piperine	Fruits	Increase digestion	(Shilpa et al., 2021)
Mustard (Brassica nigra)	Allyl isothiocyanate	Seed	Improve digestibility	(Salem et al., 2022)
Garlic Allium sativum)	Alkin	Bulb	Improve digestibility and antiseptic	(Khalesizadeh et al., 2011)
Thyme (Thymus vulgaris)	Thymol	Whole plant	Improve digestibility, antioxidant and antiseptic	(Lorenzo et al., 2019)
Shatavari (Asparagus racemosus)	Sapogenins, saponins and flavonoids	Root	Treat gastric ulcers, dyspepsia and act as galactogogue	(Khan and Sahu, 2021)
Shatavari (Asparagus racemosus)	Shatavarin 1-4 Quercetin,rutin,hyperoside	Root	Galactagogue	(Khan and Sahu, 2021)
Nutmeg (Myristica fragrans)	Sabinene	Seed	Improve digestibility and antidiarrheal	(Akbar and Akbar, 2020)
Cloves (Syzygium aromaticum)	Eugenol	Cloves	Improve digestibility and appetite, antiseptic	(Mandey, 2022)
Coriander (Coriandrum sativum)	Linalol	Seeds and leaves	Improve digestibility	(Kholif et al., 2021)
Anise (pimpinella anisum)	Anethol	Fruits	Galactogogue and enhance digestibility	(Singletary, 2022)
Parsley (petroselinum crispum)	Apiol	Leaves	Enhance appetite and digestibility, antiseptic	(Punoševac et al., 2021)
Capscicum (Capsicum annuum)	Capsaicin	Fruit	Improve digestion	(An et al., 2022)
Mint (Mentha piperita)	Menthol	Leaves	Improve digestion, appetite and act as antiseptic	(Arshad et al., 2023)
Jivanti (Leptadenia reticular)	Stigmasterol, flavonoids, pregnanel glti sides	Twigs and leaves	Antimicrobial, antiinflammatory and Galactogogue	(Ps and Ts, 2023)

Effects of Herbal Feed Additives on Digestibility, Feed Intake and Performance of Animals

The active ingredients present in the herbs and spices when taken by animals through feed result in improvement of digestion differently (Kuebutornye et al., 2024). Some of these additives like curcuma, mint, ginger, cumin, onion and anise etc. increase the bile synthesis and excretion which help animals in digestion and lipid absorption. Some active ingredients increase saliva production. Pancreatic enzymes like protease, amylase and lipase are stimulated by some spices and increase the digestion process. Plants extract fastens the digestion of feed and decreases the time of passage of feed to digestive tract. The beneficial microbes of the gastrointestinal tract are also maintained by these herbs like lemongrass, peppermint and garlic etc. (Bąkowski and Kiczorowska, 2021).

Antimicrobial Effects of Herbal Feed Additives

The plants extract called as phytobiotics have strong antimicrobial activity against many gram +ve and -ve bacteria (Aroche et al., 2023). To protect themselves from herbivores, insects and microorganisms many plants synthesize substances for their defense, and they also produce some secondary metabolites during growth in case of stress and have antimicrobial effects. When these herbs are consumed as feed additives by the animals they result in decreased harmful bacteria count and improve growth and performance (Elghalid et al., 2020). Examples of herbs with antimicrobial properties are *Dictamnus dasycarpus, Angelica dahurica, Artemisia argyi, Sophora flavescens, Hydrastis canadensis, Allium sativum, Polygonum cuspidatum, Geranium thunbergii, Anguisorba officinalls, Fraxinus rhynchophylla* and *philodendron* etc. (Yan et al., 2020). The major active ingredients like flavonoids, cinnamaldehyde, baicalin, limonene, eugenol and carvacrol etc. of these herbs have strong antimicrobial effect on the animals. These herbs change the composition of fatty acids which increase hydrophobicity and decreases microbes' survivability. The herbal additives also change the properties of cell membrane and cause ion leakage hence result in decreased virulence of microbes (Nourbakhsh et al., 2022).

Antioxidant and Immunostimulant Effects of Herbal Feed Additives

The herbal feed additives with antioxidant properties inhibit lipid oxidation, minimize rancidity and stop formation of oxidative products which outcomes in disease resistance, health improvement and decrease chances of heart attack, stroke, high blood pressure and cancer in the consumers (Tsiplakou et al., 2021). Due to the presence of vitamins like vit., A, C, E and phenolic substances like phenolic acid, tannins, flavonoids, phenolic terpenes, hydrolysable and proanthocianidins etc., in some herbs enhance the antioxidant features. Certain examples of such herbs are rosemary, oregano, garlic, onion, thyme, green tea, dandelion and ginkgo etc. These herbs' addition also prevent anti-oxidation during storage of feed (Galli et al., 2020). Carotenoids, vit. C, and flavonoids rich herbs are used in animals as immune modulators. Plants containing echinacea, cat's claw, garlic and liquorice molecules which are immunostimulants, improve the activity of natural killer (NK) cells, macrophages and lymphocytes which increase phagocytosis so animal immune systems become active (Alanazi et al., 2023).

Probiotics, Prebiotics and Synbiotics

The introduction of beneficial microorganisms in diet to improve the activity of rumen microflora and enhance the process of digestion are called as probiotics (Bąkowski and Kiczorowska, 2021). These can be used to minimize loss of gases produced during fermentation process and enhance utilization of feed and efficiency of feed and performance of dairy animals. These friendly microbes are used to compete with harmful microbes. Yeasts are commonly used probiotics used to improve immunity and positively alter the gut microflora and improve disease resistance. The probiotics lessens the lactic acid substance and stabilizes the rumen pH by modulating the rumen microbes and inhibit lactic acid producing bacteria (Reuben et al., 2022). The probiotics improve nutrients absorption and reduce ruminal ammonia creation.

The prebiotics are non-digestible food ingredients like non-digestible oligosaccharides that function to promote the growth of beneficial microorganisms in the digestive tract of humans and inhibit the harmful pathogenic bacteria from the body (Peng et al., 2020). Some examples of prebiotics are inulin, lactulose, fructo-oligosaccharides, trans galacto-oligosaccharides etc.(Guarino et al., 2020). These prebiotics in dairy animals inhibit growth of pathogenic bacteria *E. coli* from their digestive tract which cause diarrhea in animals and results in curing diarrhea.

Symbiotics are the combination of both prebiotics and probiotics and have synergistic effect on animals and help to reduce the population of food borne pathogenic bacteria and enhance immunity (Melara et al., 2022).

Essential Oils

EOs are compounds extracted from plants mainly by steam distillation and are volatile in nature and have beneficial effects on animals when added to their feed (Reyes-Jurado et al., 2020). EOs effects the population of rumen microflora and also affects fermentation patterns and reduces ruminal methane and ammonia. These have antimicrobial and antioxidant properties, enhancing the shelf life, quality and palatability of feed (Mucha and Witkowska, 2021) (Table 2).

(Dorantes-Iturbide et al., 2022)

Fatty acids in different essential oils help to prevent different diseases and improve quality of animal products (milk, meat and eggs). EOs enhance digestibility by increasing digestive enzymes secretion, reduce pathogenic bacterial load, improve nutrients absorption and stimulate immune system (Chowdhury et al., 2021).

Ionophores

These are organic compounds mostly gained from *Streptomyces spp*. and used in animals to inhibit acidosis and prevent coccidiosis and improve feed efficiency by altering fermentation process (Dec et al., 2020). Monensin sodium, laidlomycin propionate potassium, lasalocid sodium, narasin, maduramicin, semduramicin and salinomycin are declared as ionophores (Ekinci et al., 2023). These ionophores decrease methanogenesis by changing the rumen fermentation by converting the fiber digesting gram +ve bacteria to concentrate utilizing gram-very bacteria. The ionophores are administered to cows at a dose of 300-350 mg/day per cow. The ionophores work by penetrating into the cell membrane of gram +ve bacteria and cause outward movement of intracellular K+ from cell and inward movement of extracellular Na^+ and H^+ (Kharga et al., 2024). This results in increased acidity of cytoplasm and causes death of gram +ve bacteria. The ionophores improve feed efficiency of lactating cows and decrease metabolic disorders in dry cows. The ionophores enhance feed utilization in the dairy animals by decreasing acetate and increasing propionate that also reduce methane production.

Benefits and Limitations of Herbal Feed Additives

Herbs are the natural ingredients added to feed of animals and have no harmful effects on animals and are environment friendly, these herbal additives minimize the issue of drug resistance and also helps to remove the residual effect present in the animal products (Kuralkar and Kuralkar, 2021).

Table 2: Essential oils dose and effects

Essential oils (EOs)	Use in animal	Effect on ruminants
Red pepper oil	Sheep (ewes)	Carcass attributes improved
Thyme and clove essential oils	Sheep (ewes)	Improve milk quality, milk fat and milk yield, antioxidant, decrease cholesterol level.
Juniper oil	Goats	No effect on volatile fatty acids, feed intake and pH of rumen and fecal material, act as antioxidant and enhance feed efficiency.
Callistemon viminalis (weeping bottlebrush) oil	Goats	Improves nutrients digestibility and absorption and also improve intake of dry matter.
Oregano oil	Cattle	Enhance animal growth and performance and also improve feed efficiency. Increase daily weight gain, dry matter intake and alters microbial count of rumen and decrease methane formation. Reduces diarrhea in cattle. Effects changes with increase and decrease dose given
Combination of essential oils	Cattle	Dose dependent variation in effects. Improves digestibility of neutral detergent fiber, improves daily weight gain, dry matter intake and immunity and lowers chances of diarrhea, decrease the acetate : propionate ratio
Thyme oil	Sheep	Improves fermentation in the rumen, nutrients utilization and decreases the ratio of acetate : propionate
Eucalyptus oil	Buffaloes	Increase volatile fatty acids concentration and reduces methane production, acetate: propionate, protozoal count. Show no effect on nutrients digestibility, blood urea nitrogen, feed intake, temperature, and ruminal pH.
(*Coriandrum sativum*) Coriander oil	Cattle	Improves milk yield, dry matter intake, nutrients digestibility and decreases concentration of ammonia nitrogen.
Thyme oil	Cattles	Improve milk yield and decrease oxidation of lipid, methane production and digestibility of nutrients.
Garlic oil	Sheep (ewes)	Improved digestibility of crude proteins and digestibility of total nutrients and not affect calcium and phosphorus concentration in blood and feed conversion ratio.
(*Foeniculum vulgare*) Fennel essential oil	Goats	Decrease concentration of ammonia nitrogen in blood and also decrease methane production.
Mixture of essential oils	Sheep	Decreases ammonia nitrogen concentration in rumen and show no effect on ruminal pH and methane production
Oregano and linseed oil	Goats	Antioxidant, improve quality of carcass
Orange peel	Sheep	Antioxidant and increase feed intake
Cashew and caster oils	Cattle	Alter ruminal pH and no effect on nutrients digestibility and feed intake
Ajwain oil	Buffaloes	Improve nutrients digestibility, dry matter intake and protein metabolism. Reduces methane production and ratio of acetate : propionate.
Rosemary and clove oil	Cattle	Effect on oxidation and no effect on carcass quality.
Chavil essential oil	Sheep	Increase antioxidant capacity of meat and decrease saturated fatty acids.

Herbal feed additives are beneficial for animals because of antimicrobial, anti-inflammatory, antioxidant, anti-parasitic, immuno-stimulant, insecticidal, antiviral properties which improves animal health, growth, performance and decreases the chance of disease development (Mandey and Sompie, 2021).

As these additives are natural, harmless and no residual effect so that's why the animal products have good quality and no harm to humans' health. The herbal feed additives have limitations in case of overdose given to animals than requirement. Due to the variations in soil types, weathers, seasons, locations, harvesting methods, storage conditions and altitudes in which plant grow and store, results in effect on the composition of plants. Light and heat may cause harm to photo labile and thermo labile plants so these may be less stable. Microbial contamination and anti-nutritional factors of plants may restrict the use herbal additives (Pathaw et al., 2022).

Conclusion

Due to restrictions on growth promoters' usage, natural and herbal feed additives are now preferred to be used in animal diets to improve digestibility, nutrients absorption, intestinal environment that results in weight gain, increased productivity and performance of the animals. Due to the beneficial effects like antibacterial, antiviral, antiparasitic, anti-inflammatory, anticoccidial, insecticidal and antioxidant, the use of phytogenic feed additives are now increasing. Because of safety, less toxicity, ecofriendly nature their preference over synthesized growth promoters has increased. For advantageous effects and to get high quality products from animals, the use of these natural feed additives has been encouraged. Always use the correct dose of natural feed additives to avoid any harmful effect.

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Chapter 06

Role of Feed Additives in Pet's Nutrition

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ABSTRACT

The aim of this chapter is to take an insight on the feed additives which can be used for making nutrition better. A balanced nutritious diet is essential for the health and well-being of pets. Nutritional requirements are in consistent with the view that a dog is an omnivorous and cat is carnivorous. Balanced nutritious diet includes carbohydrates, vitamins, amino acids, minerals, enzymes and antioxidants. Antioxidants are compounds added to feeds at concentrations lower than those of oxidizable substrates to greatly reduce the substrates' oxidation. Calcium and phosphorous are two essential minerals in a pet's diet. It has been demonstrated that the use of exogenous enzymes improves the digestibility and bioavailability of nutrients in Agro-industrial and agroforestry wastes used as animal feed. It also assists in the removal of some anti-nutritional elements. Farmers use a diverse range of vitamins as feed additives in the feed of monogastric animals. Proline, glycine, taurine, and hydroxyl proline serve as commonly used feed additives in ruminant and non-ruminant diets, excluding glycine. Many probiotics and prebiotics have beneficial health effects on the gastrointestinal and immune system.

KEYWORDS		
Feed additive, Nutrition, Dog, Cat, Health	Received: 12-June-2024 Revised: 27-July-2024 Accepted: 24-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

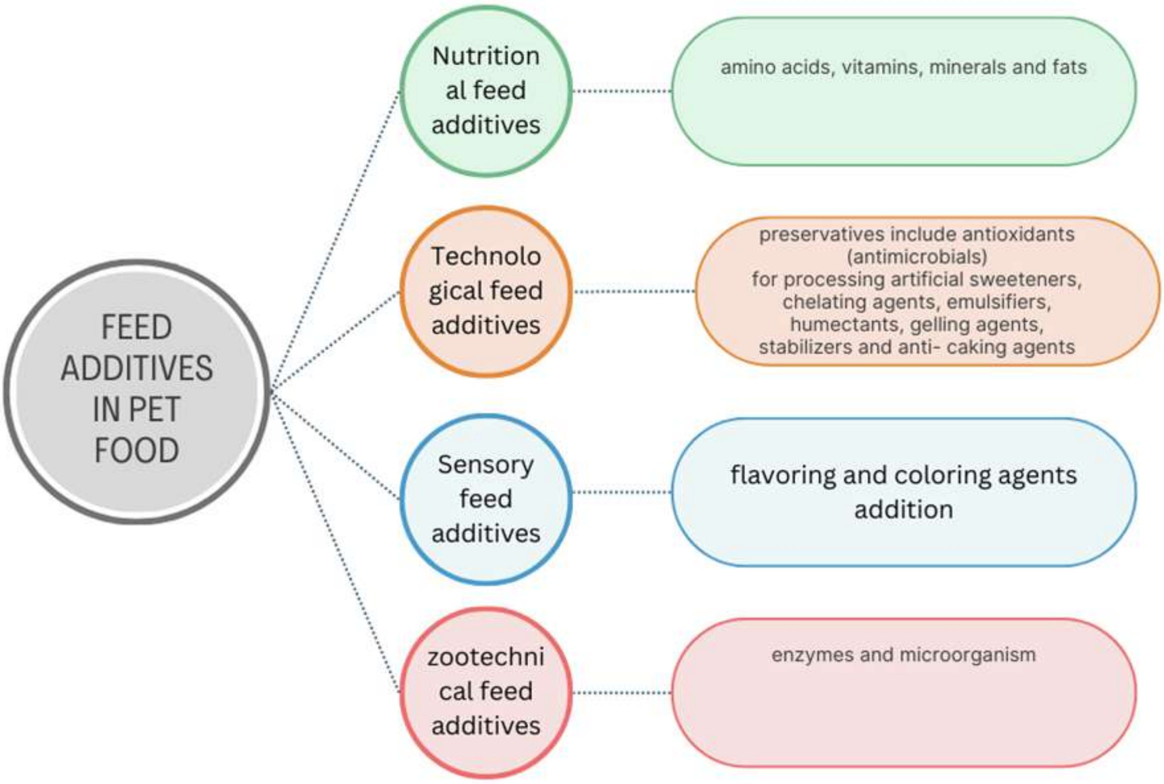
A balanced nutritious diet is essential for the health and well-being of pets. The manufacturers add feed additives to the processed feed to offer nutritional health benefits (Buff et al., 2014) and provide food safety by ensuring color, texture, flavor, and resistance towards spoilage. Feed additives are categorized into natural and synthetic additives (Pandey et al., 2019). Nowadays, feed additives are increasingly in demand in humans and animal's feed (Bai et al., 2022). Selection of feed additives depends upon the nutritional requirements for the body of cats and dogs that depend on the body condition, signalment, life stage and habitat (Ardente, 2023). It is the responsibility of the nutritionists to complete the nutrient profile when an animal stops eating in order to avoid negative energy balance in the body. Many of the commercially available feeds ensure an adequate amount of the required nutrients. In this chapter, we will cover feed additives in dogs and cats. Additives in pet food are categorized into various categorize that depicted the overall picture of feed additives as represented in Fig. 1.

Nutritional Requirements

Nutritional requirements are dependent upon the body type and working of the animal.

Cats

Nutritional requirements are in consistent with the view that a dog is an omnivorous and cat is carnivorous. Cats have high obligatory protein requirements with a view of high nitrogen requirements. They have limited ability to urea cycle enzymes and aminotransferases, because of the presence of enzymes' activity of essential amino acids degradation in the first irreversible step and have less amino acid requirements (National Research et al., 2006) . Because of less activity to urea cycle enzymes and aminotransferases, cats instantly use and metabolize amino acids for gluconeogenesis and energy source (Tazerji et al., 2024). This enables the cats to maintain blood glucose levels in starvation as compared to dogs. As cats are carnivores, they have a smaller number of carbohydrates metabolizing enzymes (Verbrugghe and Hesta, 2017). Glucokinase is not present in the liver and can digest cooked starch very efficiently. Many other essential nutrients in the feline feeds are vitamins A and D, niacin, amino acid taurine and arginine. Due to reduced activities of the pyroline-5-carboxylate and ornithine aminotransferase, there is low-level synthesis of citrulline in GIT that results in total dependance of cat upon dietary intake of arginine (Buff et al., 2014). The depletion of taurine in the body is because of less activity of enzymes of cysteinesulphinic acid decarboxylase and cysteine dioxygenase. Fewer enzyme's activity in synthetic pathway combines with less active N acetyltransferase for glycine and bile acid production that promotes a low level of taurine stores in the body (Fascetti and Delaney, 2023). Vitamin D and niacin are required because of enhanced activity of picolinic carboxylase and 7-dehydrocholestrol-reductase that consequence in the degradation of precursors, involve in their synthesis (Li and Wu, 2024).



Dog

Dogs share some metabolic and nutritional characteristics with that of cats, that's why the term adaptive carnivore is sometimes used for dogs. Dogs like other carnivores can make taurine from sulfur amino acids acid precursors and vitamin A (Bosch et al., 2015). Like cats, dogs cannot make vitamin D and can conjugate bile acids with taurine and require dietary arginine less than the cats to acquire nitrogen balance in the body (National Research et al., 2006). Table 1 enlists various feed additives used in dogs and cats.

Antioxidants

Antioxidants are compounds that, when added to feeds and foods at concentrations lower than those of oxidizable substrates, greatly prevent the substrates oxidation (Mendonça et al., 2022). Potential anti-oxidative compounds include metal chelates, oxygen scavengers, free radical scavengers, deactivators of peroxides and other reactive oxygen species and quenchers of secondary lipid oxidation products that give off rancid odors (Salami1a et al., 2016). The antioxidants found in animal feeds are broadly classified as natural and synthetic, and their functional properties are thought to be similar to those found in diet. Natural antioxidants are those that are primarily vitamins and poly phenolic chemicals found naturally in materials derived from plants (Flieger et al., 2021). Even though there are many antioxidants in nature, only a few of them are marketed as supplements to prevent feed peroxidation. Two most important natural antioxidants utilized in feeds are vitamin C (ascorbic acid) and vitamin E (tocopherols). It also includes carotenoids and vitamin A (retinol). Vegetable oil, lentils and grains are among the feed items that contain significant amounts of these natural antioxidants (Tanprasertsuk et al., 2022). Vitamins can be extracted from natural sources, fermented or chemically synthesized to create commercial forms. Temperature and molecular structure of tocopherols affect their antioxidants stability action (Corino and Rossi, 2021). These are produced chemically and are needed in small amounts to stabilize diets that contain fat, oil or lipids. The majority of them are nitrogen and phenolic compounds with phenolic derivatives having several methoxy or hydroxyl groups. Butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), tert- butylhydroquinone (TBHQ) and propyl gallate are the most widely utilized synthetic phenolic compounds (Al-Mamary and Moussa, 2021). Synthetic antioxidants are thought to be more potent and more resistant to processing losses than equivalent amounts of natural antioxidants (Gulcin, 2020).

Table 1: Different feed additives in dogs and cats

Feed additives	properties	Role in feed	others	References
xylitol	Sugar alcohol	Artificial sweetener, flavor enhancer and antimicrobial agents	In dogs, it stimulates the release of insulin and fatal loss in blood glucose concentrations and liver failure	(Lowe and Anthony, 2020)
Guar gum	Gelling agent	In dogs have some nutritional benefits and high fecal output. In aged cats, its level should be low in order to increase nutrient digestibility		(Craig, 2021)
Cassia gum	Gelling agent	In purified form use at restricted level		(Herath et al., 2022)
Propylene glycol	Synthetic antimicrobial preservative	Add in semi moist feeds in dogs.	FDA approves it to be used as feed additive in all animals feed except cats	(Deliephan, 2022)
Sodium nitrite	Antimicrobial preservative	Inhibits the growth of botulinum bacteria and stops lipid oxidation. It improves the flavor and pink coloration of animal proteins.	More common to be used in cat's feed as compared to dog's	(Craig, 2021)
Potassium sorbate	Mold inhibitor	It is safe for cats and dogs at a rate of 5000mg/kg semi moist feeds		(Kiprotich et al., 2023)
Aluminum silicate	Adsorbent clays	It is used as a binder, mold inhibitor and anti-caking agent in dog feed	It is also known as bentonite.	(Damato et al., 2022)
emulsifiers	Emulsifying agent	These are widely used to prevent separation of constituents and gel in sachet, caned and moist feeds		(Vasconcellos et al., 2023)
carrageenan		It is commonly used in canned cat and dog feed.		(Additives et al., 2022)
Polysorbate-80 and carboxymethylcellulase		It is used to increase shelf life and enhance texture	Carboxymethylcellulase has been approved to be used in an animal feedstuff in the European union	(Craig, 2021)

Minerals

Calcium and phosphorous are two essential minerals in a pet's diet (Zafalon et al., 2020). The primary function of calcium is to maintain the structure and strength of bones and teeth. It also acts as muscle relaxant and helps in neurotransmitter release. Phosphorous helps in bone growth and is essential in energy production, protein synthesis, regulation of hormones and enzymes (Ciosek et al., 2021). It is an important component of phospholipids. It also helps to balance and maintain the metabolic functions in animals. Calcium deficiency results in many bone diseases such as osteomalacia and rickets (Li et al., 2020). Imbalance in calcium and phosphorous mostly affects growing animals and causes lameness, enlarged costochondral junctions, and nephrosis. Chloride, sodium and potassium help in regulation of osmotic pressure and acid base balance. Chloride also aids in the formation of gastric juice (HCL). Potassium and sodium regulate transmission of nerve impulse and muscle contraction. Magnesium improves immune health and is a component of bone formation. It also regulates the function of nerves and muscle (Bijsmans et al., 2021).

Enzymes

It has been demonstrated that the use of exogenous enzymes improves the digestibility and bioavailability of nutrients in Agro-industrial and agroforestry wastes used as animal feed (Velázquez-De Lucio et al., 2021). It also assists in the removal of some anti-nutritional elements. Animals are naturally endowed with endogenous digestive enzymes, but these enzymes cannot fully break down and absorb all the nutrients they contain (Sureshkumar et al., 2023). As a result, treating animals with exogenous enzymes has been shown to increase animal yield and productivity. The use of fibrolytic enzymes is one of them. These fibrolytic enzymes break down the soluble and insoluble fiber by producing tiny amounts of oligomers when introduced to fibrous substrates (Spotti and Campanella, 2020). Enzymes increase the availability of nutrients, minerals, proteins, carbohydrates and amino acids. Furthermore, enzymes often exhibit positive performance response, although environmental and dietary factors influence their catalytic efficiency. The most often utilized enzymes in the animal feed are those with carbohydrates, protease, and phytase and lipase activity (de Oliveira Simas et al., 2024).

In dog food, the use of exogenous enzymes as feed additives is common practice. Various enzymes for increasing the efficiency of feed have been used. Porcine pancreatic lipase, protease, amylase are the most commonly used enzymes in the dog food industry (Additives et al., 2023). In addition to these, the dog food industry also uses xylanases, phytases, β glucanases, pectinases, mannanases, and α galactosidases. Yet some vets recommend the use of animal and plant enzymes for all the pets. Expected benefits range from improvement in digestibility to maintenance of immune system. During the preparation of dog feed, wheat and barley are commonly used. But because of the high dietary fiber content, there is a negative impact on digestibility (Golder et al., 2020). Glucanases can reduce this negative impact by the digestion of some amount of dietary fibers (Shoveller et al., 2024).

Vitamins

Diverse range of vitamins are used as feed additives in feed of monogastric animals (Chuang et al., 2021). A study was carried out regarding addition of vitamin E in food of dog (Yang et al., 2020). The theme of which revolves around that the natural antioxidants (amalgam of vitamin E and essential oils) replace chemical antioxidants in its addition to pet feed. Experimentally, two treatment groups were control treatment (synthetic antioxidant feed contains butylhydroxytoluene) and test treatment (natural antioxidant feed contain mixture of vitamin E and essential oils), using 10 beagle dogs. The experiment noted the efficiency of feed conservation, which demonstrates that these natural antioxidants not only stimulate feed conservation but also accelerate systemic antioxidant levels. Besides this natural antioxidant treated dogs' group had decreased bacterial count in their fecal matter on the 28th day of the experiment. In both of treatment groups, there was no effect on hematological variables. However, in the test treatment group, dogs had reduced level of oxygen reactive species (which minimize oxidative stress) and increased level of glutathione S-transferase.

Amino Acids

Proline, glycine and hydroxyl proline are commonly used as feed additives in ruminants and non-ruminants' diets, except glycine (Li and Wu, 2023). Remaining ingredients are of an expensive nature, therefore their inclusion in ration is somehow excluded. Alternatively (HFM) hydrolyzed feather meal containing 5% hyp, 9% glycine and 12% proline hold prime importance regarding both low cost and availability of amino acids for both ruminants and non-ruminants (Oberbauer and Larsen, 2021).

Amino acid taurine (β amino acid) is involved in many physiological processes. It is considered efficient feed additive in pet's diet, especially dog and cats and is of high significance (Che et al., 2021). Taurine allowance and requirement level is within a safe zone for the diet of cats. Use of taurine is restricted and meant only for dog and cat food (Delaney and Fascetti, 2023). It is not of prime importance when used as feed additives in other non-ruminants and ruminants' diet according to FEEDAP panel (Panel on Additives and Products and Substances used in Animal Feed). Environmental risk from use of taurine is not foreknown. In cat, dog and fish, diet addition of synthetic taurine is considered highly efficacious (Wu, 2024).

L-cysteine (non-essential amino acid); the product of hydrolyzed natural keratin, typically of duck feather. It is safe for dog and cat feed as flavoring additive, if balance between methionine and cysteine is maintained (Tantamacharik et al., 2022).

L-tyrosine (essential amino acid); the product of hydrolyzed feather keratin is considered as safe feed additive for many animal species. The condition for its use in conventional diet is its specific percentage for food-producing animals (0.5%) and for nonfood producing animals (1.5%). The expected risk from L-tyrosine preparation for consumer is 0%. Besides consumer's safety, L-tyrosine product used as feed additive pose no environmental risk (Samant et al., 2021).

Probiotics and Prebiotics

Many probiotics and prebiotics have beneficial health effects on the gastrointestinal and immune system (Savvidou et al., 2023). They show their beneficial effects when used in adequate amounts. Probiotics are live microorganisms. Yogurt is a natural probiotic source. Vegetable like carrot and asparagus are also a good probiotic (Moura et al., 2021). These are very essential during stressful conditions in which immunity become low (Wernimont et al., 2020). Probiotics are in use during different phases like weaning, vaccination, medication, change of feed or environment (Lin et al., 2023). These are very helpful for the absorption of nutrients and also help in the synthesis of proteins and vitamins. Natural prebiotic containing foods are dandelion greens, raw garlic and chicory root (Yang and Wu, 2023). Prebiotics stimulate the growth of beneficial microbiota and, hence, provide less space for pathogens (Zha et al., 2024).

Adverse Effects of Feed Additives

Feed additives may have negative effects on weight management, GI disease, oral health, diabetes, and kidney disease, so management of nutrients is very essential (Craig, 2021). In cats, propylene glycol causes hematological abnormalities (Zafalon et al., 2021).

Conclusion

Due to reduction in family numbers in industrialized countries, companion pets play a positive role in the physical and mental health of people. So, the health of pets has given prime importance. It is a need of time that health care professionals should work with food nutritionists to educate the owners about the advancements in nutrition. Antibiotics with expected high risk are banned in an animal's diet. Therefore, alternatives to antibiotics in animals' feed minerals, prebiotics, probiotics, and various enzymes are used in animal's feed as feed additives. As an alternative to antibiotics, exogenous enzymes hold key significance regarding the growth of animals. For efficient feed digestibility and utilization of dietary ingredients such as amino acids, lipids, energy, starch, protein and enzymes such as xylase, β glucanase, amylases, pectinase and protease are used. Enzymes affected microbial colony of GIT resulting in an improvement in nutrient utilization. Oligosaccharides formation from non-starch polysaccharides, consequently, help in better growth performance of pets.

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Chapter 07

Role of Feed Additives on the Health and Performance of Poultry

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ABSTRACT

The poultry industry is an important source of food for humans and plays an important role in fulfilling the demand for protein in the form of eggs and meat throughout the world. Pakistan is ranked 11th among the largest poultry producers of the globe and this sector is the important segment of livestock that offers employment to over 1.5 million individuals with an investment of more than 1056 billion. This sector has demonstrated remarkable growth; approximately averaging 7.3 % annually over the past decade. Over the past few years, there has been phenomenal growth in poultry production that has primarily been restricted to large and small organized poultry industries. To take advantage of the broiler industry, a variety of feed additives are employed, including antibiotics, probiotics (also known as bio-growth promoters), prebiotics, exogenous enzymes, and antioxidants. Currently, feed additives are broadly used in the poultry industry for multipurpose and replacing antibiotics used in feed. The use of feed additives is not limited to growth promoters but also as immunity boosters and to improve production quality. This chapter will highlight commonly used feed additives in poultry and their effect on health and performance.

KEYWORDS		
Antioxidant, Feed additives Growth-promoter, Immunomodulator, Prebiotic, Production	Received: 22-June-2024 Revised: 20-July-2024 Accepted: 19-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Pakistan is classified as a lower middle-income country with a population of 229.22 million in the year 2022, making it the fifth most populous country in the world. The agriculture sector has a key role in the economy of Pakistan, employing 37.4% of the workforce and contributing 22.9% of its GDP from 2022 to 2023 (Islam et al., 2023). The livestock sector including poultry emerges as the predominant agriculture sector, contributing 62.68 % of total agricultural output and 14.36% to the national GDP during the 2022-2023 Ministry of Finance Economic Survey, 2023 (Rana et al., 2023). By implementing farmer-friendly policies and interventions, the Government has been encouraging both rural and commercial poultry production. The estimated output of commercial and rural poultry products including egg production amounted to 23,819 million with meat production totaling 2,160 tons in the year 2022-2023. However, in the last couple of years, the country has faced climatic shocks such as floods which adversely affected the agriculture and livestock sector (Islam et al., 2023). Over the past few years, there has been phenomenal growth in poultry production that has primarily been restricted to large and small organized poultry industries. This has mostly been made possible by utilizing a variety of contemporary growth-promoting tactics and appropriate disease prevention measures (Angelakis et al., 2013). Most countries have banned the use of antibiotics as a feed additive in animal and poultry production. In response, natural products that are derived from natural resources such as plants, herbs, spices, essential oils, cold-pressed oils, minerals, and microorganisms have been used as natural feed additives in poultry to promote the health, growth, and performance of poultry (Hayajneh, 2019).

The study aims to explore commonly used feed additives in poultry and their effect on health and performance. The use of feed additives is currently rising quickly and taking the place of antibiotics as research indicates that they have a negative impact on consumer health.

Effect of Feed Additives on Different Body Systems

Feed additives are compounds that are added to a nutritionally balanced diet to elicit a response from the host that maximizes its genetic potential for growth and feed conversion efficiency. To take advantage of the broiler industry, a variety of feed additives are employed, including antibiotics, probiotics (also known as bio-growth promoters), prebiotics, exogenous enzymes, antioxidants, etc. (Dhama et al., 2011; Angelakis et al., 2013). Probiotics, prebiotics, synbiotics, organic acids, vitamins, minerals, herbs, and carnitine are among the feed additives that are used to promote poultry health and production (Angelakis et al., 2013). Antibiotics are also added to feed as a feed additive and administered at sub-therapeutic dosages to stabilize the intestinal microbiota, enhance overall performance, and prevent some particular intestinal pathological conditions (Hassan et al., 2010).

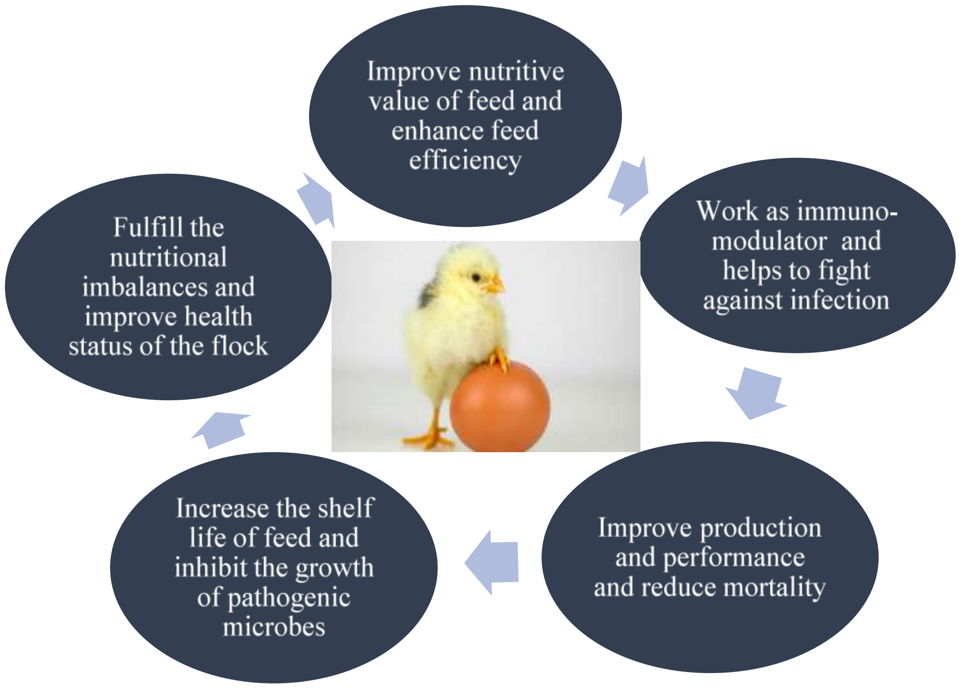

Fig. 1: Feed additives affect multiple functions of different body systems; some of them are briefly mentioned.

Effect of Antibiotics

Antibiotics are not utilized for therapeutic purposes; rather, they are used in poultry feed at low levels on a contagious basis to enhance growth and feed conversion (Chowdhury et al., 2009). Antibiotics primarily work by regulating and maintaining the ideal balance of avian intestinal microflora between gram-positive and gram-negative organisms (Yadav et al., 2016). Over 90% of the bacteria in the well-balanced gut microbiota are Gram-positive, mainly Lactobacillus. An imbalance of microflora results from a rise in pathogenic organisms like Escherichia coli or other gram-negative organisms during times of stress or digestive disorders (Jandhyala et al., 2015). Further colonization of the intestines by the gram-negative bacteria results in intestinal mucosal inflammation and attachment to the intestinal epithelium, which reduces nutritional absorption and ultimately stunts the growth and production of birds (Ma et al., 2022). Antibiotics can also modify the processes of mucin biosynthesis. Changes in mucin dynamics can also affect nutrient uptake and gut function and may change nutrient uptake hence, for eliminating the chances of imbalance under practical conditions, antibiotics are added to the feed or water as a prophylactic measure (Van et al., 2018). In contaminated environments, the use of anti-coccidial medications in addition to antibiotics as feed additives improved the growth and immune state of chickens (Lee et al., 2012). Sub-therapeutic doses of antibiotics are used to improve overall function, stabilize the gut flora, and prevent some specific pathological illnesses of the intestine. However, it's important to remember that utilizing antibiotics as feed additives might lead to resistance in the gram-negative bacteria group of microorganisms, thus prolonged usage of antibiotics should be avoided (*E. coli* and *Salmonella spp*.) (Hassan et al., 2010; Seniya et al., 2012).

Effect of Probiotics

The overuse of antibiotics has led to the development of antibiotic-resistant bacterial strains and an imbalance between pathogenic and normal microbiota. Therefore, there is a growing interest in discovering alternatives to antibiotics to produce poultry. Natural feed additives in poultry such as live probiotics have the potential to reduce poultry enteric diseases subsequently causing contamination of poultry products (Dhama and Singh, 2010; Gupta and Das, 2013). Probiotics are live microbial feed supplements that work to produce a variety of substances that help balance the bacteria population in the intestine. The host receives a "boost" to develop a correct microbial population in its gut and positively affects itself by increasing the features of the native gastrointestinal microbiota, if robes which contribute to the proper microbial balance, are added to the feed (Schwarzer et al., 2018). Additionally, probiotics have been shown to enhance nutrient absorption and utilization as well as aid in mineral metabolism and vitamin production (Biotin, Vitamin B, and K), all of which are necessary for healthy growth and metabolism (Roshanfekr, H., and Mamooee, 2009). Probiotics considerably enhanced the immunological response in the diet of broiler chicks. Additionally, feeding probiotics has been shown to raise antibody titers against viral illnesses such as Infectious Bursal Disease (IBD) and Newcastle Disease (ND) (Talebi et al., 2008). To establish gut microbial balance and prevent early chick mortality, probiotic use is recommended for newly hatched chicks. Other stressful conditions include deworming, overcrowding, vaccination, temperature, and environmental stresses, changing feed or ingredient types, and management. Probiotics are thought to be beneficial substitutes for antibiotic growth promoters, which aid in reducing the number of antibiotic residues in chicken products and the emergence of drug-resistant microbes (Dhama et al., 2011).

Effect of Prebiotic

Supplementation of the diet with small fragments of carbohydrates (such as oligosaccharides) is another method used to manipulate the gut ecosystem. Prebiotics that are specifically fermented by beneficial microflora into Short Chain Fatty Acids (SCFA) successfully keep out pathogenic microorganisms by lowering the pH in the G1 tract through the creation of lactic acid, which prevents pathogenic bacteria from colonizing. However, the impact varies depending on the kind and quantity of carbohydrates as well as the rate at which the beneficial organism’s ferment those (Fallah et al., 2013). These indigestible substrates, known as oligosaccharides, are regarded as "food for beneficial microbes," as they stimulate the intestinal absorption of many minerals while simultaneously inhibiting infections during fermentation. Prebiotics work by feeding the good bacteria to the detriment of the bad ones, therefore providing the host with selective benefits. Since these oligosaccharides are indigestible by Salmonella, E. coli, and numerous other gram-negative pathogenic microorganisms, their growth is impeded (Liu et al., 2023). The commercially available prebiotic products mainly include oligosaccharides of galactose, fructose, or mannose viz, galacto-oligosaccharides (GOS), mannan oligosaccharides (MOS), and fructo-oligosaccharides (FOS) have been tried in poultry with much success (Dhama et al., 2011; Roberfroid, 2007). Feeding MOS and FOS has been shown to improve immunological status, increase macrophage activity, and stimulate T-helper cell activity (Shohani et al., 2013). Currently, probiotics and prebiotics, sometimes known as synbiotics, are combined to counteract the impacts of infections or stress factors in chicken production systems because they have demonstrated synergistic effects (Mookiah et al., 2014).

Effect of Vitamins and Minerals

Multivitamin-mineral premixes have been utilized in chicken feed, especially for broiler feed, to improve feed utilization and broiler growth, which has led to improved production and economic outcomes (Peric et al., 2009). They also have positive effects on immunity and immunological function, as well as gut health. An improved appetite has a positive impact, despite differences in the mode of action. In addition, there is enhanced feed conversion, immune system stimulation, increased vigor, and intestinal microbiota modulation. Ascorbic acid or vitamin C also can reduce weight loss in birds due to heat stress. it resulted in enhanced performance in broiler chicks exposed to multiple concurrent environmental stressors diets enriched with tocopherols or vitamin E, in addition to ascorbic acid, improved the feed conversion efficiency, and led to improved growth performance. Tocopherols and tocotrienols are the two forms of vitamin E that are accessible. Vitamin E is degraded in its unesterified form after absorption. Vitamin C can also be added to L-arginine to improve the quality of meat (Al-Darajih and Salih, 2012; Suliburska et al., 2014).

Symbiotic

Symbiotic refers to the concurrent use of Probiotics and probiotics. According to reports the most likely method for reducing infections in poultry is the highly targeted support that these two products provide for one another (Vandeplas et al., 2010). When fed symbiotics demonstrated a synergetic impact in reducing the population of food-borne pathogenic bacteria in food of animals and birds (Melara et al., 2022; Naseem et al., 2023).

Role of Feed Additives on the Health and Performance of Poultry

Natural Feed Additives used in Poultry and their Effect on Consumer Health

A satisfactory diet is needed for animals, including poultry throughout the world that improves the growth rate and prevents infectious diseases. In the poultry sector, antibiotics have been used on a large scale for the treatment of birds against disease and have been used for improving growth, weight gain, and increase in the production such as meat and egg in sub-therapeutic levels as a feed additive (Saleh et al., 2024). The continuous or extensive use of antibiotics produces an adverse effect on the production and performance of poultry and their residues have accumulated in the birds' tissues and produce resistance in birds and in humans through the food chain ultimately the result this causes therapeutic failure (Cervantes, 2015).

Phytogenic

Phytogenic or Phyto-biotics also called plant secondary metabolites are plant extracts including herbs, spices, and essential oils, which are used as a feed additive in animal and poultry to increase production, digestibility, absorption of nutrients, and improve growth promotion (Alghirani et al., 2021). Phytogenic have antimicrobial, antiviral, anti-inflammatory and antioxidants properties which eliminate the pathogens and prevent the risk of pathogen resistance to antibiotics (El-Sabrout et al., 2023). Mostly used spices and herbs as a phytogenic feed additive for poultry production are garlic, peppermint, thyme, horseradish, chili, cinnamon, rosemary, cayenne, pepper, and sage and respective plant extracts are used in the form of essential oils (Windisch et al., 2008).

Garlic

Garlic (*Allium sativum L.)* is a commonly used herbal plant that is divided into segments. Garlic is used in vegetables for cooking in the form of crude. Garlic is considered a total phenolic compound among mostly consumed vegetables. Garlic has cardio-protective, anticancer, antioxidant, immune modulator, antibacterial, antifungal, and anti-inflammatory properties. In Poultry, garlic supplement improves digestion, feed intake and immune response, improve growth performance, and decreases the mortality of birds due to their antibacterial and antioxidant effects (Fadlalla et al., 2010). The use of garlic in poultry also raises the total protein, globulin, and albumin of the chicks (Oleforuh-Okoleh et al., 2014). Garlic supplements increase the activity of pancreas enzymes and help in better absorption of nutrients (Khan et al., 2012).

Rosemary

Rosemary (*Rosmarinus officinalis*) is an herbal medicinal aromatic plant from the Lamiaceae family, mainly found in Mediterranean countries. This plant has different colors of flowers such as white, blue, pink, or purple, and currently, this plant is famous for medical and industrial uses (Habtemariam, 2018). This plant is mostly used to treat kidney and respiratory problems and this plant's extracts have been used to treat stress and anxiety (Oluwatuyi et al., 2004). This herbal plant has rosemeric acid, phenolic, and flavonoids, that have powerful antioxidant and antimicrobial properties and its products also prevent oxidative damage and control the blood cholesterol level into the normal range. The main biologically active rosemary oils are carnosol, carnosic acid, and esters (Govaris et al., 2007). In poultry, rosemary oil has been used to improve egg and meat production. The extracts of rosemary improve feed conversion ratio, carcass quality, and microbiological composition of the cecum in poultry birds. Rosemary leaf meal extract delays the rancidity appearance in poultry products. These rosemary leaf meals could have been used in poultry diets to promote growth and increase the immunological response of the birds (Ghazalah and Ali, 2008; Petricevic et al., 2018).

Turmeric

Turmeric (*Curcuma longa*) is a seasonal flowering plant belonging to the Ziniberaceae family, and this plant grows in tropical regions such as Southeast Asia (Devi et al., 2014). This is a stemless plant, which is about three to five feet long having yellowish leaves, rhizomes, or root having white clustered flowers (Kurp et al., 2013). Turmeric is an herbal plant mainly used in diet as an ingredient to increase the appearance, flavor, palatability, and shelf life of feed (Sethy et al., 2016). Turmeric has anti-bacterial, antioxidant, anti-fungal, anti-viral, anti-protozoal, anti-inflammatory, anti-hypersensitive, and anti-carcinogenic effect. Turmeric has beneficial effects on blood parameters of layers and broilers. Turmeric powder regulates the stimulation of T cells, B cells, K cells, macrophages, neutrophils, and dendritic cells and decreases the harmful effect of aflatoxin B1 in poultry (Arslan et al., 2017). According to researchers, 0.5 % to 1.0% of turmeric powder improves the immune response and antioxidant enzyme concentration in poultry; turmeric also acts as an antibacterial agent and prevents intestinal problems such as diarrhea (Sethy et al., 2016). Feeding turmeric meal to broilers increased the growth performance and final body weight and improved the feed conversion ratio (FCR) without any adverse effects. Turmeric supplementation improves the retarded growth caused by Eimeria infection by increasing the villae (Rajput et al., 2013).

Essential Oils

Essential oils are aromatic oils obtained from plant materials such as flowers, seeds, buds, leaves, herbs, wood, roots, and fruits by fermentation, extraction, or distillation. There are two classes of essential oils: Terpenes and Phenylpropenes. In poultry feed additives, essential oils work as antibacterial, antioxidant, digestive stimulants, growth promoters, anti-parasitic, flavoring agents, immunomodulators, antiviral and insecticidal. The supplementations of essential oils in the poultry diet result in improved growth performance, body weight gain, egg production, and increased digestibility of macronutrients and production of lean meat which decrease the risk of hyperlipidemia in the consumer (Gopi et al., 2014). Many essential oils stimulate the growth of beneficial microbes and inhibit or limit the growth of pathogenic microbes, such as terpenoids and phenolic cause membrane disruption and inhibit the growth of pathogenic bacteria in poultry (Kirshan and Narang., 2014). Feeding of Carvacrol and thymol reduces the parasitic effects in poultry like they have anti-coccidial action against *Eimeria tenella* (Giannenas et al., 2003). The combination of essential oils like cinnamaldehyde, carvacol, and capsicum oleoresin produces an antioxidant effect and improves the hepatic concentration of coenzyme Q10 and carotenoids (Karadas et al., 2014).

Organic Acids

Dietary acids used in poultry feed are divided into two organic and inorganic acids. Organic acids, also known as carboxylic acids are compounds that contain the functional group -COOH. This group contains a carbonyl group (C=O) and a hydroxyl group (OH) attached to the same carbon atom. The most used acids are short-chain organic acids such as propionic, acetic, formic, butyric, lactic, malic, tartaric, fumaric, and citric acids (Polycarpo et al., 2017). In poultry, supplementation of organic acids is used as a substitute for antibiotics due to its impact on pathogenic bacteria, especially salmonella, coliforms, and Escherichia coli. and fungi such as mycotoxins, Organic acids decrease the pH of the gastrointestinal tract increase the digestion process of the birds, and improve the absorption of various nutrients, further, they improve growth performance, feed intake, disease resistance, and the immunological status of the bird (Islam, 2012). The supplementation of 2.25 g/kg of humic acid in the feed of poultry chickens improved weight gain, meat quality, and the feed conversion ratio (FCR) and decreased the cholesterol level and low-density lipoproteins in the blood. The inclusion of humic acid in poultry feed has improved the meat quality (Abd El-Hack, 2016).

Prebiotics

Prebiotics are non-digestible food ingredients that promote the growth and activity of beneficial bacteria in the colon. Prebiotics provide a substrate or a food source for beneficial microbes present in the gut. Probiotics increase the role of endogenous beneficial microbes in the gut, and these can be used as alternatives to growth-promoting antibiotics (Samal and Behura., 2015). Commonly used prebiotics in poultry are Fructo-oligosaccharides (FOS), Mannan-oligosaccharides (MOS), inulin, galacto-oligosaccharides (GOS), soya-oligosaccharides (SOS), pyrodextrins, xylo-oligosaccharides (XOS), isomalto-oligosaccharides (IMO), and lactulose (Shehata et al., 2022). The use of prebiotics in broiler feed increases lactobacilli and Bifidobacteria levels while decreasing the clostridia, *salmonella*, and coliform bacteria. Prebiotics increase the villi size of the intestine, which leads to the elimination of harmful bacteria and enhances the healthy bacteria population in the digestive tract. Prebiotics improve the feed efficiency, mineral intake, and quality of bone, and eggshell, and decrease the yolk cholesterol concentration without affecting the yolk weight and performance of the layer (Janssens et al., 2004). Continuous usage of prebiotics such as Aspergillus oryze, and Aspergillus meal (AM) can enhance the performance of poultry at low protein levels, promote growth, and increase the feed ingredient absorption and digestibility (Torres-Rodriguez et al., 2005). Beta-glucan acts as an immunity booster by affecting the villi of the intestine which helps to fight against viral and bacterial infections (Hooge et al., 2003). Yeast cell walwallsich are derived from baker's yeast and used as a prebiotic feed additive in brobroilersat increase humoral immunity, increase growth performance, reduce the cholesterol level in eggs, and reduce the abdominal fat in poultry (Yalcin et al., 2014).

Probiotics

Probiotics are the living micro-organisms (Bacteria, yeast, or fungi) incorporated in the feed of animals or poultry as feed additives or supplements to enhance gastrointestinal performance, and gut microbiota, improve the absorption of nutrients, and also improve the immunity of the birds, which improve the feed conversion ratio (FCR) and increase the production of the poultry in the form of egg and meat (Abd El-Hack et al., 2020). Probiotics can be obtained from various sources such as traditionally and commercially, the main sources from probiotics that can be isolated are milk, fermented food, gut microbiota, or the feces of the different animals (Fontana et al., 2013). The bacteria such as *Bifidobacterium* spp., *Lactobacillus* spp., *Bacillus* spp., *Lactococcus* spp., *Streptococcus* spp., and yeast-like *Candida* spp., are used to make probiotics (Park et al., 2016). The use of bacterial Probiotics or yeast in the diet of poultry produces antibacterial proteins like bacteriocins, which prevent toxins and promote the development, enhance immunity, and improve the resistance against pathogenic bacterial colonization such as *Salmonella Typhimurium, Clostridium perfringens, Staphylococcus aureus, and Escherichia coli*. Probiotics increase the pH, digestive enzyme production, meat quality, meat color, the profile of fatty acids, body chemical composition, the capacity of water retention, and oxidative status. Feeding probiotics to poultry has increased the antibody titer against viral diseases such as Infectious Bursal Disease (IBD) and Newcastle Disease (ND) and improved innate and humoral immunity (Talebi et al., 2015; Molinaro et al., 2012).

Effect of Feed Additive on Health and Production of Poultry

Feed additives that support overall health and growth performance include probiotics, organic acids, enzymes, probiotics, prebiotics, functional foods, and nutraceuticals. It may have important functions in promoting general health and growth efficiencies (Hoste et al., 2015; Abd El-Hack et al., 2020). In the chicken industry, botanical products are essential and natural ingredients that are frequently added to food. Their dietary and therapeutic qualities enhance performance. They consist of essential oils, flavonoids, phenols, probiotics, and tannins, all of which have various functions in the health of the birds. They can improve digestion and promote health in a variety of poultry species (Liu et al., 2020). Additionally, botanical or herbal products are regarded as photogenic feed enhancements for poultry birds to reduce the levels of trimethylamine in the yolks of laying hens and enhance egg weight and ovarian features (Saki et al., 2014). The seminal features and reproductive performance of roosters can be improved by dietary supplementation of various botanical feed additives, such as camphor (50 mg/kg of feed) (Raei et al., 2021).

One of the main probiotics used in the production of chickens is *Saccharomyces cerevisiae* hydrolysate (SCH), which is employed as a growth booster and is disease resistant. SCH is rich in nucleotides, B vitamins, amino acids, and polysaccharides found in yeast cell walls. As an essential component of SCH, nucleotides provide several advantages for enhancing development, controlling immunological response, and healing animal gastrointestinal tracts (Superchi et al., 2012). In the meanwhile, because of their capacity to strengthen disease resistance, improve intestinal health, improve intestinal nutrition digestibility, and reduce inflammatory responses, SCH has been regarded as one of the most potent substitutes for antibiotic growth promoters (AGP) in animals (Fu et al., 2019; Bu et al., 2020). Nutraceuticals are believed to be substitute feed additives. Bioceuticals, another name for nutraceuticals, are naturally occurring chemical substances that support and alter normal physiological processes in a healthy host (Das et al., 2012). Because of their many growth and health advantages, they are commonly utilized as alternative feed additives in chicken diets to improve animal production and welfare (Alagawany et al., 2021). Additionally, they could enhance the balance of the gut microbiota, which is critical for controlling vitamin production, intestinal epithelial growth, and metabolism (Dhama et al., 2015). Nutraceuticals are compounds that are produced as nanoparticles to cure a variety of diseases, such as coccidiosis and nutritional deficiencies (malnutrition). In addition, nutraceuticals in chicken diets can promote several gene expressions linked to immunity, growth, and metabolism (Alagawany et al., 2022).

Essential oils of cinnamon and rosemary enhanced hen productivity, quality of egg production, immunity, liver and kidney functions, and antioxidative ability. Because of its antioxidant and hypocholesterolemic qualities, cinnamon oil enhances the quality of broiler meat (Abo et al., 2020). Garden cress or Lepidium sativum, can be given to a broiler's feed in amounts up to 1% to enhance its body weight, biological performance, and general health (Hassan and El Shoukary, 2019). By supplementing with 5 g/kg of ginger, the antioxidant status and body weight of broiler chickens were improved enhancing the humoral immunity, body weight, and feed conversion ratio of birds (Zhang et al., 2009). In broiler chicks under heat stress, turmeric powder (0.5 g/kg diets) enhanced final body weight, feed conversion ratio, digestibility, and lipid status, and rise in the yield of eggs. According to a study results, layers were given 4% turmeric in their diet, the cholesterol in their eggs decreased by 25% (Kosti et al., 2020). Broiler diets supplemented with 200–400 mg/kg of chamomile oils show improvements in weight increase and ultimate body weight as well as a reduction in microbial activity (Jakubcova et al., 2014).

Probiotics control the innate and adaptive immune response by influencing B and T lymphocytes, dendritic cells (DC), and macrophages. In addition to their ability to interact with intestinal epithelial cells and draw in macrophages and mononuclear cells, probiotics also enhance the production of anti-inflammatory cytokines (Petruzziello et al., 2023). Likewise, probiotics can use the gut-brain axis to produce neurotransmitters in the gut. The amounts of serotonin, gamma-aminobutyric acid (GABA), and dopamine can be modulated by some probiotic strains, which can impact mood, behavior, gastrointestinal motility, and stress-related pathways (Gangaraju et al., 2022).

Conclusion

In this study, it is concluded that feed additives exert a positive effect as a growth promoter and improve FCR and the immune system. Increase production and improve the quality of meat and eggs. Feed additives alter gut motility and improve the population of the normal flora of the gut, thus helping to improve the digestibility of the feed. Studies also suggest that feed additives play an important role in limiting the harmful microbes in the gastrointestinal system. Recent studies show dietary organic acids are commonly used in poultry to reduce the pathogenic microorganisms in the gastrointestinal tract. Feed additives are crucial to overcome feed toxicity and work as the best detoxifying agents in the poultry industry currently. Feed additives also play a vital role in combating any kind of stress in poultry birds due to disease, weather, vaccination, or travel. This study also highlights the mechanism of action of various commonly used feed additives in poultry and the effect of these feed additives on different body systems. Currently and in the future, the use of feed additives will become more extensive because of their negligible effect on the health of consumers.

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Chapter 08

Role of Milk Thistle (*Silybum marianum*) as a Therapeutic Feed Additive in Livestock, Poultry and Humans

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ABSTRACT

Hepatoprotection is essentially the only application for silymarin (SM), the polyphenolic component from the milk thistle (*Silybum marianum*), including its primary constituent silybinin. Silymarin has received tremendous attention in medical science for the last few decades. The last five to ten years have seen the majority of the scientific interest and practical applications of this phytochemical mixture in poultry, livestock nutrition, and human health. Therefore, this chapter briefly summarizes data on SM in poultry, livestock, and humans. The presented data indicates that SM showed promising results as feed additives in poultry, livestock, and humans. The most important findings related to SM are their protective effects under various stress conditions, including mycotoxin feed contamination and heat stress. The Anti-stress and anti-toxic activities of SM put this phytochemical mixture into the veterinary category of dietary supplements. Its therapeutic uses in humans include treating liver cirrhosis, alcoholic liver illnesses, viral hepatitis, poisoning from Amanita mushrooms, and liver ailments brought on by toxins and drugs. The identification of novel silymarin compounds provides fresh avenues for liver treatment use.

KEYWORDS
Silymarin, Antioxidant, Toxins, Livestock, Human, Poultry

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INTRODUCTION

Milk thistle, or *Silybum marianum*, is a plant that belongs to the Asteraceae family. The herb milk thistle has been used for liver and gallbladder issues for over 2,000 years. More recently, the liver's defense against environmental and chemical poisoning, such as alcohol addiction, snake bites, insect stings, and poisoning from mushrooms (*Amanita phalloides*) (Křen and Walterová, 2005). A distinct combination of polyphenolic chemicals, including the flavonolignans, silychristin, silydianin, silybin, and isosilybin (together referred to as silymarin), is present in the fruit of the milk thistle plant. While silychristin could additionally exist in the diastereomeric form, some of these compounds, such as isosilybin and silybin, are naturally occurring as diastereomers (A and B) (Lee et al., 2006; Shibano et al., 2007). Fig. 1 displays the chemical structures for the seven main active components in SM.

Silymarin's potent antioxidant and tissue-regenerative qualities have led to research on it as a protective component for the liver, brain, heart, and kidneys. Numerous recent thorough reviews have examined the numerous pathways and modes of activity of SM in human trials and animal models, frequently highlighting its antioxidant qualities (Milić et al., 2013; Testino et al., 2013; Madrigal-Santillán et al., 2014; Vargas-Mendoza et al., 2014; Zholobenko and Modriansky, 2014). Pharmacological research has shown that SM is a safe herbal medication since, when taken at physiological levels, it is not hazardous unless therapeutic dosages are administered incorrectly (Toklu et al., 2007; Ramakrishnan et al., 2009).

Silymarin significantly increased the activity of liver enzymes such as the aminotransferase aspartate and the aminotransferase alanine (AST) in grill meals (Amiri Dumari et al., 2014). SM markedly lowered plasma levels of cholesterol, ALT, AST, and triglycerides in diabetic rats (Tuorkey et al., 2015). Silymarin is believed to primarily function by stimulating liver cell regeneration and acting as an antioxidant and anti-inflammatory (Vargas-Mendoza et al., 2014). Aflatoxin M 1 and its B1 metabolites were less frequently seen in the milk of dairy cows fed SM, indicating an antitoxic effect (Tedesco et al., 2003). Because SM is a widely used plant with a potential cure for liver diseases, this chapter discusses its use as a medical feed supplement in humans, poultry, and animals.

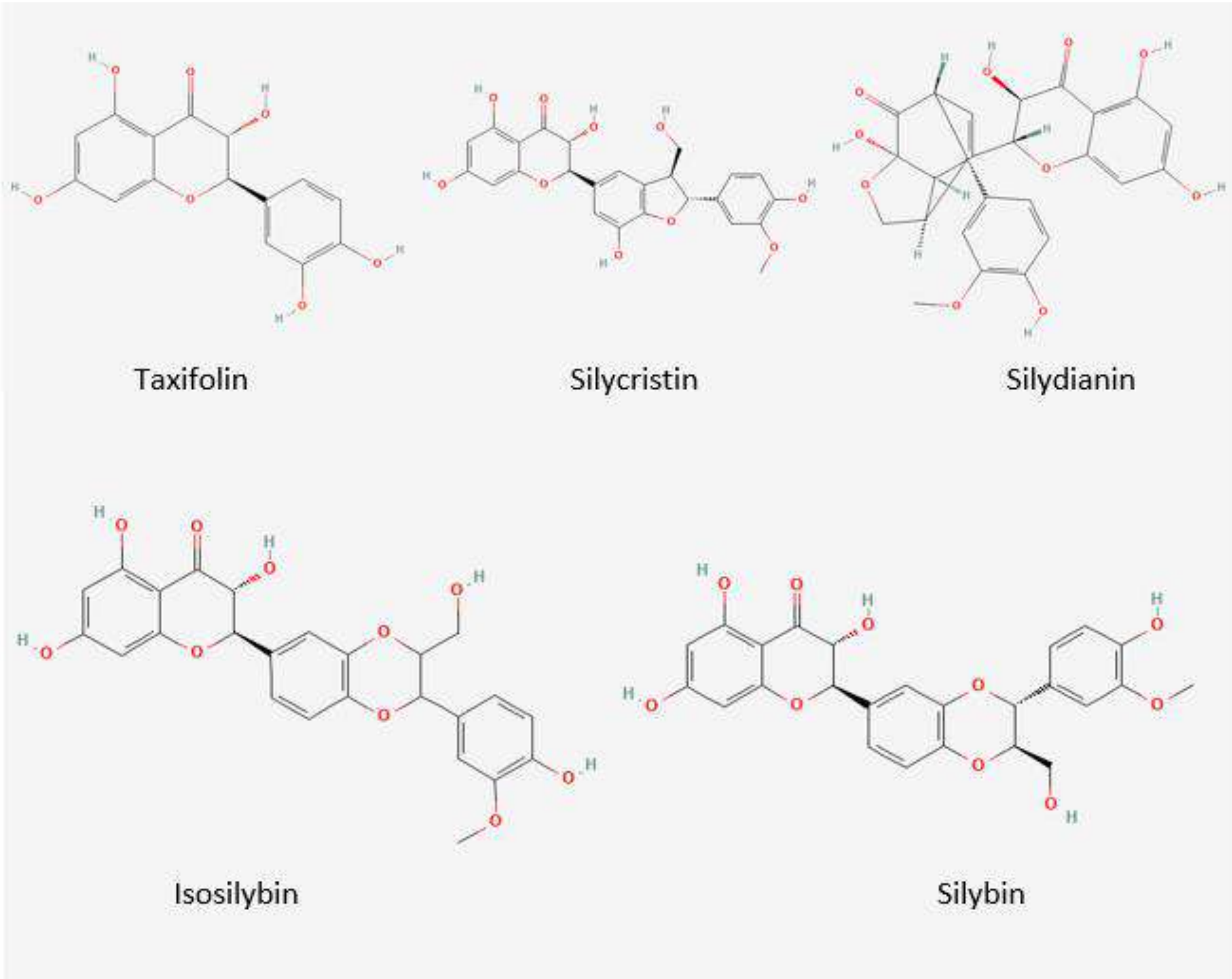

Fig. 1: Chemical composition of silymarin's primary ingredients.

Effects of Silymarin on Livestock

Several researchers have examined the use of SM as a source of feed for livestock (Potkanski et al., 1991; Szumacher-Strabel et al., 2009; Nikzad et al., 2017). Numerous studies have shown that the plant is a promising source of bioactive chemicals that can reduce oxidation and metabolic stresses in animals. It also functions as a useful tool for raising livestock productivity and quality, for example, the quantity and quality of milk and meat (Marceddu et al., 2022).

Impact of Silymarin on Productive Performance

Adding milk thistle to the food ration would serve as a flavonoid supplement and boost milk production and quality. It would also be good for the health of the animals and their general productivity (Piłat et al., 1999; Grabowicz et al., 2001). Promising outcomes were observed when milk thistle seeds were added to dairy cows' diets. When compared to the initial milk yield of the trials, the test cows' milk output increased by 3.4-7.7%, while the control groups' cows' milk production declined over the trial (Vojtisek et al., 1991).

Even two weeks after the milk thistle seed was removed from the test of the cows' diet, differences were still evident in their metabolic parameters and milk production. As compared to the control group, the cows fed 10g of SM per day demonstrated a week earlier commencement of the peak of milk production as well as a higher total milk yield (Tedesco et al., 2004). There were no observed changes in the milk's composition, nor did SM have any impact on the liver's histology or biochemistry (Vojtisek et al., 1991). Numerous studies conducted in Sicily demonstrated the benefits of adding milk thistle to the diet of Comisana sheep. The study showed that SM extract had positive effects on the number and production of squamous cells in sheep’s milk between the middle stages of lactation to the end. Otherwise, no benefits in milk quality were noted in cattle fed raw milk thistle seed; this is most likely because animals ingested less silybin when milk thistle was given in this form (Stringi et al., 2004).

Impact of Silymarin on Fatty Liver and Liver Enzymes

When dairy cows give birth, they have mild to severe fatty livers. This affects liver function and causes ketosis, which can be fatal to the cows and severely reduce milk production. Hepatoprotective medications like SM can lessen the severity of peripartum fatty liver (Gazak et al., 2007). In cows, SM had a favorable effect on the metabolic pattern of the liver enzymes during the commencement of lactation (Grabowicz et al., 2004; Tedesco et al., 2004).

Ameliorative Impacts of Silymarin on Mycotoxins

Since milk thistle has a long history of usage as a medical herb, it seems sense that ruminants have long used it as a food supplement in their diets, believing it to be able to lessen the harm caused by feeding them fodder contaminated with aflatoxin (Stringi et al., 2004; Tedesco et al., 2004; Radko and Cybulski, 2007). In compliance with Tedesco et al. (2003), SM can reduce but not block the excretion of aflatoxin M1 (AFM1, a key metabolite of AFB1) in cow's milk. In dairy cows and ewes, higher milk production was noted throughout lactation, and no harmful effects were seen (Stringi et al., 2004; Tedesco et al., 2004).

Effects of Silymarin on Poultry

Various methods and milk thistle preparations have been examined in poultry to determine their effectiveness. As an illustration, consider dried milk thistle seeds, milk thistle seed extract, and SM supplementation (Ebrahimi et al., 2014; Zarei et al., 2016; Armanini et al., 2021; Bendowski et al., 2022).

Beneficial Effects on Growth Performance

The majority of research demonstrated that milk thistle products improved poultry birds' ability to produce. Grill performance and the related weights of the body's immune organs were shown to be enhanced through the inclusion of 100 milligrams of milk thistle grains/kg of feed during low-level heat stress (Zarei et al., 2016). Under conditions of heat stress, the study employed hundred or two hundred milligrams of extract from milk thistle seeds per kilogram of food. In poultry administered a diet comprising 100mg/kg of *Silybum marianum* extract, the highest feed intake (FI), lowest feed conversion ratio (FCR), daily weight increase, and ultimate body weight (BW) were observed (Morovat et al., 2016). The ingestion of powdered milk thistle seeds with two concentrations (0.24 or 0.36g/day/broiler) into their water supply improved the well-being and production performance of the broilers under normal growth conditions (Bendowski et al., 2022).

Laying hens are more vulnerable to a range of stressors throughout their extended production cycle, including high temperatures and illnesses that cause oxidative stress and initiate their cellular death programme. Because of this, hens lay fewer, lower-quality eggs with lower production (Mehaisen et al., 2016; Eid et al., 2022). For 12 weeks, the meals of 80-week laying hens were supplemented with 200 milligrams of nano- or lecithinized SM per kg of body weight, which improved the intestinal morphology and nutritional digestibility of the birds. The performance of the hens and parameters of egg quality may benefit from this (Faryadi et al., 2021). Meals contaminated with aflatoxin (0 and 2.2mg/kg) supplemented with 1000mg SM/kg were found to mitigate the negative effects of aflatoxin on quail performance (Khaleghipour et al., 2019).

Because *S. Marianum* is so versatile, it can be added to feed additives or added to drinking water, making it an effective growth booster. Numerous flavonolignans found in SM also improve immunological and physiological processes, reduce stress, and promote the development of poultry birds (Khaleghipour et al., 2019; Abdulwahid and Oleiwi, 2021; Shanmugam et al., 2022). As a result, scientists concentrated on using SM as a harmless feed additive to promote the growth of chicken species.

Hepatoprotectant Effect of Silymarin

Understanding how SM functions as a liver stimulant is essential to maximize its use and speed up the creation of a powerful feed additive that protects the liver. With its intricate chemistry, the liver is essential to the physiology of chickens (Trease and Evans, 1989). Toxins that are consumed and absorbed from the digestive tract initially reach the liver, where they can build up and cause illness. Immunological response, inflammation, necrosis, fibrosis, apoptosis, altered gene expression, regeneration, and ischemia can all result in liver damage, which can vary from acute hepatitis to hepatocellular cancer. While the exact mode of action of SM is yet unknown, it has been suggested that SM can address these issues through immunomodulatory, anti-oxidant, anti-proliferative, anti-fibrotic, and anti-viral effects. Because SM has a brief half-life and quickly combines in the liver, it is primarily excreted in bile (Shaker et al., 2010). Oral administration of high or frequent doses is recommended to decrease hepatic inflammation in vivo (Morishima et al., 2010). In patients with chronic active hepatitis, SM (silybin) dramatically reduced total bilirubin and serum liver, a biomarker of liver stress and damage, when given at a dose of 240mg per day (Salmi and Sarna, 1982; Buzzelli et al., 1993).

Antioxidant Effect of Silymarin

Because they reduce lipid peroxidation, antioxidant mediators improve the color, taste, smell, odor and nutritional value of meat and eggs while also lengthening their shelf lives (Fellenberg and Speisky, 2006). This makes antioxidant mediators essential for poultry nutrition. Polyphenolic flavonoids are potent antioxidants that have also been demonstrated to possess immune-modulating and, more specifically, anti-inflammatory qualities (Serafini et al., 2010). The most renowned exogenous antioxidants include flavonoids like SM and oligo-elements like glycine, selenium, and amino acids (Parra-Vizuet et al., 2009). It has been shown that SM increases the expression of genes linked to enzymes known as antioxidants (CAT, SOD, GSH, and MDA), which act as defense mechanisms against the dangers posed by free radicals (Upadhyay et al., 2010).

According to published studies, SM's anti-inflammatory properties work via lowering TNF-α, stopping erythrocyte lysis, and avoiding acute nephrotoxicity brought on by cisplatin (Saller et al., 2007; Karimi et al., 2011). Several theoretical explanations have been put out regarding SM's antioxidant qualities. These include: (a) inhibiting the production of free radicals by blocking particular enzymes that generate reactive oxygen species (ROS) or protecting the viability of mitochondria in stressful situations; (b) reducing inflammatory reactions by inhibiting the activity of nuclear factor κB (NF-κB)-dependent paths; and (c) preserving the ideal redox equilibrium within the cell by stimulating nuclear factor erythroid two-related factor, which in turn activates a variety of enzymes that combat liberated radicals (GST, CAT, SOD, GSH-Px, and GR) and anti-oxidants that are not enzymatic (vitamins C and E) (Surai, 2015; Tan et al., 2015; Zhao et al., 2015).

Effect of *Silybum marianum* on Blood Biochemical

Changes in physiologic and metabolic processes may impact indices of bird's health (Emam et al., 2023). Components of milk thistle can maintain birds' blood biochemical values within normal ranges (Talebi et al., 2015). According to research, SM increased total protein and albumin levels in quails (Moradi et al., 2017). The best dosage for increasing albumin, globulin, and total protein was 250mg/kg of *Silybum marianum* (Zaker-Esteghamati et al., 2021). In addition, blood total protein concentrations in the birds who received SM were higher (Behboodi et al., 2017).

Broiler chickens' serum γ-globulins content increased when they received dietary supplements of *S. marianum* extract (0.1, 0.5, 1.0, 1.5, and 2.0 milligrams per kg BW); this positive trend in serum γ-globulins content is probably caused by an improvement in poultry resistance and stimulation of immune functions (Bagno et al., 2021). *Silybum marianum* helps lower the blood sugar levels in chickens. Chicks treated with SM exhibited reduced levels of glucose (Behboodi et al., 2017).

Silymarin consumption (0.5g/kg diet) dramatically increased the number of red blood cells (RBCs) and hemoglobin (Hb) in comparison to the control group. In comparison to the control group, the groups that were given SM (0.5g/kg diet) showed a significant rise in lymphocytes, packed cell sizes, blood white cell counts (WBCs), phagocytic activity, and phagocytic index percentage (Abdalla et al., 2018).

When compared to the untreated group of birds, the WBC, RBC, and hemoglobin levels of the birds fed a dietary regimen treated with ten grams of SM/kg food were significantly higher (Sultan et al., 2018). Broiler chickens' white blood cell count, red blood cell count, and hemoglobin level all increased when they received dietary supplements of *S. marianum* extracts at doses of 0.1, 0.5, 1.0, 1.5, and 2.0mg/kg BW (Bagno et al., 2021). This suggests that leucopoiesis, hemoglobin production, and erythropoiesis are positively impacted by milk thistle extract.

Effects of Silymarin on Human

Traditionally, milk thistle has been utilized as a medication to treat liver diseases linked to alcohol intake as well as hepatic illnesses, including chronic hepatitis (Clichici et al., 2016). Silymarin exhibits beneficial impacts on human hepatocytes among individuals suffering from nonalcoholic steatohepatitis, fibrosis, and nonalcoholic fatty liver disease (Marin et al., 2017). Silybin regulates oxidative stress, blood insulin levels, and the buildup of fat in the liver (Federico et al., 2017).

Furthermore, it has demonstrated immunomodulation and early wound healing. Silymarin inhibits the onset of diabetic nephropathy by lowering serum glucose levels, making it an effective anti-diabetic agent (Tajmohammadi et al., 2018). By lowering oxidative stress, SM significantly contributes to higher conception rates and increased human fertility (Akhtar et al., 2023).

Effect of Silymarin on Oxidative Stress

Numerous studies have demonstrated the antioxidant qualities of SM through a range of routes, such as direct inhibition of the production of free radicals, transcription factor-mediated development of the antioxidant activity of enzymes, and activation of a wide range of vitamin genes that are ultimately in charge of the synthesis of protective molecules (Surai, 2015). It is thought that the SM constituent's detoxifying and antioxidant properties stem from the hydroxyl groups in its molecular structure. Thus, by trapping free radicals and regulating inflammatory cytokines, SM can mitigate the negative effects of oxidative stress and the inflammatory process.

By combating free radicals such as 1,1-diphenyl2-picryl-hydrazyl (DPPH) and 2,2'-azino-bis (3-ethylbenzene-thiazoline-6- sulfonic acid diammonium salt) (ABTS), SM was able to demonstrate it's *in-vitro* antioxidant activity (Köksal et al., 2009). Silymarin's antioxidant qualities can function in several ways. These include promoting the synthesis of protective compounds, activating antioxidant enzymes, decreasing the creation of oxygen radicals that are activated by enzymes, and preventing the formation of free radicals by intestinal ion chelation (Surai, 2015).

Non-alcoholic Fatty Liver Disease

Numerous randomized control trials (commonly referred to as RCTs) that highlight the curative effects of SM have demonstrated excellent outcomes when utilized in nonalcoholic fatty liver disorder (Zhong et al., 2017). Two of the nonalcoholic fatty liver disease clinical signs are inflammation and hepatic fibrosis. This is due to SM's metabolic impact on diabetes and hyperlipidemia and its anti-oxidant, anti-inflammatory, anti-fibrotic, and pro-regenerative qualities related to nonalcoholic fatty liver disease (Shakya, 2020). Silymarin is a promising treatment for nonalcoholic fatty liver disease prevention, although larger, standardized RCTs are still needed. According to a recent meta-analysis involving 500 people, using SM medicines improved liver function (Zhong et al., 2017).

In patients with acute hepatitis, SM (140mg, three times per day for 28 days) has a higher bioavailability and no adverse effects. The participants in this clinical study got another exam for a further four weeks after starting SM medication (Soleimani et al., 2019). In a different trial, subjects having nonalcoholic fatty liver disorder were given 194mg of phosphatidylcholine, 94mg of silybin, and 89.28mg of vitamin E every day for a year. The drug was not causing any significant negative effects at that point. However, side symptoms have surfaced, such as itching, diarrhea, and dysgeusia (de Avelar et al., 2017).

Effect of Silymarin on Tumor Cell

Silymarin medication with a 140mg SM level given twice daily to cancer patients before cisplatin drug ingestion for one week has no side effects and is bioavailable (Momeni et al., 2015). In a different research, individuals with cancer were given 420mg of SM daily for 20 days. No known adverse effects have been reported (Shahbazi et al., 2015). In a different trial, selenium and SM were administered in various combinations to a group of individuals with prostate cancer. When SM was taken for six months at a selenium level of 570mg/d, had no adverse effects and effectively slowed the progression of prostate cancer (Elyasi et al., 2017).

Silymarin exhibits anti-cancer characteristics that are thought to be related to the induction of apoptosis, growth cycle arrest, blockage of the mitochondrial pathway, and inhibition of oxidative stress. SM treatment for hepatocellular carcinoma has demonstrated anticancer benefits at different phases of hepatocarcinogenesis cells. Silymarin's ability to encourage hepatic regeneration makes it a prime candidate as a potential treatment for patients with chronic liver disease (Mastron et al., 2015).

Effect of Silymarin in Reproductive System

Human infertility is significantly influenced by oxidative stress. In addition, several other factors are thought to be triggers that directly affect spermatogenesis and consequently cause infertility, including heat, chemicals, heavy metals, alcohol abuse, obesity, chronic stress, inflammation of the reproductive system, urogenital trauma, and electromagnetic radiation (Walczak–Jedrzejowska et al., 2013). Numerous plant extracts support cell defense and free radical scavenging. Therefore, antioxidants such as SM can help increase conception rates.

Furthermore, multiple studies have demonstrated that SM possesses antioxidant properties and can protect sperm and eggs from the harm that chemotherapeutic medications and environmental contaminants can inflict. Research conducted on both male and female animals has demonstrated the beneficial effects of SM on fertility. Antioxidants have been shown in numerous studies to improve sperm and oocyte motility, which increases the likelihood of healthy births (Kamkar et al., 2018). Infertility in both males and females is caused by oxidative stress, which damages the cells in the reproductive system (Dutta et al., 2021).

Stimulation of Protein Synthesis

Silymarin can penetrate the nucleus and influence RNA polymerase I enzymes as well as rRNA transcription, which increases the production of ribosomes. This accelerates DNA and protein synthesis as a result (Sonnenbichler and Zetl, 1986), strengthening the cytoplasm's biosynthetic machinery and raising the rate at which structural and functional proteins are synthesized. In theory, at least, this stimulation would allow cells to compensate for the loss of enzymes and transporters that occur in many diseased situations. This action has significant therapeutic ramifications for the restoration of the liver's normal activities and the replacement of damaged hepatocytes.

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Chapter 09

Boosting Animal Health and Growth Traits with Herbal Feed Additives in Different Animals

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ABSTRACT

Herbal feed additives are increasingly significant in sustainable livestock production due to the restriction on the usage of antibiotics as boosters of growth, and increasing awareness of the detrimental residual effects of antibiotics. The incorporation of herbal feed additives is becoming increasingly important in animal husbandry because they are inexpensive, have no adverse consequences, and prevent the application of some antibiotics. Feed additives, also known as probiotics and manufactured from many kinds of plants across nearly a hundred plant families are utilized, primarily as flavorings or zootechnical additions. Medicinal plants showed the capacity of plants bioactive substances such as phenolics, phytochemicals, polyphenols, terpenoids, alkaloids, saponins, flavonoids, polysaccharides, tannins, essential oils, etc. These secondary metabolites of plants accelerate the growth of animals, improve nutrient digestion and absorption, enhance feed status and animal feed intake, modulate immune status, reduce oxidative stress through antioxidant properties, modulate gut microflora, and improve the egg and meat quality of animals. Dietary supplementation is a valuable approach in preventing and treatment of many diseases and for improving people's welfare since it makes use of food components that are abundant, low in toxicity, and inexpensive.

KEYWORDS Feed additives, Antibiotics, Phytobiotics, Metabolites, Supplementation	Received: 18-June-2024 Revised: 13-Julyu-2024 Accepted: 06-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Herbal feed additives are increasingly significant in sustainable livestock production due to the restriction on the usage of antibiotics as boosters of growth, cost-effectiveness, and increasing awareness of the detrimental residual effects of antibiotics. The application of several feed additives, including ascorbic acid, prebiotics, probiotics, and herbal extracts, benefits the animal husbandry industry. It is important to investigate the medicinal qualities of herbs to enhance immune-stimulant activity, digestibility, antibacterial, anti-inflammatory, and antioxidant characteristics in animal nutrition as well as safe human nutrition (Pandey et al., 2019). Plants manufacture a wide variety of low molecular weight secondary metabolites that help in defense against pathogens as well as minimize physiological and environmental stress. Flavonoids, glucosinolates, and isoprene derivatives constitute most of these active secondary metabolites (Dalle Zotte et al., 2016).

Feed Additives

Feed additives are nonnutritive items that are mixed into the basic feed to improve animal health or metabolism, boost feed utilization efficiency, promote growth or other productive functions, or preserve feeds. Additives don't fulfill any dietary requirements. Feed additives are different kinds of chemicals, substances, or organisms that help with growth, health, and the ingestion, absorption, and assimilation of nutrients. They influence physiological processes like stress resistance, reproduction, and immune system presentation. Immunostimulants, essential oils, probiotics, prebiotics, and acidifiers inclusions are examples of feed additives. Feed attractants improve feed consumption (Muneendra Kumar et al., 2014).

Herbal Feed Additives

The incorporation of herbal feed additives is pleasantly increasing in animal husbandry because they are inexpensive, have no adverse consequences, and prevent the application of some antibiotics. It has been reported that certain feed additives, including probiotics, prebiotics, organic acids, and herbal extracts, enhance the health and growth characteristics of animals. The qualities of medicinal herbs, which enhance digestibility, and have antibacterial, anti-inflammatory, immune-stimulant, and antioxidant activities, should be utilized in animal nutrition and safe human food products (Muneendra Kumar et al., 2014). When preparing herbal mixtures, it's important to consider the flavor preferences of the animals. Herbs typically have high concentrations of essential oils, and some ruminants—like sheep—may have trouble absorbing them. By promoting rumen microbes, the herbal feed additives given to ruminants aid in the stimulation of digestive processes (Foksowicz-Flaczyk et al., 2022).

Worldwide, there is a noticeable rise in the use of herbal products. Most of the animals were treated with herbal treatments, roughly 70% are cattle, goats, horses, sheep, and pigs; poultry comes in second (9.1%), rabbits (4.3%), and dogs (5.3%). This is caused by the availability of substantial information regarding the effectiveness of natural products in managing problems. The utilization of natural products is growing in significance. Individuals are beginning to choose natural over synthetic items because they consider—whether correctly or incorrectly—that natural products have fewer negative impacts and unfavorable outcomes (Kuralkar and Kuralkar, 2021). Herbal feed additives are important for nutrition and overall health. As feed additives, also known as phytogenics, botanicals, or phytobiotics, and other plant preparations from 100 plant species across nearly 100 herb families are utilized, primarily as flavorings or zootechnical additions. According to a review of European ethnoveterinary research 600 herbs species derived from more than a hundred different botanical families are recognized for use in livestock in the EU. These species are being researched for their potential uses in animal therapy (Franz et al., 2020).

Common Herbal Feed Additives

Aloe vera Tests have shown that aloe vera, the ancient natural plant used in human cosmetology, is effective in controlling ulcer-related stomach issues in horses as well as hoof health. Anthraquinones, polysaccharides (Acemannan), saccharides, salicylic acids, vitamins, enzymes, saponins, minerals, sugars, lignin, and amino acids are among the 75 potentially active ingredients in the extract or gel. These constituents may have a range of functions, such as cytoprotective, mucus-stimulating, antioxidant, and anti-inflammatory effects. A few experiments conducted on monogastric animals have demonstrated that aloe vera extract can enhance intestinal microbial ecology by reducing the overall E. Coli count and elevating the Lactobacillus count (Elghandour et al., 2018). Turmeric the well-known spice turmeric (*Curcuma longa L.*) is also frequently added to animal feed. Its strong antiviral, antibacterial, and antifungal properties as well as its ability to reduce intestinal inflammation are effectively employed in far-reaching manufacturing because they enhance animal health and increase productivity (Kiczorowska et al., 2017). Fenugreek (*Trigonella foenum*) has long been recognized and esteemed as a therapeutic herb. Many people utilize fenugreek as a medicinal herb. The pharmaceutical industry finds its seeds to be a valuable source of diosgenin, an important steroid. Protein, total carbs, fat, and minerals like calcium, phosphorus, zinc, iron, magnesium, and fatty acids (mostly linoleic, oleic, and palmitic) are all abundant in fenugreek seed. Additionally, it contains trimethylamine, neurons, and biotin, all of which have an appetite-stimulating effect on the neurological system (Abd El Latif, 2022). The Labiatae family of plants includes the herbal rosemary (*Rosmarinus officinalis*), whose leaves resemble needles. The Mediterranean region has seen widespread cultivation of it. Rosemary can have pink, purple, white, or blue flowers. It is widely acknowledged that rosemary is among the species with the highest antioxidant activity. According to a chemical analysis, rosemary contains a variety of antioxidants, including volatile oils and flavonoids like rosmarinic acid, carnosic acid, and carnosol. The most powerful antioxidants in rosemary are carnosol and carnosic acid, which are among the plant's main bioactive components along with rosmarinic acid, caffeic acid, betulinic acid, ursolic acid, and camphor. It's interesting to note that carnosic acid has three times the antioxidant activity of carnosol and seven times the activity of butylated hydroxyanisole and butylated (Abd El-Hack et al., 2020). Chamomile flowers reduce inflammation by preventing dangerous intestinal microorganisms from growing excessively. Nettle (*Urtica dioica*) has been attributed to health benefits. Nettle has been tested by numerous investigations and fifty distinct chemical components were identified. After an extensive examination, it was shown to include two resins, sugar, gum, albumen, and starch. There's also serotonin, choline, acetylcholine, and histamine are present. Thyme (*Thymus vulgaris*) contains two phenols: 15% carvacrol and 40% thymol. Traditionally, this plant has also been used for medical purposes (Omar et al., 2016). Two aromatic herbal plants from the Lamiaceae family—basil *(Ocimum basilicum* L.) and sage (*Salvia officinalis*)—are utilized for their antibacterial, antiviral, antioxidant, antimicrobial, and antiseptic qualities. Since they are blends of phenolic and antioxidant chemicals, adding them to animal diets is a fascinating method to supplement with biologically active molecules. Sage is more commonly employed as an essential oil extract than in its natural state (Vlaicu et al., 2021).

Bioactive Compounds

Numerous researchers have experimented with a wide variety of medical plants; some of them have shown the capacity of plant bioactive substances or phytobiotics, to both prevent disease and accelerate growth. The natural synergistic impact of all the substances within the plants is the primary reason why phytogenic feed additives are superior to synthetic growth boosters. (Ashour et al., 2020).

Phenolics

Phenolics are manufactured by plant secondary metabolism. A substance with a benzene ring and one (phenol) or more (polyphenol) hydroxyl groups, such as esters, methyl esters, etc., is referred to as a phenolic compound. Phenolics' strong antioxidant properties are one of their fundamental characteristics. Certain phenolics may also have extra advantageous qualities like antibacterial activity, immunity, gastrointestinal health, and anti-inflammatory effects. Over the past few decades, phenolic compounds have gained a lot of attention in human nutrition and medicine. Due to their strong antioxidant activity, phenolic chemicals may be very beneficial to health. Even so, phenolics continue to be acknowledged by animal scientists as useful feed additions (Mahfuz et al., 2021).

Phytochemicals

Phytochemicals are non-nutritive molecules obtained from plants and are among the many distinct types of dietary components that are vital for the animal body's diverse activities. Dietary supplementation is a valuable approach for the prevention and/or treatment of many diseases and for improving people's welfare since it makes use of food components that are abundant, low in toxicity, and inexpensive (Lee et al., 2017). Thousands of phytochemicals that may have significant physiological and biochemical effects are the focus of several investigations. Many phytochemicals have been linked to a range of health-promoting benefits, including flavonoids, polyphenols, stilbenes, carotenoids, and anthocyanins (Kamboh et al., 2015).

Polyphenols

Nearly all plants contain polyphenolic chemicals, yet they are not evenly distributed among tissues, cells, or subcellular structures. Polyphenol content is more in plants' outer layer than that of their inner layers. the insoluble polyphenolic compounds are linked to the cell wall, while the soluble ones are located in the cell vacuoles (Gessner et al., 2017). They are commonly found in fruits and vegetables. The possible uses of polyphenols could be strongly related to their unique ability to effectively regulate the gene pathways linked to antioxidants and their possible defense against lipid peroxidation (LPO) in organisms. Moreover, there is growing awareness that the potential health advantages of polyphenols may be significantly influenced by gut bacteria. Dietary polyphenols may be metabolized by the microbiota in the gastrointestinal tract (GIT) into additional bioactive substances with various physiological implications. As a result, they might also alter the gut bacterial communities' diversity, composition, and/or activity (Ahmadifar et al., 2021).

Terpenoids

Terpenoids are a group of significant secondary metabolites in plants with various structural variations. They are the supreme prevalent molecules in natural products. Terpenoids were also frequently employed as raw materials in the food, cosmetics, and pharmaceutical sectors (Yang et al., 2020).

Alkaloids

Alkaloids exhibit an extensive range of activity among plant secondary metabolites. In the natural world, they not only inhibit the growth of herbivores but also lessen the presence of bacteria and fungi. Therefore, they are compounds with great potential for use in toxicology, veterinary medicine, plant protection, or medicine. Additionally, the range of activity of alkaloids is relatively broad. Among them, compounds exhibit antibacterial, antiviral, anti-inflammatory, and anticancer effects (Adamski et al., 2020).

Saponins

Several plant components, including the roots, rhizomes, stems, bark, leaves, seeds, and fruits, have been found to contain saponin chemicals. Plants produce secondary metabolites called saponins, which are present in over 100 families of both domestic and wild plants. Generally, saponins have been proven to have anticancer, antibacterial, antiviral, antifungal, hypocholesterolemic, immunostimulatory, and antiparasitic properties (del Hierro et al., 2018).

Flavonoids

Flavonoids have antimicrobial and antioxidative qualities, they are thought to increase animal growth and develop the quality of animal products. There is a great deal of interest in researching how naturally occurring bioactive chemicals might alter the ruminal microbial ecology and bring about desired adjustments to fermentation conditions like pH, propionate concentration, and protein breakdown. Flavonoids and other phenolic compound members are now commonly utilized as feed additives in ruminant production (Kalantar, 2018).

Polysaccharides

A type of naturally occurring macromolecular polymer, polysaccharides are often made up of over ten monosaccharides joined together in either linear or branching chains by glycosidic bonds. It is widely found in mammals, algae, microorganisms, and plants. In addition to being a necessary macromolecule for all living processes, polysaccharides are also crucial for immune system molecular recognition, cell adhesion, and cell-cell communication. Particularly, it has been demonstrated that glycoproteins and β-glucans obtained from mushrooms, sulfated polysaccharides generated from seaweed, galactomannan, arabinogalactan, and pectic polysaccharides derived from higher plants all exhibit immunomodulatory and antioxidant properties (Yu et al., 2018).

Tannins

Plant tannins are polyphenols that are abundant in both terrestrial and marine plants. For a long time, plant tannins have been added to animal production. To enhance functionality or meat quality, they might have an impact on the gut flora or metabolism. Plant tannins are significant for protein, and adding plant tannins to ruminant meat in the right amounts offers nutritional benefits (Tong et al., 2022).

Protease Inhibitors

Protease inhibitors (PIs) are necessary for controlling proteolytic activity and are involved in several biological processes that are connected to cell physiology and metabolism [3]. Furthermore, certain PIs have been reported to serve as growth factors in animals and as receptors in cell-signaling pathways or during the processes involved in carcinogenesis. Storage protein mobilization, endogenous enzyme activity regulation, apoptosis and programmed cell death modulation, and stability of defensive proteins or chemicals against animals, insects, and pathogens have all been linked to them (Clemente et al., 2019).

Essential Oils

Essential oils are becoming progressively more popular in animal nutrition because of their advanced biological activity than the raw material from which they were produced. Essential oils are bioactive substances derived from plants that have a different chemical make-up and concentration. Essential oils are pungent, secondary plant products that mostly consist of hydrocarbons (terpenes, sesquiterpenes, etc.), oxygenated compounds (alcohol, aldehydes, ketones), and a minor amount of non-volatile residues (paraffin, wax). These compounds make up the majority of the plant's active ingredients. They are mostly obtained by steam distillation from the raw components (Yitbarek, 2015).

Effects of Herbal Feed Additives on Animal Health

Improver Nutrient Digestion and Absorption

Phytochemicals perform countless biological processes involving the functions of the intestinal zone, mainly secretions linked to digestion and absorption of nutrients. Improved salivary gland secretion (higher amylase), activation of mucus secretion in the stomach and intestine (which inhibits pathogen adhesion on the intestinal villi and encourages the extension of intestinal villi), and increased gastric secretion (activation of pepsin) are the main mechanisms responsible for these biological activities. enhanced production of bile acids in the liver and their excretion in bile for better digestion and absorption of lipids, enhanced performance of digestive enzymes in the liver, and enhanced production and function of pancreatic and intestinal enzymes, such as lipases, trypsin, chymotrypsin, carboxypeptidase, and lipase (which speed up digestion and reduced the time of feed passage through the digestive tract) (Valenzuela-Grijalva et al., 2017).

Supplementation with various herbal extracts enhanced food utilization by elevation of cellulolytic bacterial activity, in the rumen and inhibited protozoa and methanogenic bacterial growth, which reduced the amount of energy loss by methane emissions (Redoy et al., 2020).

Improver Feed Status and Animal Feed Intake

Additionally, herbs boost appetite, which encourages cattle to consume more feed and improves conversion. Experiments including the addition of 1.0% and 2.0% of several herbs (fenugreek, pansy, fennel, sage, thyme, chamomile, nettle, and mint) to the feed showed improved feed conversion, increased consumption of solid feed, and higher body weights. Bull calves and heifers had the best performance when offered feed containing 2% herb content. The animals showed negative for any illnesses. The control group's average daily gains were 707 g, the 1% herb addition group's was 760 g, and the 2% herb addition group's was 782 g (Paskudska et al., 2018).

Immune Status

The immunomodulatory properties are usually related to the manufacturing of cytokines and mediators. This is somewhat reasonable, as the immune system works by the interaction of T-, B-cells, natural killer cells (EC cells), macrophages, and mediators (interferons, interleukins, etc.). We are persuaded to rely on the upgrading of colostrum quality and, as a result, the immunological status of newborn calves due to the effects of herbs is directly related to the composition of the plants that share this feed additive (Kozyr et al., 2019).

Reducing Oxidative Stress by Herbal Antioxidant

Oxidative stress is the damaging state that arises from an imbalance between the body's inherent antioxidant defense systems and the endogenous production of free radicals. Because they lack a paired electron, free radicals are unstable and extremely reactive chemical entities that seek to neutralize themselves by absorbing electrons from biological macromolecules including proteins, lipids, and DNA. Free radicals react with biotic molecules to cause oxidative harm to these macromolecules, possibly leading to cellular damage. Antioxidants must be taken externally when free radical generation is abundant to minimize the risk of cellular damage. Antioxidants either directly scavenge free radicals or stabilize them by providing the necessary electron donation as part of a counter-protective response (Salami et al., 2016).

Modulation of Gut Microflora

Gut microbiota includes unicellular eukaryotes like yeast and fungus and bacteria, viruses, and archaea. In addition to the diversity of microbial composition, the host's state of health is significantly induced by changes in the relative presence of microbial species and the range of functional chemicals they emit, known as metabolites.

First, the microbiota in the stomach release enzymes that are essential for breaking down complex carbohydrates such as non-digestible oligosaccharides, plant cell wall polysaccharides, and resistant starches. Second, the production of cobalamin, or vitamin B12, is carried out by the gut microbiota and is limited to anaerobic gut microbes. Furthermore, the synthesis of vitamin K, folate, biotin, nicotinic acid, pyridoxine, pantothenic acid, riboflavin, and thiamine is supported by gut flora. Thirdly, the formation and operation of the host immune system depend on the gut bacteria (Čoklo et al., 2020).

Impact of Herbs on Meat Quality and Fatty Acid Profile

Numerous studies have demonstrated that altering the diet of ruminants can transform the conventional perception of meat and meat products into one of healthy living, removing lipids, reducing saturated fat acid, and adding herbs, spices, fibers, and extracts, among other things. When it comes to meat, the goal of including functional elements in meals is to enhance the meat's brand during these health-conscious times, in addition to giving it some appealing properties. However, meat has satiating qualities and is good for one's health in terms of obesity. It is possible to alter the amount of fatty acids and vitamin E in ruminant diets. For instance, supplementing lambs' diets with herbal plants may enhance the fatty acid composition of their muscle. Natural bioactive substances should make it possible to produce new meat foodstuffs that have a lot of health advantages. For the meat industry, these meat stuffs would open up an entire new market (Odhaib et al., 2021).

Impact of Herbs on Egg Quality

The pigment found in laying hens' egg yolks cannot be synthesized, although it can be transferred from diet to yolk. Egg yolk color is influenced by the diets of laying hens. Egg yolk color has been altered by the use of certain feed additives, including canthaxanthin, dried carrot powder, and dietary corticosterone (Gumus et al., 2018).

While improving egg quality indices was the main goal of most herb extract experiments on laying hens, botanical extracts (a combination of oils from thyme, black cumin, fennel, anise, and rosemary) also had a positive effect on egg weight and egg mass without influencing egg production rate, feed intake, or feed conversion ratio. Herb extract supplements and citrus peel oils) have been shown to increase feed conversion ratio and egg production (Świątkiewicz et al., 2018).

Conclusion

The goal of this research topic is to generate original research findings on the utilization of herbs, as substitute feed additives in livestock nutrition, given the existing limitations on the usage of antibiotics, especially as feed additives. Natural feed additives can boost digestibility preserve and stabilize the beneficial microbiota in the gut, and enhance animal performance and production while also having a good environmental impact.

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Chapter 10

Enhancing Livestock Health with Nanoparticles as Feed Additives

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ABSTRACT

The field of nanotechnology has the potential to transform worldwide livestock and agriculture. The production of nanoparticles with reducing substances alters the physical and chemical properties of the molecules being studied. Nowadays, nanoparticles are extensively employed in many fields, including targeted medicine delivery, nutrition therapy, vaccine development, etc. Nanotechnology is utilized in animal nutrition to prepare nano-minerals, particularly trace minerals with low bioavailability. Furthermore, intestinal mineral inhibitors can be reduced by nutrients in nanoparticle form in a safer way. It helps to improve the trace dietary efficacy of livestock. Their use will improve absorption at low additive concentrations and consistent quality when combined with other components. Nanoparticles' smaller size allows them to readily cross the GIT mucosa, penetrating the enterocytes' inner layer and functioning more successfully as a substrate's operational site before being absorbed via the GIT membrane. These NPs can enhance growth performance, lower the microbial load, and minimize a range of health risks, such as treatment resistance in endemic populations and drug residues in poultry meat. According to studies, the nanoparticles enhanced performance, immunity, and digestive efficiency. This paper addresses several aspects of nanotechnology, their use in animal feed, and their future potential.

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INTRODUCTION

To meet the demands of this rapidly expanding population, there needs to be a substantial boost in agricultural output and effectiveness globally. According to Food and Agriculture Organization (FAO), 200 million tons of beef must be generated annually by 2050 to sustain the growing human population (Ghasemzadeh, 2012). Modern technologies, such as nanotechnology in the food and agriculture sectors, will be implemented to enhance productivity, effectiveness, efficiency, and health. Hence, the poultry business is being explored with the intention that nanotechnology will enhance the efficiency required to transform agriculture.

Definition of Nanoparticles

The Greek word nano 'dwarf', is employed in the name nanoparticles. Nanoscience primarily focuses on the size-dependent aspects of materials by analyzing matter at the nanoscale. The development, usages, and findings of nanomaterials, or particles smaller than 100 nm is known as nanotechnology (Mulvaney, 2015; Hasan, 2015).

The areas of biology (molecular and cellular), biotechnology, mineral diet, physiological requirements, development, and pharmacology in both animal and human models—are using this as a new tool. Nanotechnology has a wide range of utilization, including both the scientific and engineering fields of food, animal, and crop production. Agriculture is the primary economic driver in many nations, and nanotechnology will be crucial to livestock now and in the future (Sri Sindhura et al., 2014).

The field of nanotechnology can be administered to the diet as an additive to improve feed utility, boost animal development, and improve livestock economics. This aids in enhancing the livestock's trace nutrient efficiencies. The potential benefit of utilizing nanoparticles as a feed alternate is anticipated to be enhanced absorption at minimal additive dosages and consistent quality when integrated with other ingredients. Due to their reduced dimensions, nanoparticles can readily pass through the GIT mucosa, entering the inner layer of intestinal cells and acting as a substrate's functional site more effectively before being absorbed through the GIT barrier (Mishra et al., 2014).

Characteristics of Nanoparticles

Nanoparticles exist in different shapes, sizes, and structures (Joudeh and Linke, 2022).

Surface Functionalization

It is possible to functionalize nanoparticles by adding various compounds to their surface, such as polymers, immunoglobulins, or specific cells. The Nano platform's design considers these functionalization's' reliability and effectiveness into attention (Yusuf et al., 2023).

1. **Core Stability**

The core of iron oxide nanoparticles is durable and does not compact or break down in biological structures.

2. **Biocompatibility**

The nanoparticles must not induce any harmful effects on the structure of the body.

3. **Release Kinetics**

For the application of nanoparticles in a therapeutic way the release kinetics of the payload must be considered from the Nano platform. The release should be controlled in a manner that is effective and safe.

4. **Targeting and Accumulation**

The nanoparticles must selectively target the desired location and accumulate in a way to maximize the therapeutic efficiency of drugs.

5. **Particle Size**

The size of the nanoparticle and its distribution are the significant characteristics through which the *in-vivo* distribution, fate of nanoparticles, and targeting ability are determined.

6. Surface Morphology

Nanoparticle exists in a variety of structures, like flat, tubular, spherical, cylindrical, and irregular with surfaces crystalline or amorphous with uniform or irregular surfaces (Yusuf et al., 2023; Ealia and Saravanakumar, 2017; Singh and Lillard, 2009).

Types of Nanoparticles used in Livestock Feed

1. **Nano-Selenium (Se-NPs)**

The selenium nanoparticles have enhanced developmental efficacy, cell damage activity, high uptake rate, and the production of egg capability. The nutritional status of broilers is profoundly impacted by the addition of Se-NPs to chicken feed (Cai et al., 2012), When such nutritional additives are administered to livestock in nanoforms, anxiety levels are lowered, improving livestock breeding and the flavor of meat.

2. **Calcium Phosphate (Ca-P) NPs**

Nutrients such as calcium (Ca) and phosphorus (P) are necessary to animals for their growth and performance. Inadequate Ca and P intake in livestock might result in ruptured bones and hemorrhage of meat when the carcass is processed. According to Vijayakumar and Balakrishnan (2014), Ca-P NP intake can enhance an animal's reproductive efficiency while lowering the amount of mineral dietary supplementation.

3. **Polystyrene NPs**

In chickens, polystyrene nanoparticles may have an impact on iron transport and absorption. The breakdown of cellular lining by NPs may be the cause for enhanced iron transfer in cells of the GIT. By altering the lining of the intestine to create additional surface area for consumption, extended contact with polystyrene NPs may improve iron absorption. NPs can enhance iron absorption in this manner, which could lead to a raise in weight retention (Gangadoo et al., 2016).

4. **Nano-silver**

A potent antibacterial agent is silver. *Escherichia, salmonella, Clostridium*, and *Streptococcus* are examples of both gram-positive and gram-negative microbes that are significantly impacted by the presence of silver, even at low concentrations.

5. **Nano-zinc**

Employing ZnO- in the diet enhance the carcass traits and flesh nutritional value of livestock reared in hot summer conditions, as demonstrated by the correlations between different dietary fatty acid compositions (FAs). It has been demonstrated that administering ZnO-NPs enhanced both the development and antioxidative capacities of livestock. The ZnO-NPs added to dry meals raised the proportion of the weight of the animal's immunological and gastrointestinal systems and enhanced carcass yield (Gangadoo et al., 2016). Because zinc has antibacterial and antimicrobial qualities, animal feed contains nano-zinc, which is employed to make use of these minerals (Cho et al., 2015).

6. **Nano-copper**

The cardiovascular system and other organs all require copper for proper development and proliferation. Additionally, it aids in the body's immune activation and the detoxification of free radicals, which seriously harm cells (Scott et al., 2018).

7. **Nano-Iron**

Since iron is thought to be a necessary component for microbial growth, it has been observed to promote the development and proliferation of a wide range of bacteria. According to Qiu et al. (2018), it exhibits certain harmful effects on commensal microorganisms such as *Bacillus subtilis, E. coli*, and *Staphylococcus aureus*.

8. **Nano-Titanium**

The interaction between titanium oxide (TiO2) and *E. coli* is the subject of research's focus. They have little effect on the gut microbiome. When there is no light, some intestine bacterial species are susceptible to the cytotoxicity of nano-TiO2. (*in-vitro*) (Waller et al., 2017).

9. **Nano-Gold**

Au-NPs are an appropriate choice for utilization in livestock due to their huge surface area-to-volume ratio, which allows dozens of molecules to be covered on their exterior. By triggering cellular processes such as the expression of growing cells' nuclear antigens to boost development efficiency, it improves the organization of the pectoral muscle.

10. **Diamond (D) NPs**

The D-NPs are non-hazardous readily absorbed by cells and have a tremendous capacity for adsorption due to their allotropic nature and wide surface area. The administration of D-NPs increased the expression of genes linked to both the growth and differentiation of muscles (Osama et al., 2020).

Mechanisms of Action of Nanoparticles in Animal Nutrition

The mechanisms through which nanoparticles act in animal nutrition illustrated in Fig. 1 as follows;

1. It helps in increasing the available surface area to link with biological systems.
2. It increases the duration of residence of a compound in GIT.
3. It lowers the impact of the intestinal clearance mechanism.
4. It pierces the tissue extremely deep through fine capillaries.
5. It crosses the lining of epithelial fenestration (liver).
6. Enable the cell for efficient uptake.
7. Proper delivery of active drugs to the targeted sites inside the body (Chen et al., 2006; Singh, 2016).

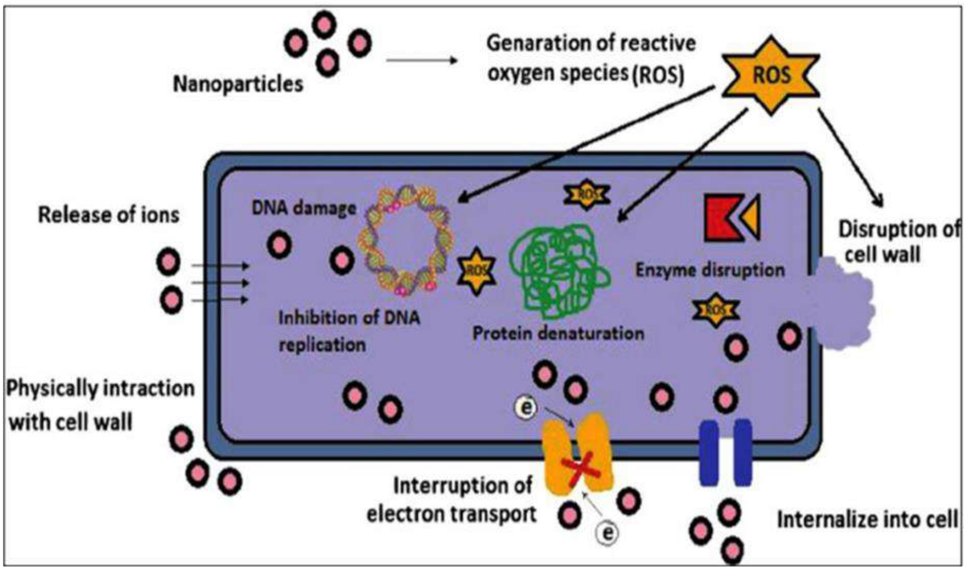

Fig. 1: Mechanism of action of nanoparticles (Meena et al., 2018)

The Rationale for using Nanoparticles as Feed Additives

Food additives, which are used to enhance the integrity of foods during preparation and preservation, optimize product features, or boost the efficacy and absorption rate of nutrients, make up the majority of nanomaterials used in the processing of food. When compared to traditional usage, the use of food enhancers and dietary supplements encapsulated in nanoparticles offers significant advantages (Fig. 2). The method of microencapsulation can minimize the amount of fat, salt, sugar, and preservatives used in food products while also improving taste and the capacity of fat-soluble ingredients to disperse. Lowering the salt content is crucial and a major problem for the meat business. (Weiss et al., 2010; Bošković et al., 2013).

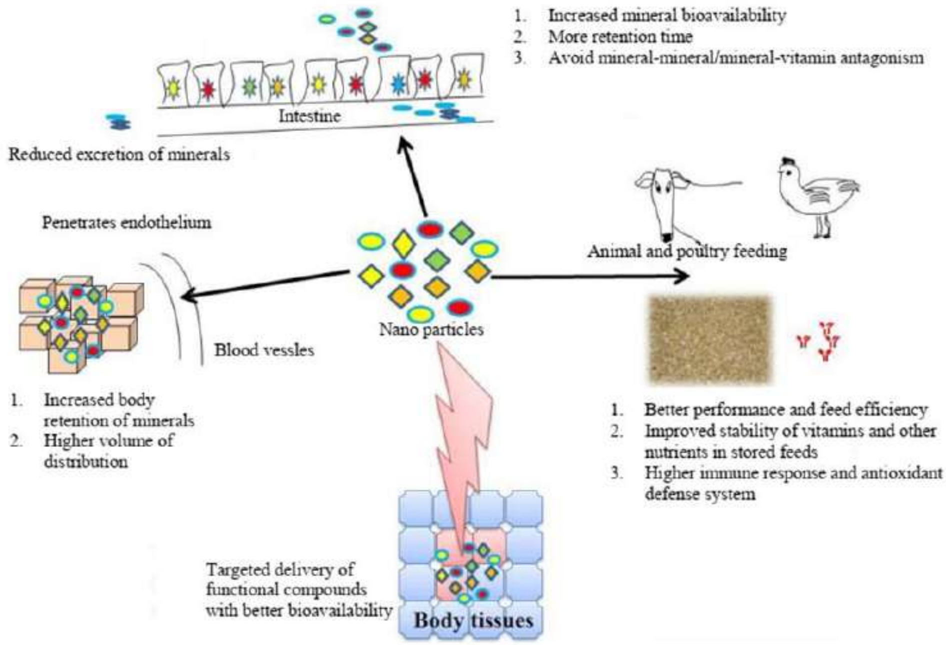

Fig 2: Benefits of nano-particles in animal feeding (Marappan et al., 2017)

The advantages of employing nanoparticles are as follows;

A. Enhanced Nutrient Absorption and Carrier

The nanoparticles interact more like gases and penetrate tissues more readily than solid particles do. Additionally, the nanoparticle interface contains polypeptide particles—enzymes—for bonding. The capacity of nanoparticles to promote protein durability is significant in biological activities (Singh, 2016).

B. Improved Digestive Health

a) Digestion and Absorption

Several pathways allow nanoparticles to enter the GIT. According to Khan et al. (2021), inhaled nanoparticles can also be consumed and make their way through the pulmonary system to the GIT system. Additionally, oral or smart delivery into the GIT (oral channel) depends on contact with GIT cells, mucosal permeability, and diffusion for particle assimilation in the GIT.

b) Ingestion or Swallow Pathway

Nanoparticles are absorbed in the GIT system, and nothing is known about how they are assimilated beyond that point. Active transport mechanisms, passive absorption across epithelial cells, and interstitial uptake are the ways that ingested nanoparticles are taken up and ultimately end up in the GI tract. The polystyrene nanoparticles of 100 nm or smaller show that after being taken in from the GI tract, nanoparticles may spread to the liver and spleen via the lymphatic system. It is anticipated that natural source nanoparticles, like casein micelles, will perform similarly to their macro- or micro-sized counterparts in terms of administration and accessibility (Bunglavan et al., 2014; Oberdörster et al., 2005).

Similar to absorption, physical and chemical properties including size, charge, and mobility will dictate how nanoparticles disperse, dissolve, and excrete in the body. It is anticipated that these nanoparticles will be dispersed swiftly and efficiently disassembled into their component molecules, and then eliminated from the body (Bunglavan et al., 2014).

c) Inhalation Pathway

The particle size-dependent inhaled tiny particles settle in the nasal cavity and the upper and lower respiratory tract. They discovered that solid ultrafine particles in the air could target the brain and CNS, with the nasal region serving as the most likely site of deposit. Many medications, such as antibiotics, antineoplastic, and many other medications that operate on the CNS, particularly neuropeptides, find it difficult to cross the blood-brain barrier. Scientists have successfully transported drugs through this barrier of drug delivery to the brain by using nanoparticles (Oberdörster et al., 2005).

d) Oral or Smart Pathway

Proteins and peptides are administered orally using nanoparticles. Because these chemicals' accessibility is limited by the GIT's epithelial barriers and their susceptibility to the degradation of digestive enzymes, the discovery of appropriate carriers continues to be a challenge. Naturally occurring compounds have been embedded in polymeric nanoparticles to prevent enzymatic and hydrolytic degradation (Bunglavan et al., 2014). The nanoparticles are occasionally employed as a carrier for the delivery of proteins and peptides. To get around this issue, the medication must be administered via an impermeable carrier method, such as nanoparticles, which improves drug delivery to the GIT epithelium (Singh, 2016).

e) Nanoparticles Enhancing Nutrient Absorption

Mobasser and Firoozi (2016) claim that tiny particles are more refined, have a greater surface area, and are more successful in absorbing nutrients. It was shown that 50 nm nano-chelates efficiently give nutrients without changing the color or flavor of the feed, making the insertion of nano-capsules in the feed an essential part of the approach (Tiwari, 2022).

f) Improvements in Feed Conversion Efficiency

The FCR, which shows how well livestock can convert feed into body mass, is the weight acquired to be consumed. The most successful individuals in the flock are those organisms with the lowest FCR, meaning they need the least feed per kilogram of weight gain. (Benyi et al., 2015).

To optimize effectiveness using the most economical feed materials, one of the primary contributors is the diet, which includes things like dietary fat and protein sources and ease of digestion, which may be adjusted with specialty additives to the feed. The needs for poultry feed vary depending on what the hens are being raised for; normally, the nutrition consists of a variety of sources of protein and energy with a small number of specialized additives to supply essential nutrients and important amino acids (Walk et al., 2012).

The focus of research has shifted to the gut microbial ecosystem due to recent developments in sequencing technologies. Hundreds of varieties of bacteria can be found in the GIT of livestock, and these species are important for the animal's potential to consume food energy and use it for growth, as well as for aiding the host's defense against pathogen invasion (Stanley et al., 2014).

C. Enhance the Livestock Production

Livestock productivity can also be grown through nanoparticles. To increase their bioavailability, antioxidant nature, taste, coenzymes, essential oils, vitamins, minerals, and coenzymes are delivered using nano capsules, also known as minute micelles (Fig. 3) (Elamin, 2006; Heller, 2006).

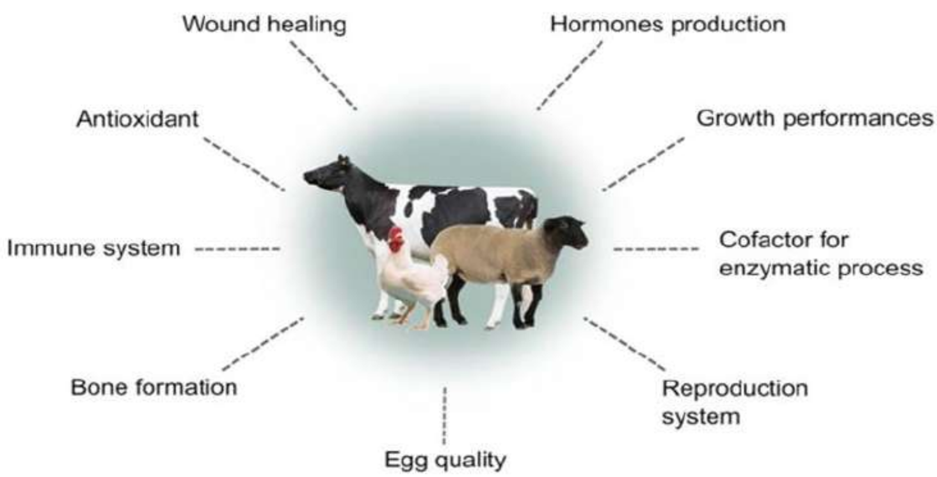

Fig. 3: Role of NPs supplementation in poultry and livestock (Mohd Yusof et al., 2019)

D. Enhancing Immune Function

a) Role of Nanoparticles in Modulating Immune Responses

The primary function of the body's immune system is to recognize and eliminate foreign substances. A compromised immune system affects a person's general health. To reduce infectious agents and help treat autoimmune disorders, there are many ways to improve immune function. As the body's first line of defense against viruses, innate immunity relies on pattern-recognizing receptors (PRPs) to recognize massive pathogen-associated molecular patterns (PAMPs). It is composed of several elements that cooperate to protect against intruders, such as cells, serum protein, and physical barriers (Khan et al., 2023). The autoimmune system is more prone to cell-mediated absorption because of its intrinsic mechanisms and defense against external substances (Hilligan and Ronchese, 2020).

b) Applications in Reducing Antibiotic use and Promoting Animal Welfare

Alternatively, humoral defenses or immunity generated by cells can be used to categorize adaptive immune responses (Roche and Furuta 2015). It depends on the antibody-presenting pathway because it supplies the data required to control immunological effectors downstream. APCs scavenge and remove external pollutants, among them being dendritic cells (Smith et al., 2004). Over-activation of the immune system is undesirable and will have negative effects. Three immune-related effects should be considered while creating a nanomaterial for use in vivo (Boraschi et al., 2012). The various features of nanoparticles (NPs), notably size, content, surface charge, and shape, impact their ability to adhere to immune cells. The majority of NPs cause an inherent immune reaction. Enhanced innate immune cells, including natural killer cells, mast cells, neutrophils, dendritic cells, monocytes, and macrophages, and pattern recognition receptors such as toll-like receptors (TLRs). Likewise, the interaction of nanomaterials with adaptive immunity triggers Th1/Th2 processes and increases the formation of cytokines. The impact of nanoparticles on B cells tends to increase resistance after vaccination and B cells are usually directed by specially functionalized nanoparticles that target B cells with lymphoma to eliminate lymphoma and produce a chemotherapeutic effect from using the NP (Fig. 4) (Aljabali et al., 2023).

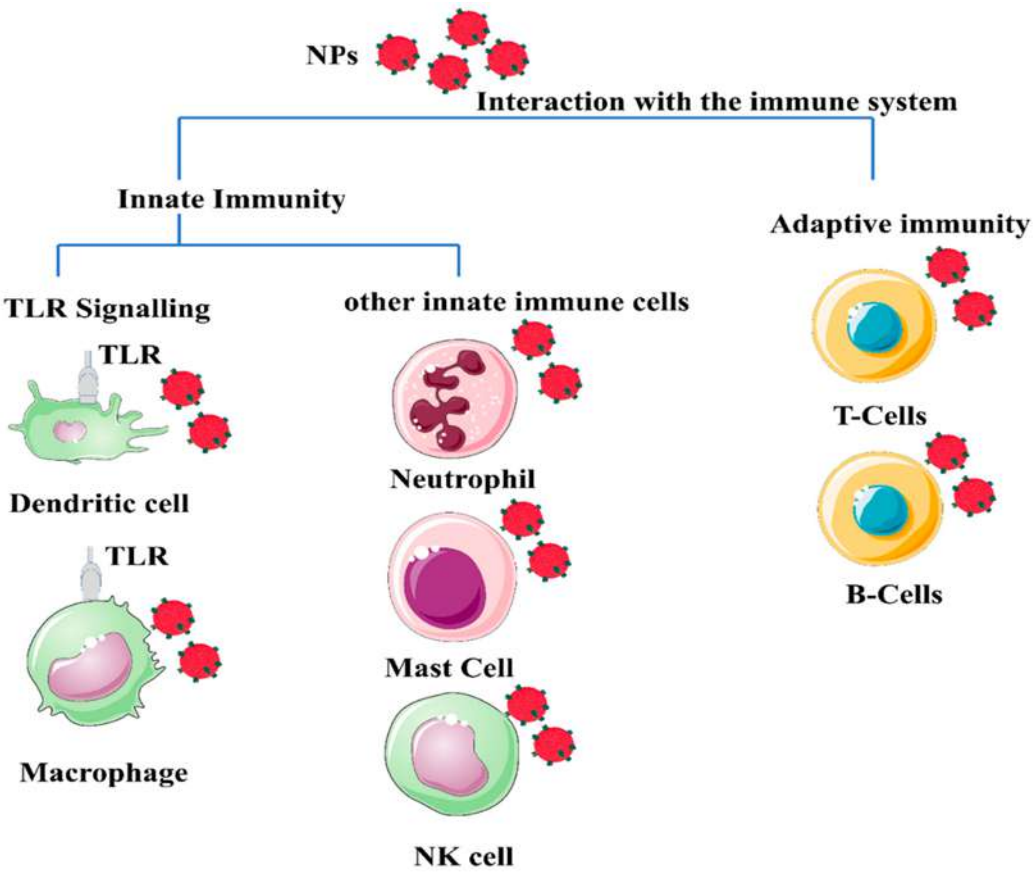

Fig. 4: Different types of nanomaterials (polymeric or metal-based) represented in red spheres, indicating their possible interaction with different immune system cells (Aljabali et al., 2023).

E. Improving Health and Meat Quality

There are three separate phases in the growing process of muscle during the developmental stage: myoblast creation, myoblast fusion to produce myotubes, and myotubes conversion to form myofibers. Numerous genes govern and control this growth pattern, which is dependent on the nutrients accumulated in the embryo. As a result, sufficient nutrition is essential for the development of the fetus (Sobolewska et al., 2011).

a) Role of Nanoparticles in Muscle Development

The remarkably high surface-to-volume proportion, muscular activity, and chemical resistance of nanoparticles set them apart from their larger counterparts in terms of both physical and chemical properties. Because of their small size, nanoparticles can pass through cell membranes and enter tissues. The studies conducted *in-vivo* showed that modest concentrations of silver nanoparticles were safe and had no effect on immune system responses. It has recently been demonstrated that nanoparticles control the production of vascular endothelial growth factor (VEGF) and fibroblast growth factor 2 (FGF2) (Hotowy et al., 2012; Peng et al., 2012).

b) Proliferation of Satellite Cells

The results show that pectoral muscle cells' differentiation and proliferation are positively impacted by nanoparticles, which speed up the cells' growth and development processes. Keeping in view the potential applications of NPs to improve poultry health (Peng et al., 2012).

F. Industrial Application

It is also used in the food industry i.e., liposomal carriers are used for the encapsulation and transportation of ingredients like enzymes, proteins, antimicrobial compounds, and flavors (Wen et al., 2014).

a) Enhance milk production

Nanoparticles are too small to pass through the wall of the stomach to the body cells. Singh, (2016) noted an increase in the production of milk, immunity, and the reduction in mastitis with its use.

b) Precision in Nutrition

The supplementation of chromium nanocomposite in pigs shows a reduction in urea nitrogen, cholesterol, serum glucose level, and non-esterified fatty acid. When the piglets are supplemented with Nano copper it shows improvement in their growth rates.

c) Environmental Benefits

Those compounds/materials that are insoluble in water are differently soluble in water and can be made water soluble by extending their use in feed and potentially changing their bioavailability (Singh, 2016).

Applications of Nanoparticles in Livestock Health

1. Application of Nanotechnology in Animal Nutrition

Certain types of nanoparticles have been demonstrated to encourage the growth of beneficial bacteria, hence increasing both performance and growth, while others have been utilized in poultry feed to reduce the number of pathogenic microbes in the chicken microbiota (Mahmoud, 2012). Microencapsulation reduces the need for fat, salt, sugar, and preservatives while improving flavor and increasing the absorption of lipid-soluble chemicals in feed. The unique transport and uptake capabilities of nanoparticles achieve higher absorption efficiencies by the specific transport and uptake capabilities of nanoparticles (Zha et al., 2008). The water and livestock feed can directly absorb nanoparticles, or they can be incorporated into feed wrapping (Haben Fesseha, 2020).

2. Nano feed Additives and their Application in Animal Nutrition

Khalid and Arif (2022) state that natural feed ingredients, protein tiny particles, and capsules all are included in nano-additives. Additionally, it is believed that using nano-capsules will increase the effectiveness of antioxidants, flavors, and crucial oils. The liposomal microvesicles are thought to transport nutrients, enzymes, flavors, and antimicrobial agents in food, according to Pateiro et al. (2021). Feed additives are essential raw materials in the modern feed industry, improving product quality, cost-effectiveness, animal health, and nutritional value (Pandey et al., 2019).

3. Applications of Nanotechnology in the Feed Industry

The application of nanotechnology for the feed industry includes:

a) Small adjustments to organic components to improve their flavor, accessibility, and sensory qualities like color and texture.

b) Improving the nutritional value of food nutritionally by maintaining substances like dietary supplements in feed matrices, packaging, and new product development.

c) Enhancing uptake and focusing on the administration of bioactive substances to increase the bioavailability of important nutrients.

d) Creating biosensors to identify and diagnose pathogens, as well as antimicrobial substances to eradicate harmful bacteria found in feed.

e) Enhanced understanding of food substances at the nanoscale enables nano-delivery of bioactive/nutrient components in livestock feed or *in-vivo* in the body.

4. Applications of Nanotechnology in Veterinary Diagnostics and Therapeutics

Expectedly, shortly, nanotechnology will be a major factor in veterinary care worldwide. The One Health Initiative's greatest accomplishment is the use of nanotechnology tools to diagnose illnesses in animals and humans. *In-vitro* and *in-vivo* respiratory virus (RSV) detection has been made quick and precise with the use of customized nanoparticles coupled to monoclonal antibodies. It can bridge the gap between the present laborious virus detection assays and the requirement for more rapid and sensitive detection of viral agents by offering regulate fast, and effective recognition of viruses (Tripp et al., 2007).

5. The Role of Nanotechnology in Animal Reproductive Biotechnologies

The objectives of nanotechnology-based studies on reproduction in livestock are as follows: create nano biosensors for recognizing indicators of physiology in nature or influenced (by infectious agents and disorders) life-sustaining status; create chemical methods for the synthesis of metal nanoparticles for utilization in procreation control; create nanodevices for the safe cryogenic preservation of gametes and embryos; and create sustained release systems for various molecules, including hormones, vitamins, antibiotics, antioxidants, and nucleic acids, among others. (Wang et al., 2014; Weibel et al., 2014).

6. Case studies demonstrating the effectiveness of nanoparticles

The identification and treatment of individuals as well as livestock could be significantly impacted by nanotechnology. The distinct size-dependent characteristics of nanoparticles have a wide range of clinical uses, including MRI contrast agents and diagnostic biosensors with imaging nanoprobes. It has great potential for veterinary care, animal health, and other aspects of livestock farming. It also plays a significant role in the treatment of illnesses by enabling the development of intelligent drug delivery systems (Gupta et al., 2013)

A recent medical use of nanotechnology is the delivery of medications, heat, light, or other chemicals to target cell types (e.g., cancer cells) via nanoparticles. The creation of such a method lessens harm to the body's healthy cells and enables early illness identification. On the other hand, an enzyme that stops viral molecules from replicating in the bloodstream of the individual is delivered via nanoparticles, not the virus itself (Bollo, 2007).

Safety and Regulatory Considerations

a. Assessing the Safety of Nanoparticle Feed Additives

The feed additives, therapeutic administration methods, novel instruments for molecular and cellular biology, the safety of livestock and food supply chains, new materials for bacterial identification, and environmental protection are a few examples of possible uses of nanotechnology in the science and engineering of food and crops (Thulasi et al., 2013).

Future Directions and Challenges

a. Emerging Trends and Prospects in Nanoparticle Research for Livestock Health

Although NPs have been successfully employed in broiler research to enhance the growth and performance of chickens, it is important to acknowledge that silver can accumulate and become cytotoxic in the body's tissues, which can have a significant effect on the body's defenses. Due to the foreign environment of materials like silver, the immune system naturally attacks them, causing an inflammatory response. As a result, nutrients and minerals are given more attention; selenium is one such example; it is already necessary for healthy cell function and does not put the body under stress in this way. The body needs selenium for the initial line of defense, and studies have shown that selenium nanoparticles significantly boost a broiler's immune and general health (Gangadoo et al., 2016).

b. Addressing Challenges in Nanoparticle Formulation and Delivery

The primary responsibility of Nps is to reduce the FCR while increasing the overall well-being of chickens through more efficient growth. A low FCR lowers the amount of feed needed to reach market weight and lowers waste disposal costs. Drug-encased NPs, such as the Newcastle virus vaccine encapsulated in a polymer, are among the other NPs being researched to enhance broiler efficiency. Because polymers are disposable and extend the duration of the medication's retention in the body, they are currently frequently used for drug delivery in the body (Hasan, 2015).

Therefore, NPs might be a cutting-edge way to give chickens the nutrients they need at deficient concentrations. To fully comprehend the significance of NPs in the synthesis of metabolites and beneficial gut microorganisms, more research on their impact on the intestinal microbiota of chickens is necessary. Recent developments in sequencing technology have made molecular microbiology options available that enable simultaneous screening of the culturable and non-culturable microbiota (Gangadoo et al., 2016).

Challenges Related to Efficacy, Safety, and Sustainability

The following are some of the issues facing livestock science research in the future: improving feed efficiency; creating dynamic feed; managing macro- and micro-nutrients absorption; addressing disorders epidemics; delivering targeted drugs; altering the composition of eggs to make them void of cholesterol or full of animal protein; cutting down on energy and protein waste for ineffective physiological uses to improve feed efficiency; and lowering the cost of chicken meat. Furthermore, more investigation and testing are required before the nanoparticle is prepared for usage in the far future (Thulasi et al., 2013).

Conclusion

This chapter concludes with the findings that nanotechnology can be the most widely used utility in the near future in the field of nutrition, diagnosis, and treatment of animal and human ailments together with their better preventive options. There is a dire need for extensive research work on the safety and precise use of nanotechnology for the well-being of humans, animal and environment.

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Chapter 11

The Crucial Role of Feed Additives and Nutrition in Animal Health

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ABSTRACT

Expression of genetic potential for production requires an adequate supply of nutrients. Animals suffering from malnutrition may develop severe health issues. Additives to feed enhance the health and performance of animals. Using feed additives is advised to improve the meal's quality and efficacy as a means of boosting output. These are classified as sensory, nutritional, zootechnical, coccidiostat, histomonostat, and technological according to rules set out by the European Commission. Various categories of feed additives include of probiotics, essential oils, polyphenols, antimicrobials prebiotics, amino acids, exogenous enzymes, vitamins, trace elements, antioxidants, and acidifiers.

The purpose of writing this chapter is to give a thorough summary of the role that appropriate nutrition and feed additives play in preserving animal health. This chapter emphasizes the relationship between nutrition, feed quality, and animal performance such as growth rates, reproduction, immune system function, and disease resistance. This chapter will be helpful in future research directions and advances in nutrition and feed additives with the goal of improving animal production, welfare, and health.

KEYWORDS		
nutritional additives; Digestibility; Antioxidants, Natural feed additives, Polyphenols, Probiotics, Prebiotics	Received: 11-June-2024 Revised: 15-July-2024 Accepted: 03-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

The European Commission defines feed additives as substances added in animal diets to enhance the quality of feed and animal growth, by increasing health (Pandey et al., 2019). Poor nutrition negatively effect health and well-being, resulting in deficiencies in key vitamins and minerals. Malnourished animals may be more susceptible to sickness, injuries, and less capable of healing (Wu, 2022).

The consumption of supplemented diets has been advised to improve the uptake of nutrients from alternative feed raw materials to improve production (Okey et al., 2023).

Feed additives have been used since the beginning of time when farmers would season animal feed with salt to make it more palatable. These gained popularity in the early 1900s as researchers looked into the dietary requirements of animals. Vitamins were discovered in the 1920s and included into the animal feed. The findings cleared the path towards innovative feed additives, especially minerals, amino acids, vitamins, and proteins. They are utilized for enhancing nutrition efficiency, growth, and animal health (Wani et al., 2023). Antibiotic-supplemented diets have undesirable consequences such as immunopathological reactions, transfer of resistant bacteria to populations, allergies, hepatotoxicity, nephropathy, reproductive problems etc. Hence, it is imperative to regulate the usage of antibiotics in animals consumed by human. Fortunately, there are now numerous substitutes, such as prebiotics, herbal additives, probiotics, enzymes, active plant metabolites and organic acids. These alternatives can enhance production performance and boost immunity in livestock and poultry without consequences (Dutta et al., 2019).

Types of Feed Additives

Classification of feed additives describes their function in the animal that provides guidelines to farmers for their applications (Okey, 2023). Based on European Commission regulations feed additives are categorized as nutritional additives, coccidiostats, histomonostats, sensory additives, zootechnical additives, and technological additives (Fig. 1).

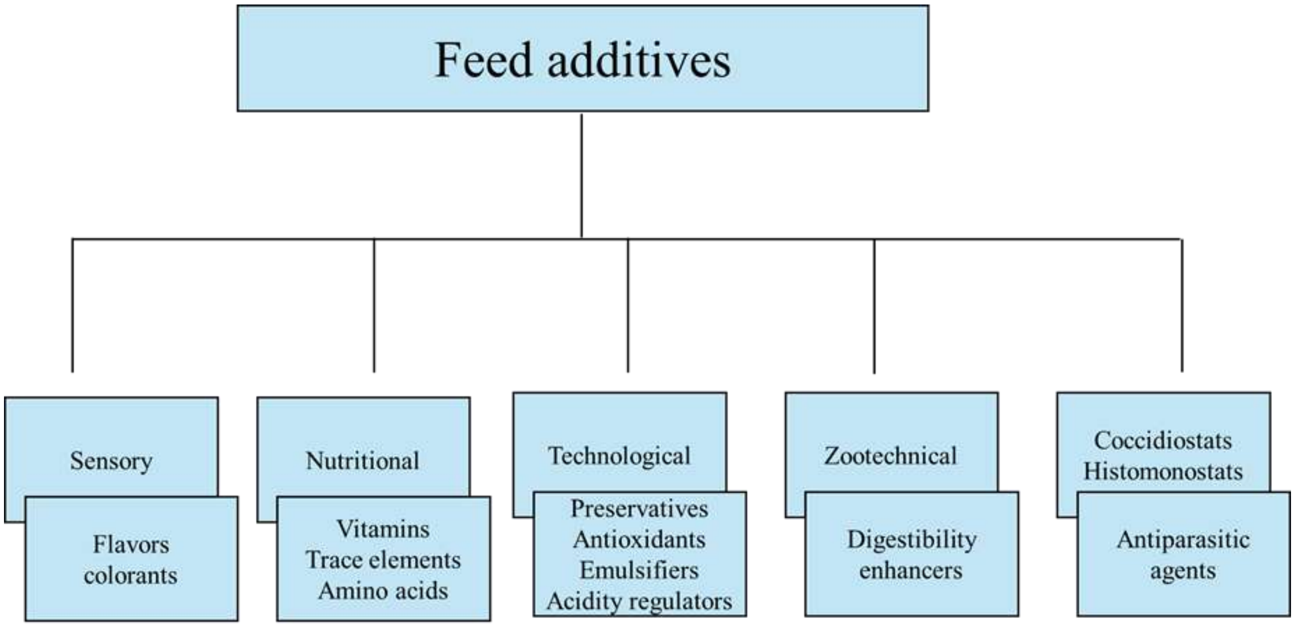

Fig. 1: Classification of feed additives

Numerous feed additives can be produced chemically or naturally from a variety of sources, including microorganisms, minerals, algae, fungi, and plants. Different classes of feed additives include polyphenols, essential oils, antimicrobials, probiotics, prebiotics, amino acids, exogenous enzymes, vitamins, trace elements, antioxidants, and acidifiers (Pandey et al., 2019). The properties of feed additives may overlap, making it challenging to create clear boundaries within each category or type.

Sensory Feed Additives

Additives with sensory qualities are substances, such as colorants and flavoring compounds, which enhance or modify the organoleptic aspects or visual attributes of the feed (Anadón et al., 2018). Studies on Guppies and Rosy barb have shown that the diet supplemented with dried powder of the marine algae *Enteromorpha intestinalis* is a powerful skin colour enhancer and growth stimulator (Monica Joicy et al., 2021). Carotenoids are frequently added to foods like egg yolks, white meat to enhance their colour. Zeaxanthin, capsanthin, canthaxanthin, lutein, β-carotene are commercially used carotenoids. These compounds can be isolated from microalgae species such as *Haematococcus, Chlorella, Dunaliella*; yeast, *Xanthophyllomyces dendrorhous*, *cyanobacterium*, *Spirulina* (Foong et al., 2021). Supplementation of Sumac (2g per 1kg) increased 3% growth efficiency and 4% feed efficiency (Shariatmadari and Shariatmadari, 2020).

Nutritional Feed Additives

Vitamins are nutritional substances required in trace amounts and are critical for numerous metabolic functions as well as for the effective utilization of other nutrients. Although they are naturally included in the feed, supplementation is necessary to ensure that the animals' needs are met. Vitamins C and E are regarded as exogenous antioxidants to cope with oxidative stress and maintaining the stability of cellular membranes (Righi et al., 2021). Vitamin E and citric acid additives significantly improve the activity of antioxidant enzymes, growth and the amount of polyunsaturated fatty acids (PUFAs) of juvenile cobia by promoting the relative mRNA expression of PPARα and aconitase (Xu et al., 2020). Certain trace minerals, including Se, Cu, Zn, and Mn, have a beneficial influence on the immune system's response to many infections. Moreover, chromium has been shown to improve the health of cattle under stressful conditions by lowering cortisol levels and adjusting insulin and glucose concentrations (Palomares, 2022).

Technological Feed Additives

These additives are crucial to the nutrition of animals since they enhance the food's quality, boost the animals' health and performance, and promote their overall wellbeing. For instance, curcumin is a phenolic compound with anti-inflammatory, anticancer, and antioxidant properties. Livestock and poultry feeds supplemented with curcumin plays an important role for animal growth, metabolism, reproduction, immunity, and clinical health care (Pan et al., 2022). For yellow-feather broilers challenged with heat, chitosan oligosaccharides may be a helpful feed supplement to maintain muscle glycolytic metabolism, liver function, meat quality, growth performance, and oxidative status (Chang et al., 2020). Essential oils and saponins are primarily composed of terpenes. A wide variety of bacteria, fungi, and even enveloped viruses are susceptible to the deadly or cytotoxic effects of terpenes (Reddy et al., 2020).

Zootechnical Feed Additives

These additives are used to favorably affect the animal health and growth performance or used to favorably affect the environment such as digestibility enhancers and gut flora stabilizers. Dietary inclusion of probiotics (*Bacillus subtilis* and *Bacillus licheniformis*) in broilers improved growth performance, digestibility, microbial index, and meat quality (Biswas et al., 2023). Chitosan supplemented diets significantly modulate immunity, rumen fermentation, digestibility bacterial population in ruminant animals (Shah et al., 2022). The ingestion of antinutritional components found in fish diet, such as indigestible oligosaccharides like stachyose and raffinose, phytic acid, and antigen proteins result in delayed digestion and malnutrition. It can be improved by exogenous enzymes including proteases, glucosidases, and lipase (Liang et al., 2022).

Coccidiostats and Histomonostats

Coccidiostats are synthetic compounds or biological products that suppress or eliminate protozoa, the parasites that cause coccidiosis (Martins et al., 2022). Cunha et al. (2020) investigated that the intestinal health of broilers is enhanced by zinc since it modifies the ileal microbiome. Moreover, it has been demonstrated that feeding supplements including copper and manganese during an *Eimeria* infection improves feed conversion and alters the immunological response. During an *in-vitro* examination, 2-nitro-1-propanol and nitroethanol decreased the amount of sporozoites in the Madin-Darby bovine kidney cells. In an *in-vivo* study, 2-nitro-1-propanol reduced lesion scores in the ceca and enhanced food digestion of energy, but it was unable to sustain growth in broiler chickens challenged with *Eimeria spp.* (Teng et al., 2020). In a flock of turkey breeders, a dietary supplement called adiCoxSOLPF, which contains a special blend of herbal extracts, was beneficial both prophylactically and therapeutically against histomonosis (Beer et al., 2022).

Role of Feed Additives in Improving Digestibility

Seven enzymes, including pentosanase, protease, cellulase, betaglucanase, phytase, pectinase, and amylase, can degrade pentosans, protein, cellulose, starch, and phytate, hence enhancing food digestibility and absorption in the avian gut (Ramesh and Devegowda, 2004). Broiler chicks fed enzyme-supplemented diets had higher apparent digestibility of organic matter, dry matter, ether extracts and crude protein (Khan et al., 2006). Supplementing commercial enzymes in poultry diets with sunflower meal can increase digestion of fiber and reduce its negative effects (Alagawany et al., 2015). Enzyme addition improved the energy and protein digestibility of grilled chickens (Pourreza et al., 2007). Supplementing xylanase greatly reduced the competition for nutrient utilization from gut microbiota, making more nutrients available for the birds (Hosseini and Afshar, 2017). The addition of a variety of enzymes (amylase, glucanase, and xylanase) to a corn-soy diet of 29-day-old broiler hens dramatically enhanced ileal nitrogen digestibility (Rutherfurd et al., 2007).

Olukosi, et al. (2008) found adding phytase with amylase, protease, and xylanase to the diet improved total tract nutrient retention and increased metabolizable energy. Zhou et al. (2009) demonstrated supplementing meals with multi-enzymes (xylanase, amylase, and protease) improved energy utilization, particularly in diets with the lowest levels of energy. The addition of α-galactosidase enzyme in broiler feed improved energy digestibility of soybean meal (Kidd et al., 2001). Phytogenic feed additives (PFA) are an alternative that may improve the production and health of chickens. Mehri et al. (2010) noticed exogenous enzymes may be advantageous in the digesting process. Enzymes greatly raised excreta calcium retention and improved metabolic energy levels as compared to those without enzyme. Enzyme-supplemented diets improved the nutritional absorption of birds fed diets containing sunflower meal (Mushtaq et al., 2009).

Role of Feed Additives in Enhancing Growth Performance

The rapidly growing demand for animal products (such as fish, meat, eggs and milk), which is mostly brought on by rising urbanization, income growth, and human population expansion, has led to the development of the livestock industry (Thornton, 2010). Current production methods are challenging due to the rise in demand and the cattle industry's explosive expansion. However, there is a growing interest in rearing animals without antibiotic growth enhancers as people become more aware of the possible drawbacks of these substances in livestock diets (Liu et al., 2018). It might be necessary to adjust management and dietary practices to prevent the negative effects of eliminating antibiotic growth boosters from cattle diets (Kil and Stein, 2010). Feed additives are used to increase digestion and production efficiency by minimizing pathogen prevalence and reducing the environmental effect of animals (Yirga, 2015). Ruminant nutritionists have begun to focus more on controlling the rumen protein and carbohydrate digestion to maximize feed degradation efficiency. The diverse microbial population in the rumen produces enzymes that destroy plant toxins such as tannases, including β-glucanases, cellulases, pectinases, xylanases, phytases, amylases, and proteases (Kumar et al., 2018). One of the main components of plant cell walls, hemicellulose, contains the linear polysaccharide xylan. A class of enzymes known as xylanase breaks down hemicellulose by converting xylan into xylose. Although xylanase is frequently found in bacteria, where it breaks down plant matter into beneficial nutrients, mammals do not produce this enzyme (Kumar et al., 2018).

Role of Feed Additives in Enhancing Immune Function

The gut mucosa of monogastric animals acts as the body's first line of defense against infections from the environment. Submucosal and mucosal lymphatic tissue in the intestines has developed into a sophisticated system to fight against potentially harmful and infectious substances (GALT - gutassociated lymphoid tissue). GALT accounts for more than 75% of all lymphocytes in the immune system. The intestine produces about 80% of all immunoglobulins and

50% of lymphocytes. The GALT system produces IgA antibodies, which are released on mucosal surfaces. Their major role is to trap antigens and prevent them from passing past the mucosa into the body. Antigens are collected by specialized antigen presentation cells (APC), which generate suitable cytokines, therefore dictating the development or abatement of inflammation (Butler and Sinkora, 2013). The presence of gut bacteria is required for proper mucosal immune system function. The valuable gut microflora suppresses the growth of possibly harmful microbes by producing bacteriocins (such as lactic acid bacteria), resulting in homeostasis in the gastrointestinal tract (Asgari et al., 2016). By using growth promoters such probiotics, prebiotics, and phytobiotics as feed additives, the gut immune system can be strengthened. They mainly improve the health status of animals by boosting immunity and resistance of the host mucosa to harmful bacterial colonization (Cheng et al., 2014).

Role of Feed Additives in Improving Gut Health

Jamroz et al. (2006) reported Chickens' gut morphology improved after phytogenetic feed additives supplementation. Phytogenic feed additives, which are a blend of herbs, spices, and derived products, have been related to a variety of biological activities, including growth promotion, immune system modification, and intestine shape change (Windisch et al., 2008). The treatment group had a higher villus/crypt ratio, indicating a mature and efficient absorptive surface, ideal gut health, and enhanced gut structure and function, which provided a significant barrier against possible infections (Sakamoto et al., 2000). The larger number of goblet cells in crypts could signify a more abundant source of new cells, increasing the gut's tolerance to weaning stress (Kim and Ho, 2010).

A study by Rajput et al. (2013) demonstrated PFAs can improve grill energy balance while also potentially altering metabolic enzyme activity and gut flora, resulting in alterations in metabolic profiles.

Probiotics, Prebiotics and Polyphenol as Feed Additives

Synbiotics are dietary supplements containing prebiotic and probiotic components which provide a variety of health advantages to the host. They promote intestine eubiosis and have immunomodulatory, antioxidant, anti-inflammatory and antibacterial activities (Hashem et al., 2021, Wu and Zhang, 2018). Microbial species such as *Saccharomyces* spp., *Bacillus* spp., *Streptococcus* spp., and. *Lactobacillus* spp., are frequently used as possible probiotics. Synbiotics' biological activity is influenced by a range of parameters, including the type of probiotics employed, probiotic tolerance to gastrointestinal conditions and colonization capability, prebiotic supply, production process, and storage conditions (Das et al., 2022). They have antibacterial capabilities against enteric infections, synthesize minerals and micronutrients, and generate bacteriocins and other biologically active postbiotics, such as short-chain fatty acids (Thanjavur et al., 2022). Several studies have emphasized the benefits of using multi-strain probiotics in one formula, as each probiotic strain has its own unique properties and metabolites (Melo-Bolívar et al., 2021). This medication appears to be effective against a wide range of infections and activates various biological reactions within the host (Chapman et al., 2011). Prebiotics are an instance of synbiotic material that comprise phytochemicals such soluble fiber, polyphenols, and polyunsaturated fatty acids. They have developed from insoluble carbohydrates and are a significant source of prebiotics (Hashem et al., 2021). To increase probiotic synthesis and provide the hosts additional health advantages, new prebiotic sources have been suggested (Davani-Davari et al., 2019). Cocoa-derived flavanols stimulate the growth of lactic acid bacteria (Tzounis et al., 2011). Pomegranate peel, a biomass agro-industrial byproduct, has a high concentration of phenolic components such as flavonoids, lignans, phenolic acids hydrolyzable tannins and stilbenes, all of which have strong antioxidant and antibacterial activities (Andishmand et al., 2023). The effects of green and black tea polyphenols on the nonpathogenic gut microbiome, revealed that these compounds, which include catechin, epigallocatechin gallate, epigallocatechin, epicatechin, gallocatechin, are potent inhibitors of microorganism development (Peterson et al., 2005), can limit the development of numerous infections, including *Helicobacter pylori* (Ankolekar et al., 2011). Citrus polyphenols such as diosmetin, naringenin, poncirin and hesperetin have been shown to inhibit *H. pylori* proliferation (Duda-Chodak et al., 2015). Lactulose as a prebiotic component promotes the growth of *Streptococcus, Lactobacillus* and *Bifidobacterium* while inhibiting *Enterobacteriaceae* and bacteroides (Gibson, 2004).

Mechanism of Action of Probiotics, Prebiotics, and Polyphenols

Probiotics operate through four primary mechanisms to benefit the body: they prevent and reduce the growth of potential infections, enhance the gut's barrier function, modulate the body's immune system, and produce neurotransmitters that can influence the host (Sánchez et al., 2017). Moreover, probiotics can directly influence immune cells, other host cells, or food ingredients through immune system modulation as reported by Oelschlaeger (2010). Polyphenols have the ability to interact with bacterial proteins in order to limit the synthesis of bacterial nucleic acids, influence the integrity and synthesis of bacterial cell walls, affect cell metabolism, and stop the formation of biofilms (Makarewicz et al., 2021). The non-digestible oligosaccharides galactans and fructans are dietary prebiotics with a substantial research supporting their beneficial impacts on human health (Rastall and Gibson, 2015). These oligosaccharides are preferentially metabolized by bifidobacteria (Roberfroid et al., 2010). Prebiotics are indigestible substances that alter the composition and activity of the gut microbiota through microbial metabolism in the gut, providing a positive physiological impact for the host (Bindels et al., 2015).

Regulations and Safety Considerations in Feed Additive use

Regulatory Framework for Feed Additives

Feed additive regulations cover a broad spectrum of additives: sensory additives (colorants and flavours); nutritional additives (amino acids, vitamins, and trace elements); technological additives (emulsifiers, acidity regulators, antioxidants, and preservatives); zootechnical additives (digestibility enhancers); and coccidiostats and histomonostats (antiparasitic agents). Regulatory bodies such as the FDA (Food and Drug Administration (United States), EFSA (European Food Safety Authority (European Union), CFIA (Canadian Food Inspection Agency (Canada), MARA: Ministry of Agriculture and Rural Affairs (China), MAFF (Ministry of Agriculture, Forestry, and Fisheries (Japan), APVMA (Australian Pesticides and Veterinary Medicines Authority (Australia), FSSAI (Food Safety and Standards Authority of India (India), MAPA (Brazilian Ministry of Agriculture, Livestock, and Food Supply (Brazil) and PFA (Pakistan Food Authority (Pakistan) oversee the approval process for these additives, ensuring they meet safety and efficacy standards (Pressman et al., 2017). The registration and licensing process includes the taking toxicological testing and other detail analysis to ensure the safety of these feed additives for animal uses.

Analysis for the Security of Additives to Feed

For an assessment of the legality of additives to feed for livestock, toxicological analysis was essential. To mitigate potential hazards involved with such additives, a threat assessment and control strategy has been developed. The appropriateness for additives used in food for animals remains intact by continuous surveillance and evaluation (Neveling et al., 2017).

The Compliance of Standard Manufacturing Processes (GMP)

Implement GMP standards throughout the production process to ensure the healthfulness and effectiveness of feed additives. GMP ensures that nutritional supplements are produced in compliance with stringent quality standards in an organized and reliable setting (Mtewa et al., 2020). For the sake of the safety and effectiveness of food additives, quality assurance procedures are implemented through the entire production process.

312 Assessment for Additives to Feed Effectiveness

Safety assessments are a crucial component of the licencing method for feed additives. To reduce potential hazards associated with these unwanted modifications, risk evaluations and management initiatives, in addition to toxicological evaluation, have been implemented to ensure their safety for animal feed. According to Neveling et al. (2017), present oversight and management ensure the secure consumption of nutritional supplements used in food for animals.

Implementing the Specifications for Effective Processes in Manufacturing (GMP)

GMP procedures are essential for ensuring the security as well as efficiency of additives to feed across every stage of the manufacturing procedure. According to Mtewa et al. (2020), GMP enables security and effective feed additive production.

Case Studies and Examples

Important insight into the complications and achievement of regulation pertaining to the use of feed additives are offered by case studies and illustrations. They stress the importance of adhering to the law and provide sage advice for increasing the law and guaranteeing the safety of feed additives by ensuring that regulations are improved; lessons learned from the past can assist that feed additive safety in animal feed (Mantovani et al., 2022).

Future Trends in Animal Feed Additives and Nutrition

Improvements in feed additives technologies are bringing changes in animal nutrition. Changes in the encapsulation and nanotechnologies are transforming feed additive delivery and effectiveness tendency to more precisely target substances and control their release is made feasible by these advancements, new feed additives, animal health and performance (Pandey et al., 2019).

Precision Nutrition and Feed Additives

Accurate nutrition is becoming more and more crucial for the optimizing the use of feed additives. Precision feed, or tailoring the use of feed additives to each animal's particular needs, increase both performance and health. Additionally, (Gaillard et al., 2020) tailored feeding schedules for various animal species and developmental stages are being created, which will boost the efficiency of feed additives (de Toro-Martín et al., 2017).

Sustainability and Environmental Impact

During feed additives production, sustainability is given first attention with the purpose of reducing the detrimental impacts of animal husbandry on the environment through the utilization of sustainable sources. Chojnacka et al. (2021) made efforts to establish production procedures for feed additives that decrease the environmental hazards are motivated by environmental concerns (Hu et al., 2017).

Integration of Feed Additives with other Technologies

Feed additives are becoming more effective when combined with other technologies, such as probiotics and prebiotics (Anadón et al., 2019). To improve the benefits offered additives in animals feed, this synergy must be known and utilized. They enhance the ability to improve the overall animal productivity and health (Fleischhacker et al., 2020).

Outcomes

While there are chances for the expansion and innovation in the feed additive sector, there are limitations that prevent the adoption of navel technologies. Regulatory obstacles and farmer acceptability are two of the industry main issues. However, with the true legislation and outreach, the feed additive sector can offer effective and long-lasting solutions for animals feed. To sum up feed additives are important for maximizing animals' performance and health because they support genetic potential for production and alleviate nutritional shortage. A range of feed additives and their classification by the European Commission indicate the different roles play in enhancing feed quality and efficacy. Feed additives with a different importance, either from natural or artificial sources, such as polyphenols, essential oils, probiotics and others.

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Chapter 12

Impact of Natural Feed Additives on the Health of Humans and Animals

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ABSTRACT

This study examines the possible advantages and difficulties of incorporating natural feed additives into dietary habits while also examining the effects of these additions on the health of both humans and animals. Herbs, essential oils, probiotics, prebiotics, and plant extracts are examples of natural feed additives. Positive outcomes like better immune responses, better gut health, and greater nutrient absorption are revealed by the studies. According to these findings, there may be less need for synthetic pesticides and antibiotics in animal husbandry, which would be in line with the increasing desire for environment-friendly and sustainable farming methods. The research also emphasizes difficulties including the requirement for dosage calculations, standardization, and long-term impact evaluations. To guarantee the safe and efficient use of natural feed additives in the diets of both humans and animals, these problems must be resolved.

KEYWORDS		
Natural feed additives, Human health, Animal health, Antibiotic reduction, Probiotics	Received: 22-May-2024 Revised: 26-July-2024 Accepted: 13-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Compounds called natural feed additives are incorporated into the diets of animals to improve their general health, performance, and well-being. These materials may come from microbes, minerals, plants, or animals. These substances can be used to boost growth, reduce disease risk, improve feed efficiency, and support the immune system. Natural feed additives are typically chosen by producers and consumers over synthetic ones when they are searching for sustainable and environmentally safe feed additives (Carocho et al., 2015).

Types of Natural Feed Additives

Probiotics

These beneficial microbes, such yeast or bacteria, balance the microbial population in the stomach to enhance animal digestion and gut health. Probiotics can reduce the frequency of digestive issues, boost nutritional absorption, and fortify the immune system (Arowolo and He, 2018).

Prebiotics

No digestible materials called prebiotics help the good bacteria in the stomach grow and thrive. Fibers or oligosaccharides are typically what they are. Prebiotics are beneficial for gut health because they give probiotic bacteria a substrate, preserving a balanced microbial community in the digestive system (Singh et al., 2017).

Herbal Extracts

Rich in bioactive compounds with a variety of physiological effects, such as antibacterial, antioxidant, and anti-inflammatory properties, plant-based herbal extracts are very beneficial. Certain supplements have the ability to improve animal health, boost immunity, and decrease the negative effects of stress (Kumar et al., 2014).

Essential Oils

Vibrant aromatic compounds possessing antiviral, antibacterial, and antioxidant properties are abundant in essential oils obtained from plants. When added to animal feed, essential oils can improve digestion, promote overall performance, and inhibit the formation of pathogens in the stomach (Krishan and Narang, 2014).

Enzymes

By breaking down complex substances into simpler forms that an animal can more readily ingest, natural enzymes can improve feed digestibility and nutrient utilization. Sources of microbes, plants, or animals can provide these enzymes. Enzyme supplementation can increase feed efficiency and decrease the damaging environmental effects of animal agriculture (Ojha et al., 2019).

Organic Acids

In order to prevent the growth of pathogenic bacteria in the gut and reduce the risk of stomach infections, several organic acids, such as butyric, propionic, and acetic acids, have antibacterial properties. Organic acids can also improve gut health and improve the absorption of nutrients (Suiryanraynaand Ramana, 2015).

Seaweed Derivatives

Many bioactive compounds, such as polysaccharides, polyphenols, and pigments that are present in seaweeds have positive effects on animals' health. Derivatives from seaweed may modify the composition of the gut flora, increase antioxidant status, and strengthen immunity (Lomartire and Goncalves, 2022).

In this chapter, we will discuss about the impacts of natural feed additives like probiotics, prebiotics, herbal extracts, essential oils, enzymes, organic acids and seaweed derivatives on animal and human health.

Impact of Natural Feed Additives on Animal and Human Health

An increasing number of animal producers are paying attention to natural feed additives made of plants, such as fruits, herbs, spices, and other plant parts. Studies have indicated that adding natural feed additives to animal diets can improve the animal’s quality of life, development and ability to digest nutrients (Abdelli et al., 2021).

Probiotics

From mid-1970s onwards, probiotic use in animals has grown (Fuller, 2012). In agricultural animals, probiotic supplements have been utilized as therapeutic supplements to reduce morbidity and mortality (Rai et al., 2013), enhance feeding behavior (Naglaaand Azeem, 2013), and boost yields of meat, milk, and eggs (Kabir et al., 2004). Additionally, probiotics are being used in the food business because of their capacity to suppress a broad range of harmful microorganisms that come from the environment and diet (Beauchemin et al., 2006). Probiotics generate substances such as biosurfactants, bacteriocins, hydrogen peroxide, and organic acids, which are antimicrobials and can, stop the growth of harmful bacteria (Chaucheyras-Durand and Durand, 2010). Lactic and acetic acids are the most frequently generated chemicals by probiotic bacteria; they lower pH and inhibit the growth of pathogens. Additionally, by competitively colonizing intestinal adhesion sites and nutrients, probiotics increase resistance to intestinal infections (Boirivant and Strober, 2007). Only a limited population of probiotics is viable because, like other organic substances in the gut, they are partially broken down and digested. Nevertheless, research has indicated that probiotics are useful in combating microbes that harm the host's health. One significant role of probiotics against pathogenic invasive bacteria is systemic stimulation of the immune system (Bhogoju and Nahashon, 2022).

Probiotics function through a variety of pathways, including the preservation and improvement of the epithelial barrier, enhanced adhesion to intestinal mucosa and concurrent inhibition of pathogen adhesion, competitive exclusion of pathogenic microorganisms, production of anti-microbial substances, and immunomodulatory action (Bermudez-Brito et al., 2012). A key defensive mechanism that preserves gut integrity and function is the intestinal barrier. The mucous layer, peptides that are active against microorganisms, IgA, and the epithelial junction adhesion complex comprise the intestinal barrier. Probiotic bacteria increase intestinal production, which has an impact on several components of the epithelial barrier (Gogineni et al., 2013). By preventing different harmful bacteria from colonizing the gastrointestinal tract (GIT), probiotics work. By creating inhibitory substances like lactic acid, bacteriocin, and toxic oxygen metabolites, probiotics also work to stop pathogenic microorganisms from attaching themselves to enterocyt. The signal that causes the release of cytokines is started when probiotics connect to their receptors. Neutralization of dietary carcinogens and accelerated turnover of enterocytes are caused by butyric acid production. Optimized immune response is the outcome of specific serum IgA synthesis (Ahmed et al., 2016; Dimidi et al., 2017).

Prebiotics

Prebiotics are used to support probiotic bacteria that are supplied externally as well as helpful bacteria that are already established in the colon. Initially, prebiotics were described as food elements that enter the colon undigested in the upper GI tract and function to favorably affect the host by encouraging the proliferation and/or activity of specific bacteria (O’Bryan et al., 2013). Asparagus, chicory, onion, garlic, Jerusalem artichokes and leeks are just a few of the fruits and vegetables that naturally contain moderate amounts of prebiotics for consumers. However, the prebiotic levels in these foods are typically too low to have a discernible impact on the makeup of intestinal microflora (Manning and Gibson, 2004). Therefore, prebiotics are produced by enzyme synthesis or the breakdown of polysaccharides from dietary fibers or starch to concentrate and economically extract from fruits and vegetables. All prebiotics are mixtures of indigestible oligosaccharides, with the exception of inulin, which is a fructooligo-and polysaccharide combination (Gibson et al., 2000). Galactooligosaccharides, fructans and the synthetic disaccharide lactulose are the only four forms of carbohydrates that are currently recognized as prebiotics and supported by high-quality data from human trials. All currently recognized prebiotics are carbohydrates (O'Bryan et al., 2013).

Three main components make up the intricate concept of gut health: nutrition, intestinal mucosa, and intestinal bacteria. Consequently, some types of beneficial bacteria, such as lactic acid bacteria (*Lactobacillus* sp.) and bifidogenic bacteria (*Bifidobacterium* sp.), have access to prebiotic substrates, While potentially harmful bacteria have less access to them, such as toxogenic *Escherichia coli*, proteolytic bacteroides, and *Clostridium* species (Manning and Gibson, 2004). Enhancing the function of endogenous beneficial bacteria in the gut can be achieved by the use of prebiotics. They have the potential to serve as substitutes for antibiotics that promote growth. Prophylactic dosages of antibiotics and chemotherapy have been added to cattle and poultry feed for a number of years in an effort to enhance animal welfare as well as to save expenses by improving performance and lowering medication requirements (Hajati and Rezaei, 2010).

Essential Oils

All antibiotics used to stimulate animal growth were outlawed by the European Union in 2006, and substitutes were suggested (Simitzis, 2017). Naturally occurring goods are seen to be promising substitutes, including herbal extracts, essential oils (EOs), and medicinal plants (Mushtaq et al., 2018). Being often responsible for several species' health-promoting characteristics, essential oils (EOs) are among the most economically significant plant-derived goods. A significant portion of the conventional pharmacopoeia these substances are derived from a variety of plants that are typically found in temperate to warm regions, such as the Mediterranean and tropical nations. Terpenes, alcohols, aldehydes, and ketones are among the low-molecular-weight compounds that make up essential oils (EOs). These molecules are not only bioactive but also give these materials their characteristic aromatic scent (Nehme et al., 2021). 10% of the approximately 3000 EOs currently identified are significant from commercial and economic standpoint. These goods are in line with consumer's current taste for natural products and may contain a variety of bioactive chemicals with various advantageous qualities (Brenes and Roura, 2010). Additionally, they have less adverse effects and are better absorbed by the body (Liu et al., 2017).

In addition to their flavoring qualities, EOs was also used for their potential as food preservatives, as they could increase product shelf life (Fernandes et al., 2017) or lower Clostridium number concentration (Moro et al., 2015). They are frequently insufficiently strong and affect the organoleptic response when given in large enough amounts to produce the desired antibacterial effect, which is the primary barrier to their use as food preservatives. But in order to identify the most synergistic effects which are still unknown this method needs deeper understanding of how molecules interact. During the last ten years, EOs has become incredibly popular in the fields of animal health. Unfortunately, little is known about their advantageous immunomodulatory and antioxidant properties in the ruminant industry (Lykkesfeldt and Svendsen, 2007).

Since ancient times, essential oils (EOs) have been used as medicinal agents due to their diverse pharmacological and psychological characteristics. They are a complicated blend of volatile odour molecules, mostly monoterpenoids, sesquiterpenoids, benzenoids, and phenylpropanoids. Due to their attractive smells, essential oils (EOs) were used in religious ceremonies, medicine and prevention of illness (Vergis et al., 2015). Due to its biological actions, which include antibacterial, antiviral, anti-inflammatory, antioxidant, anticancer, and antinociceptive qualities, EOs have gained interest from researchers, practitioners, and therapists (Lizarraga-Valderrama, 2021). Today, insomnia, sadness, anxiety, and some cognitive impairments are all treated with aromatherapy across the globe. Growing data over the past ten years has demonstrated that the administration of EOs has quantifiable pharmacological benefits and, at the right dosage, appears to be safe and free of side effects, which are typical of many pharmaceutical psychiatric medications. To demonstrate their pharmacological efficacy in the human neurological system, additional empirical data is necessary (Bandelowand Michaelis, 2015). Both medication and psychotherapy are used to treat most diseases. Given their favourable benefit/risk profiles, selective serotonin reuptake inhibitors and selective serotonin norepinephrine reuptake inhibitors are the most often prescribed first-line medications (Thibaut, 2017).

Seaweed Derivatives

Rhodophyta, red and brown seaweeds are the three main kinds of seaweeds, often known as macroalgae, which are multicellular, large-size marine organisms (Alboofetileh et al., 2021). For ages, numerous coastal communities have utilized this biomass, which serves as a crucial ingredient for food, organic fertilizer and livestock feed (Mac Monagail et al., 2017). It is well known that seaweeds are abundant in primary and secondary metabolites. There are various kinds of primary metabolites, including proteins, lipids, and carbohydrates. These metabolites are directly engaged in physiological tasks such as growth, development, and reproduction. Together with their core metabolites, seaweeds can also acquire minerals that are vital to their survival (Matos et al., 2021). A great variety of secondary metabolites that are also produced by seaweeds have a major role in determining their potential for bioactivity (Øverland et al., 2019). Secondary metabolites do not serve as a prerequisite for tissue growth as primary metabolites do. When biotic and abiotic stressors are present, they are generated in the biomass (Metsämuuronen and Sirén, 2019). The class of secondary metabolites known as phenolics both polyphenols such as tannins and flavonoids and simple phenols like phenolic acids, is significant in seaweeds. Carotenoids and sterols are main metabolites (Salehi et al., 2019). Antioxidant action is seen by the majority of the listed substances. As "free radical scavengers," seaweed antioxidants can prevent or repair oxidative stress-related damage and have a great deal of potential applications in the treatment of a wide range of illnesses (Liu and Sun, 2020). Seaweeds develop in a constantly shifting environment, which gives them their distinct makeup. Stress factors including salinity, temperature fluctuations, and nutritional enrichment and UV radiation exposure. Seaweeds produce physiologically active compounds such as oligosaccharides, amino acids, vitamins, and phytohormones, which enable them to withstand both biotic and abiotic stress scenarios (Manlusoc et al., 2019). The major uses of seaweed-based antioxidants are explored in relation to food applications, pharmacological, biomedical and cosmetic uses; biostimulants of plant growth in agriculture; and animal health. Seaweed-derived antioxidants have a variety of positive health impacts on animals, including immunomodulatory, antibacterial, anti-inflammatory, and prebiotic actions (Rodríguez-Bernaldo de Quiróset al., 2010; Cotas et al., 2020). Prebiotics derived from seaweed biomass have been added to animal feed, and this practice has received a lot of attention lately because of the benefits they have on immune system and gastrointestinal health (Ruiz et al., 2018). Fig. 1 provides an overview of the seaweed antioxidants and how they affect animal health and performance (Michalak et al., 2022).

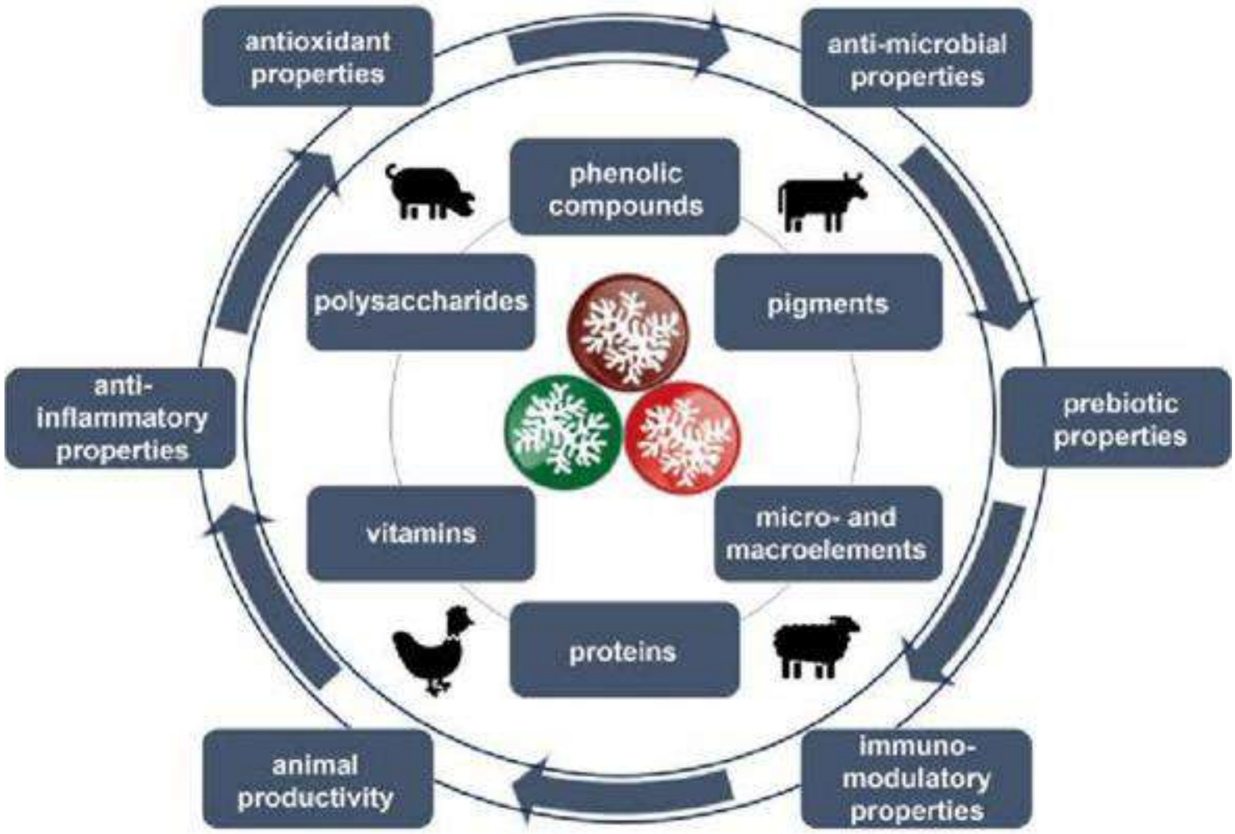

Fig. 1: Role of seaweed derivatives in animal health

In addition to dietary fibers, proteins, minerals, and vitamins, marine algae are a rich source of bioactive substances like polysaccharides, polyphenols, phytochemicals, and polyunsaturated fatty acids that may have therapeutic applications against a variety of degenerative diseases, cancer, oxidative stress, allergies, diabetes, thrombosis, obesity, hypertension, and lipidemia (Tannaand Mishra, 2019).

Herbal Extracts

Plants have been used by humans for thousands of years. Although they can be used for a variety of purposes, such as food, raw materials and one of the earliest known uses of plants for medicinal purposes is as herbal medicine. As a matter of fact, the study of plants dates back hundreds of years, and this has allowed them to be investigated for purposes other than food production. Technically speaking, a medicinal plant is defined as having pharmacologically active components that enable it to be utilized, either directly or indirectly, in a therapeutic treatment to prevent or cure a certain condition (Djeridane et al., 2006; Boscolo and Senna Valle, 2008). The potential medical benefits of plants, which may include antioxidant, antidiabetic, anti-inflammatory, and anti-tumoral activities, have been the subject of several studies (Ekor, 2014). Furthermore, many of the medications that are regularly prescribed in modern medicine have herbal roots. It is believed that these drugs' medicinal and therapeutic properties from the presence of several substances present in a wide variety of plants, including flavonoids, phenolics, terpenoids and alkaloids. According to estimates from the World Health Organisation, more than 80% of people on the planet receive their main healthcare from traditional medicine that uses plants (Who, 2013). Due to their high dietary fiber and phenolic compound contents, which have been linked to several epidemiological studies that have shown to have potentially positive effects like antioxidant, immunomodulatory, and anti-tumoral activity, eating fruits and vegetables has been seen as an essential component of a healthy diet (Ganesan et al., 2018). Furthermore, the gut microbiota is thought to have a significant influence on human health; multiple studies have demonstrated this relationship (Alkasir et al., 2017). The emergence of several illnesses has actually been linked to abnormalities in the makeup of the gut microbiota, such as variations in the kinds and quantity of bacteria present in the gut. Dysbiosis is the term for this disruption, which can cause mental health issues, gastrointestinal illnesses, inflammatory bowel disease, and cardiovascular diseases. Due to the nature of plant extracts, modifications in the gut microbiota have been investigated as potential replacements for existing therapies (O'Callaghan and Sinderen, 2016; Finegold et al., 2017).

The natural world has provided food and medicine in the form of plants for both animals and birds ever since life first began. The majority of plant-based medicinal agents utilized globally are found in traditional medicine (Sen and Chakraborty, 2017). Over the past ten years, there has been a noticeable increase in the use of plants for grain conservation and animal health prevention and recovery. This increase can be attributed to a number of factors, including the development of organic livestock production systems, drug resistance, high input costs, and concerns about toxic residues in food (Escosteguy, 2014). Thus, plant-based medications and products are now utilized either on their own or in conjunction with other treatments to treat illnesses or as a curative agent. A rising number of people are using herbal medicines because they are thought to be safe or to have little negative effects (Wachtel-Galor and Benzie, 2012). The fact that herbal preparations are becoming more and more common in cow healthcare practices, raising questions about the potential use of medicinal plants for both disease treatment and productivity enhancement in high-yielding animals such as cattle (González et al., 2011). These conventional therapies continue to be well-liked despite the many contemporary initiatives that hospitals and government agencies have put in place to improve rural health care. Tribal villages continue to use traditional medical methods for treating cattle when veterinary services are unavailable (Kuralkarand Kuralkar, 2021).

Enzymes

All animals need digestive enzymes to properly digest their food, and these enzymes are either created by the animal's body or by helpful bacteria found in the animal's colon. The feed that animals consume, 15–25% cannot be digested either the feed contains some indigestible ingredients or the animal bodies do not contain the specialized enzyme needed to break down those particular feed nutrients (Konietzny and Greiner, 2002). The phosphomonoesterases known as "phytase" are responsible for starting the process of gradually dephosphorylating myoinositol, or phytate the most abundant form of inositol phosphate in nature. They have been found in mammalian tissues, microbes, and plants (Konietznyand Greiner, 2002). Many producers add specific enzyme supplements to their feed to increase meat production per animal or to produce the same amount of meat more quickly and cheaply in order to reduce this expense (Vohra and Satyanarayana, 2002). Since the 1980s, animal feeds have included digestive enzymes due to their advantages in terms of economy, environment, and health. Phytase, which is utilized in animal feed on a global scale and makes about half of all the enzymes used in the feed business, is the most widely utilized enzyme (Selleand Ravindran, 2007). Low meat and egg production, low feed efficiency, and digestive disturbances are all caused by anti-nutritional elements, which also provide a challenge to regular feed digestion. Feed enzymes function to facilitate the availability of nutrients from feed constituents. As a result of producing less animal waste, feed enzymes also assist in lessening the damaging effects of livestock production on the environment. The proteins in these enzymes are eventually broken down or eliminated by the animal, so there are no leftovers in the meat or eggs (Greiner and Konietzny, 2006). For many of an animal's processes, phosphorus is an essential mineral. The addition of inorganic phosphate (P) to the food was necessary to meet the nutritional needs of chickens due to their inadequate utilization of phytate P. Half of the (P) in poultry feeds derived from plants is released without being digested because there is less endogenous phytase activity. Because phytase reduces excretion of (P) by 50%, environmental contamination is reduced and inorganic (P) is preserved. Fungi, bacteria, and recombinant technologies are the main sources of commercially available phytases (Greiner and Konietzny, 2006). For the synthesis of exogenous phytase, both submerged and solid state fermentation are utilized. Enhancing the use of (P) by the birds and lowering its content in their excrement is one of the industry's main concerns. The most effective way to solve these issues is to add phytase supplements to diets. The application of phytase enzymes in chicken diets was made possible by extensive study, which also contributed to a proportionate decrease in the amount of inorganic (P) fertilizer added to the feed (Imran et al., 2016).

Organic Acids

Organic acids are substances that are organic, acidic, and include one or more carboxyl groups. Carboxylic acids, whose acidity originates from the carboxyl group, are the most common organic acids, with the exception of organic acids such as sulfonic acid, sulfinic acid, and sulfuric acid. Organic acids can be divided into the following groups based on the quantity of carboxyl, hydroxyl, and carbon–carbon double bonds that they contain in their chemical structure: The number of carboxyl groups and whether they are substituted, as in the cases of acetic acid, malic acid, and citric acid, are the first two factors to consider. Other saturated or unsaturated acids are acrylic acid and acetic acid. Benzoic acid is one example of an aliphatic, alicyclic, aromatic, and heterocyclic acid. Chemical compounds known as amino acids are produced when an amino group is added to the carbon atom of a carboxylic acid to replace the hydrogen atom (Qiu et al., 2021). Basic amino acids and acidic carboxyl groups are among these molecules. Amino acids are absent in this review.

One important class of food additives is organic acids, which are used for a number of purposes, including preserving food's nutritional value and sensory appeal as well as acting as antioxidants and acidity regulators (Strazzullo et al., 2009).A typical antioxidant that can increase food stability is ascorbic acid, which works by postponing or stopping the oxidative breakdown of lipids, oils, and other food components. Citric acid, malic acid, fumaric acid, and tartaric acid are all acidity regulators that can maintain or change the pH of food. Additionally good preservatives for preventing food decomposition and extending its shelf life include propionic acid and benzoic acid. Due to the cross-modal relationship between aroma and taste, the formation of organic acids during oral food digestion affects taste perception as well (Shi et al., 2022). All around the world, hypertension is the primary risk factor for death, and it is a chronic illness that is highly prevalent among Chinese citizens, according to the World Health Organization (WHO) (Strazzullo et al., 2009). It is crucial to accomplish reduction of salt without lessening the flavor of salt in order to preserve the food's flavor. Organic acids provide an acidity that can either enhance or suppress other tastes when combined with them. An investigation conducted recently revealed that the addition of malic acid to low-sodium salts enhanced the salty flavor and lessened the bitterness caused by the potassium salts (Wangand Zhang, 2012). When it comes to their nutritional roles, One category of nutrients is organic acids that have been shown to have a number of positive health effects, including the ability to reduce inflammation, prevent osteoporosis, regulate the host immune system, produce intestinal hormones, prevent obesity, boost calcium absorption, and inhibit platelet aggregation (Ji et al., 2021).

Conclusions

The health of both people and animals may benefit from natural feed additives. Natural feed additives have been demonstrated to promote growth performance, increase immunity, and improve general health in animals through a multitude of studies and observations. These additions, which have a variety of impacts including altering gut flora, improving nutrient absorption, and bolstering the immune system, frequently comprise organic acids, plant extracts, essential oils, probiotics, and prebiotics. Utilizing natural feed additives can help animals become less dependent on synthetic growth promoters and antibiotics, which lowers the risk of antibiotic resistance and enhances food safety. Better-quality products for human consumption also result from healthier animals, which may lower the prevalence of foodborne illnesses and improve total nutritional content. Naturally occurring feed additives also help the environment and promote animal health.

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Chapter 13

Nano-feed Additives in Animal Nutrition, their Preparation, Mode of Action and Application

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ABSTRACT

Nanotechnology, an advancing field, holds the promise of transforming agriculture. and animal industries worldwide. It involves the modification of particle size to a few nanometers, allowing for the synthesis of nanoparticles with reducing agents that alter their physical and chemical properties. These tiny particles find applications across multiple domains, such as precise drug delivery nutrition therapy vaccine manufacturing, and textile purification. Previously, nanoparticles were synthesized using chemical techniques, releasing pollutants into the environment. Green synthesis, which uses plant extracts containing sugars, polyphenols, terpenoids, proteins, and other compounds as reducing agents, is becoming increasingly significant. These phytochemicals act as reducing agents, ensuring minerals remain reduced throughout synthesis. Nanotechnology plays a vital role in animal nutrition, especially in the preparation of nano-minerals, focusing on trace minerals that have limited bioavailability. Moreover, these nanoparticles have the potential to enhance immunity, digestive efficiency, and overall performance in both livestock and poultry. Nanoparticles, which contain minerals, can reduce mineral antagonism in the intestines, reducing environmental pollution and excretion. They have been found to improve immunity, efficiency in digestion, and performance in poultry and livestock, highlighting the potential of nanotechnology in animal nutrition. This book chapter discusses different facets of nanotechnology, such as nanoparticle production, its impact on animal nutrition, and its future potential.

KEYWORDS
Nanomedicine, Bioavailability, Nano-minerals, Nano-silver, Nano-sensors.

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INTRODUCTION

Nanotechnology is the precise manipulation and processing of atomic and molecular structures to create useful materials, electronics, and systems at a scale of one billionth of a meter. At the nanoscale, materials manifest distinct characteristics, as underscored within this domain of study. Nanometer-scale materials display unique features compared to bigger materials, as highlighted in this field. Nanomaterials are utilized in different fields, such as medicine, to improve drug absorption, deliver drugs to specific organs, and penetrate tissues more effectively (Sheikhalipour et al., 2022). Nanotechnology holds significant potential in livestock systems, including improving feed quality, creating biosensors for breeding, preventing disease transmission, and developing pathogen diagnosis and protection systems. Nano-sensors and capsule vaccinations can aid in embryo bulk production, precision drug distribution, and monitoring of biologically active components. Nanobots provide precise brain assessments and comprehensive capillary inspections and can be employed in packaging materials to improve thermal properties and shelf-life (Sheikhalipour et al., 2022).

Nanotechnology, as defined by the National Nanotechnology Initiative in the USA, involves the study and control of matter at a small scale, with structures typically less than 100 nanometers in size, which is significantly thinner than a human error (Suhag et al., 2023). Nanoparticles, like nano-zinc and nano-silver, have shown potential as antibiotic substitutes due to their ability to kill bacteria. The European Union banned antibiotics as feed supplements for cattle in 2006 due to microbial resistance concerns. This advancement in science and technology continues to expand their applications (Abd El-Ghany et al., 2021).

Moreover, substituting nanoparticles for their macro-scale counterparts in feed additives reduces mineral excretion and minimizes environmental contamination. Nano-formulations require lower total dosages to achieve effective serum concentrations in comparison with their non-nano counterparts (Dey et al., 2021). For example, administering nano-ZnO (zinc oxide) at 800 mg/kg significantly enhanced average gain, intestinal morphology, and plasma zinc levels, mirroring the effects of non-nano-ZnO administered at 3000 mg/kg (Wang et al., 2018). The classification of nanoparticles is broadly grouped into emulsions, inorganic, dispersions, nano-clays, and organic based on chemical characteristics (Bensebaa, 2013). Inorganic nanoparticles, produced at the nanoscale, encompass various approved feed additives like titanium dioxide, utilized as a barrier of UV protection in food packaging when employed as a nanoparticle (Chadha et al., 2022).

Nano-silver is widely employed as an antimicrobial agent, finding application in various settings including fridge panels, storage boxes, and packaging lines, all of which are in direct contact with feed during production. Storage bins for feed are now being manufactured with embedded silver nanoparticles in plastic, effectively eliminating bacteria from stored feed and reducing health risks. Inorganic nanomaterials, like nano-clay platelets, silver nanoparticles, silicon dioxide, calcium, and magnesium, are utilized for feed, feed additives, and food packaging, offering benefits such as water purification and antimicrobial properties (Sharma et al., 2023).

Organic nanoparticles, known as nano-capsules, are utilized to enhance the nutritional value of feed by delivering vitamins and nutrients without altering taste or appearance (Gorantla et al., 2021). These nanoparticles encapsulate nutrients, aiding in their absorption through the gastrointestinal tract and increasing their bioavailability. Additionally, various types of nanomaterials, including organic ones like proteins, fats, sugars, and plant-derived feed additives, are utilized in feed production. Nanoparticles are engineered to provide encapsulation systems for delivering food and feed ingredients, as well as for food and food packaging purposes, serving as identification markers, biosensors, antimicrobials, and shelf-life extenders (Sonea et al., 2021).

Nanoparticles containing minerals demonstrate the potential to mitigate mineral antagonism within the gastrointestinal tract, leading to reduced waste output and environmental pollution. Additionally, these particles enhance animals' digestive efficiency, immune response, and overall performance, underscoring the advantageous applications of nanotechnology in animal nutrition.

This chapter gives a summary of how nanoparticles are made and used in animal food, emphasizing the benefits of making them with plant extracts instead of chemicals.

Potential Application of Nano-feed Additives

Nanotechnology holds potential in several key areas concerning animals (Reddy et al., 2020).

- It can facilitate the delivery of nutrients, medication, supplements, probiotics, and some other substances.
- It enables the diagnosis and disease treatment using nanoparticles, which can detect and eliminate the cause of disease without invasive surgery.
- Nanotechnology allows for an identification registry, which can track an animal's history and its products, such as meat, milk, and eggs.

It aids in reproductive management through hormonal immunosensors (Gelaye, 2024).

Nanoparticles often exert their effects by inducing oxidative damage, disrupting cell membranes, and interfering with cellular processes such as division and death (Rudramurthy et al., 2016).

Various Types of Nanoparticles and their subsequent application are summarized in Table 1.

Nanoparticles can get inside an animal's body in different ways, like eating them in food or drinking water, getting them as medicine, or breathing them in. These particles spread around more easily than solid ones. They act a bit like gas in the air or bigger molecules in liquids, which reduce their sedimentation. The size of the nanoparticle significantly influences its behavior in the body. Smaller particles have faster diffusion through the gastrointestinal tract (GIT) mucus, reaching the intestinal lining cells and entering the bloodstream more efficiently (Gopu et al., 2023).

Nanoparticles smaller than 300nm can be absorbed into the bloodstream, while those smaller than 10nm can penetrate various tissues and organs. Once absorbed, nanoparticles may translocate to other organs through the lymph system, notably to the spleen and liver. Organic nanoparticles, like casein micelles, are readily absorbed and highly bioavailable. Additionally, bio-functionalized nanoparticles have shown promise in treating enteric infections by targeting pathogens like *Campylobacter jejuni* (Xu et al., 2023).

Despite these advancements, challenges remain, particularly in delivering peptides and proteins orally. The gastrointestinal tract poses barriers such as proteolytic enzymes, gut flora, mucus layers, and epithelial cell linings. Colloidal carrier systems, like polymeric nanoparticles, offer a solution by encapsulating bioactive molecules, protecting them from degradation, and enhancing interaction with epithelial cells. Fig. 3 demonstrates the effect of cinnamon on the gut health of poultry. For instance, insulin-loaded nanoparticles have demonstrated sustained activity of insulin and reduced blood glucose in diabetic rats following oral administration (Verma et al., 2021).

Table 1: Various Types and Subsequent Application of Nanoparticles

	Types of NPs	Example	Application
Category No. 1	Nano-emulsions/ dispersion		
	Dispersions	Calcium Carbonate	Enhanced calcium carbonate solubility can be utilized at elevated supplementary concentrations.
	Emulsions	Oil in water	Preservation of bioactive components for administering active substances: prolonged shelf-life; flavor diffusion; low-fat items
Category No. 2	Nano Particles (NPs)		
	Organic Nano-particles (NPs)		
	Protein		Make dairy protein into calcium caseinate again. This improves its performance, including its ability to form a gel, withstand heat, and other desirable qualities.
	Polymeric		Non-biodegradable: Polystyrene Biodegradable materials: Gelatin, Collagen
	Liposomes		Encapsulation and precise delivery of feed/food components
Category No 3	Inorganic Nano-particles (NPs)		
	Silver		An antibacterial agent used in feed or food supplements.
	Zinc		Feed or food supplements are used as a colorant.
	Iron		Feed and/or Food supplement
	Platinum		Feed and/or Food supplement
	Iridium		Feed and/or Food supplement
Category No. 4	Nano-clays		
		Clay composites	This substance is utilized in packaging materials to improve their shelf-life, durability, and thermal properties.

Nano-materials as Feed Additives

Nanoparticles offer significant potential as additives to enhance livestock production. They serve as carriers for various essential components such as essential oils, flavor enhancers, antioxidants, coenzyme Q10, and vitamins, thereby enhancing their bioavailability (ElAmin, 2006). Fig. 1 provides the benefits of nanoparticles on livestock. By encapsulating active ingredients like minerals, micronutrients within nanoparticles, and polyphenols, they are shielded from oxidation and taste receptors, minimizing undesirable flavors in the final product (Heller, 2006).

In the food industry, tiny bubbles called liposomal nanovesicles are used to trap and carry important stuff like nutrients, proteins, flavors, and things that fight germs. These tiny helpers can be put into little packages made of natural food ingredients, like proteins or other stuff we eat. Micelles, which are tiny oil or fat spheres coated with bipolar molecules, can contain substances like omega-3 fish oil, releasing them only in the stomach to mitigate strong tastes. Moreover, the utilization of silicon nanoparticles as food additives, derived from inexpensive feedstock via wet milling, releases ortho silicic acid in the gut is a bio-available form of silicon with proposed benefits for osteoporosis prevention (Canham, 2007). These mineral additives, with particle sizes smaller than 100 nanometers, facilitate rapid absorption through the stomach wall into body cells compared to larger particles. An experiment was done to demonstrate the efficacy of nano zinc oxide supplementation in lactating crossbred cows with subclinical mastitis. Their findings indicated improved immunity, milk production, and reduction in somatic cell counts, suggesting the potential of nano zinc oxide in enhancing dairy animal health ((Rajendran et al., 2013).

Adding Nano-Se at a rate of 3 parts per million (ppm) to the basic diet of sheep caused their stomachs' pH to drop and lowered the concentration of a substance called ammonia N. However, it increased the amount of another substance called total volatile fatty acids (VFA). The ratio of two types of acids, acetate, and propionate, changed in a smooth curve because of more propionates being produced. Additionally, Nano-Se made it easier for sheep to break down a type of fiber and protein in their food and improved how much they could absorb from their meals. The number of certain compounds in their pee changed in a curved pattern too because of Nano-Se supplementation (Shi et al., 2011).

Nanoscale Zoo-technological Activities

Feed additives used in horse nutrition have beneficial effects on their performance. These include stabilizers for gut bacteria, enhancers for digestibility, and substances that improve the environment. Additionally, other additives boost the overall nutrient balance for horses. However, unlike in other animals raised for farming, the effectiveness of antibiotics as feed additives for horses is unclear because the dosage needed may differ (Reddy et al., 2020).

Nanotechnology offers a promising solution using tiny metal particles that can break down the cell walls of both Gram-positive and Gram-negative. Foal diarrhea, a frequent problem affecting growth and health vulnerability, is caused by different bacteria. Adding nano-sized zinc oxide (ZnO) at 800 milligrams per kilogram to their diet reduces diarrhea and helps them gain weight. Similarly, round silver nanoparticles also lessen diarrhea by fighting against *Salmonella* and *Shigella* bacteria (Wang et al., 2018).

Using nano-sized copper supplements has been shown to work well against diarrhea in young pigs after weaning, which justifies its use. Since infection-related diarrhea continues to be a problem, it's important to consider using nano-compounds as long-lasting antimicrobial additives in young horses. Additionally, iron oxide nanoparticles, when combined with a stationary magnetic field and applied to equine stem cells taken from fat tissue, can be guided to particular areas of the body, showing promise for helping tissues heal in injuries such as bone fractures (Reddy et al., 2020).

Selenium nanoparticles help donkeys recover faster after exercise by boosting selenium levels in their blood and increasing the expression of HSP90, a protein involved in stress response. Gold nanoparticles activate platelets and encourage the release of growth factors, showing potential for regenerative medicine in horses, especially for racehorses prone to ligament, tendon, and joint injuries. Silver nanoparticles have excellent wound-healing properties compared to standard antibiotics, and they're used in wound dressings and as additives in bandages (Kojouri et al., 2013).

Nanoparticles are extensively used in horse medicine due to their enhanced drug delivery capabilities, as demonstrated by gelatin nanoparticles in immunotherapy for conditions like recurrent airway obstruction (RAO). Chitosan nanoparticles hold potential for drug delivery and hyper-immunization techniques in horses. Lipid-coated mesoporous silica nanoparticles show promise as carriers for antiviral drugs, while nano-formulations of vitamins and minerals enhance grooming results and prevent sun bleaching of horse hair (Youssef et al., 2019).

Chromium nanoparticles are known for their effect on leanness and muscle protein in poultry and swine. Overall, nanotechnology offers diverse opportunities to improve equine health and performance across various applications (El-Sayed and Kamel, 2020).

Nano-nutraceutical Additives

Nutritional additives are crucial for supplying animals with essential nutrients, including trace minerals, amino acids, vitamins, and polyunsaturated fatty acids, administered in precise amounts for direct consumption. Researchers are investigating the potential of nanoparticles as delivery systems for these nutraceuticals in the food industry (Pandey et al., 2019).

Designing carrier nanoparticles for equine nutrition poses challenges due to the gastrointestinal tract's unique environment and pH levels. Proteins, with their emulsifying and gelling properties, are considered safe nano-carriers. Canola protein cruciferin has shown promise as a carrier material for beta-carotene (Pandey et al., 2019).

Processed cereal grains in equine diets may lead to mineral and vitamin loss, predisposing horses to metabolic disorders. Nanotechnology improves bioavailability by enhancing bioaccessibility, absorption, and molecular transformation (Arshad et al., 2021). Heavy working and racehorses have high physiological demands for nutritional additives. Inorganic mineral salts have poor bioavailability and may increase excretory rates, posing environmental risks. Nanosized minerals could enhance bioavailability while reducing excretion. Mineral nanoparticles are believed to improve growth and performance by enhancing nutrient absorption rates (Kopittke et al., 2019).

Nano-encapsulation is a valuable technique for the delivery of Vitamins C, A, and E, enhancing absorption efficiency, and promoting reduced inflammation and improved healing. Nano Vitamin E is one of the few nano-elements in nutrition, essential for optimal neurological and muscular function, especially in performance horses (Subramani and Ganapathyswamy, 2020). Coenzyme Q-10, crucial for energy production, is available in nano-suspension form, beneficial for combating oxidative stress in racehorses. Fig. 2 demonstrates the various mechanisms involved in equine nutrition. Casein nanoparticles serve as an effective carrier for hydrophobic nutrients, aiding in the delivery of nutrients and growth in weanlings (Ali, Ijaz, et al., 2021).

Mode of Action

Nanoparticles often exert their effects by inducing oxidative damage, disrupting cell membranes, and interfering with cellular processes such as division and death (Rudramurthy et al., 2016; Liu et al., 2021). This oxidative stress arises from reactive oxygen species like hydrogen peroxide, leading to cell damage. Additionally, nanoparticles can affect intracellular ATP production and DNA replication, and even mimic biological molecules like mannose to attract bacteria (Liu et al., 2021). For instance, carbon nanoparticles repel gram-negative bacteria through electrostatic forces and alter the surface charge to deter gram-positive bacteria, ultimately preventing bacterial division and causing cell lysis (Varghese and Balachandran, 2021).

Silver nanoparticles disrupt enzymes, alter protein expression, and damage biomolecules in bacteria, while polymeric nanoparticles interact strongly with bacterial cells, leading to microbial death upon contact (Joshi et al., 2020). Nanoparticles with protruding structures, such as zinc-doped copper oxide, efficiently disrupt bacterial cell walls, hindering biofilm formation, a crucial defense mechanism for pathogens (Wu et al., 2016). Disrupting biofilm formation is particularly important as biofilms pose significant health risks. Furthermore, nanoparticles inhibit methane emissions by reducing populations of methane-producing microorganisms and suppressing key enzymes involved in methane production (Palangi and Lackner, 2022).

Nano-based food additives offer a diverse range of functions, thanks to various engineering techniques and nanoparticle types as mentioned in Table 2.

Adsorption of NPs and Uptake Pathways

The initial step involves the adsorption of NPs onto the surface of cells lining the gastrointestinal tract (GIT) or other targeted tissues. This adsorption is influenced by various factors like the presence of specific binding sites, nanoparticle size, and surface charge on the cell membrane (Rampado et al., 2020).

Table 2: Nano-feed Additives, their sources, and applicability.

Sources	Feed Additives	Applicability/ Functions	References
Microorganisms	Probiotics	Enhancing digestion and stimulating growth.	(Muzaffar et al., 2021)
Essential amino acids (A.A.) and Plant-based enzymes	Enzymes and amino acids	Enhancement of digestion, Antibacterial, antioxidative properties	(Li and Wu, 2020)
Oligosaccharides	Prebiotics	Enhancement of digestive function and promotion of growth.	(Muzaffar et al., 2021)
Carboxyl acids	Organic acid	Enhancing feed efficiency, improving digestion, and preserving feed quality.	(Nguyen et al., 2020)
Essential Oils and Herbs	Phytogenic additives	Antimicrobial properties, enhancement of digestion, and promotion of gut health.	(J. Singh and Gaikwad, 2020)
Minerals and clay, Metal oxides	Functional elements and nanoparticles	Antimicrobial properties coupled with enhanced digestion.	(Patra and Lalhriatpuii, 2020)

Nanoparticles serve as effective carriers for hydrophobic nutrients, aiding in the delivery of nutrients and growth in weanlings. This section delves into three key aspects of their interaction with biological systems: (Adegbeye et al., 2019)

Different uptake pathways then facilitate the internalization of NPs into cells. These pathways can be active (requiring cellular energy) or passive (driven by diffusion or concentration gradients). Understanding the specific uptake pathway involved is crucial for optimizing the design and delivery of nanoparticle-based therapies (Behzadi et al., 2017).

Diffusion Passage of NPs through the Mucosal Laye

Following adsorption and uptake, NPs encounter the mucosal layer, a protective barrier lining the GIT. The ability of NPs to diffuse through this layer depends on their size, charge, and interactions with the mucosal components. Smaller and neutral NPs tend to diffuse more readily, while larger or charged NPs might require specific carrier systems or surface modifications to facilitate their passage. Understanding these diffusion processes is essential for predicting the bioavailability and efficacy of orally administered NPs (Lotfipour et al., 2021).

Passage through GIT and BBB

For systematic delivery beyond the GIT, NPs face the challenge of passing through the intestinal epithelium and potentially the blood-brain barrier (BBB). The intestinal epithelium presents a barrier with tight junctions, and only certain NPs with specific properties can permeate it (Kulkarni et al., 2023).

The blood-brain barrier, on the other hand, is an even stricter gatekeeper for access to the brain, posing a significant hurdle for most NPs. Strategies like using specific targeting ligands or modifying the surface properties of NPs are being explored to overcome these barriers and enable targeted delivery to specific organs or tissues (Niazi, 2023).

By understanding these key aspects of the NP mode of action, researchers can design more effective and targeted therapies while minimizing potential off-target effects

Preparation of NPs as Animal Feed Additives

Various methods exist for preparing nanoparticles, and the choice among them depends on specific objectives and conditions governing the particles' intended use. Factors to consider encompass the physical and chemical stability of the active agent, its toxicity, release profile, and various other elements (P. Singh, 2016).

The Cross-linking Emulsion method involves creating a water-oil emulsion where a watery solution is emulsified within an oily phase (Fig. 5). Through vigorous agitation, the particles separate and solidify, necessitating agents to facilitate the union of compounds (Sawant et al., 2021).

The Precipitation/coacervation Method

Particles are generated by introducing the active agent into an alkaline solution. This approach provides precision control over the shape, composition, and size of the nanoparticles, allowing customization to produce diverse nanomaterials with targeted properties. These tailored materials find applications across various fields including catalysis, biomedical imaging, and nanoelectronics (He et al., 2019).

The precipitation or coacervation method is a technique used for the synthesis of nanoparticles. Here's a general outline of the process:

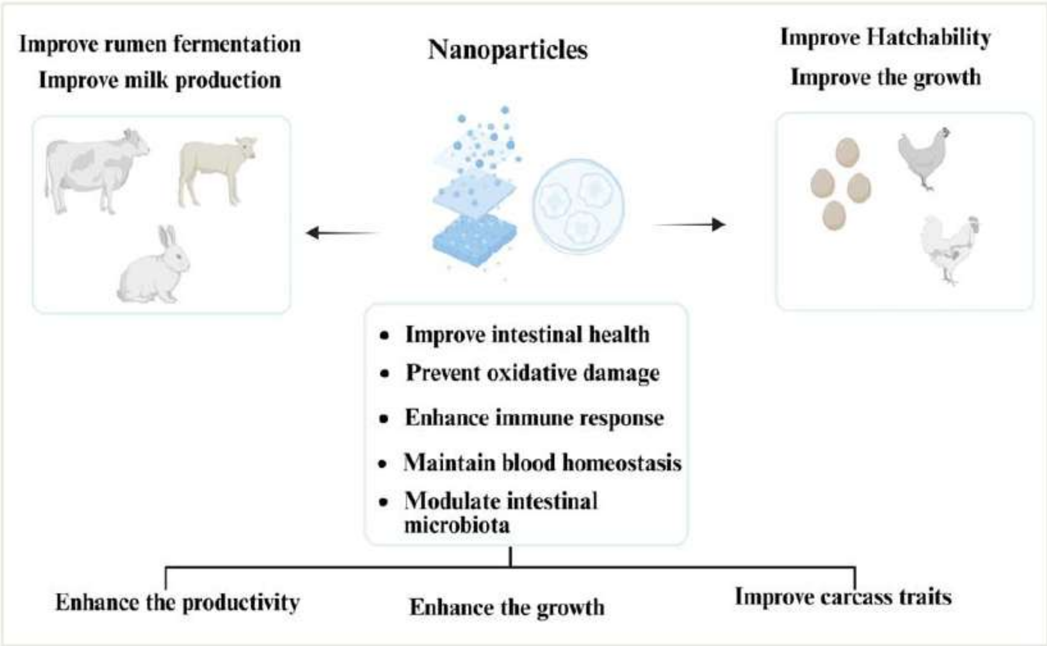

Fig. 1: Enhancing Animal Health and Performance through Nanoparticles (Michalak et al., 2022)

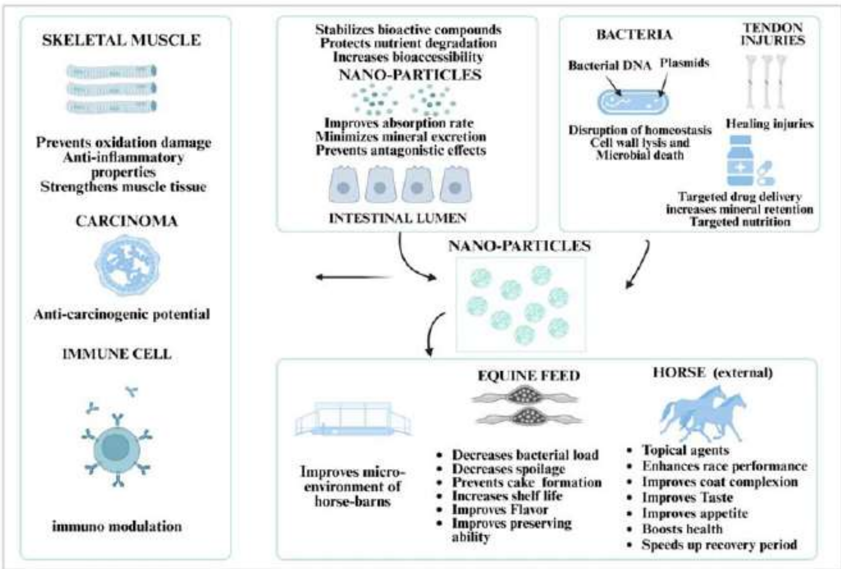

Fig. 2: Various nanotechnology-based feed additives operate through different mechanisms in equine nutrition (Reddy et al., 2020).

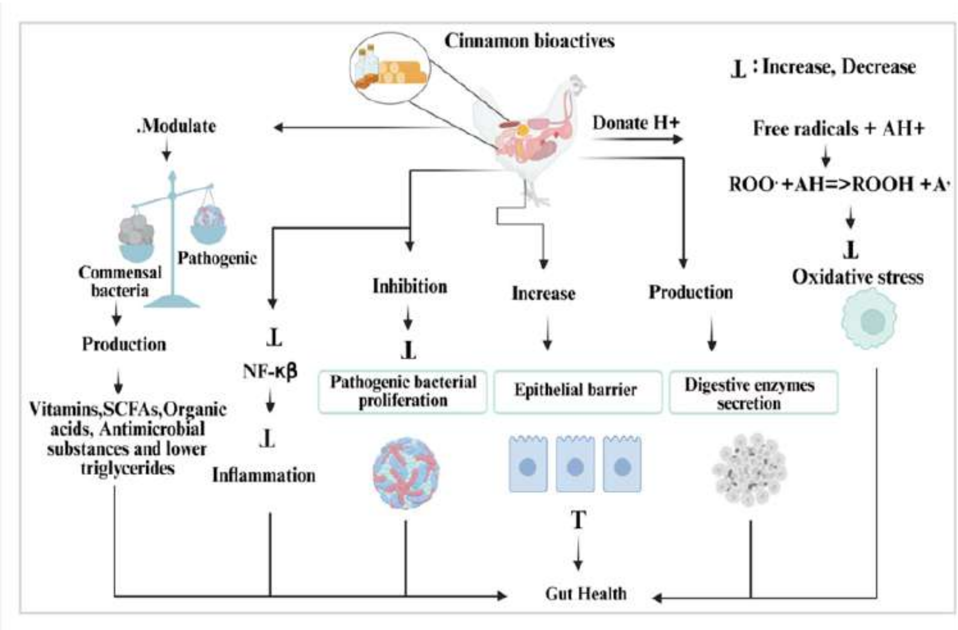

Fig. 3: Effect of cinnamon on the gut health of Poultry (Ali, Ponnampalam, et al., 2021)

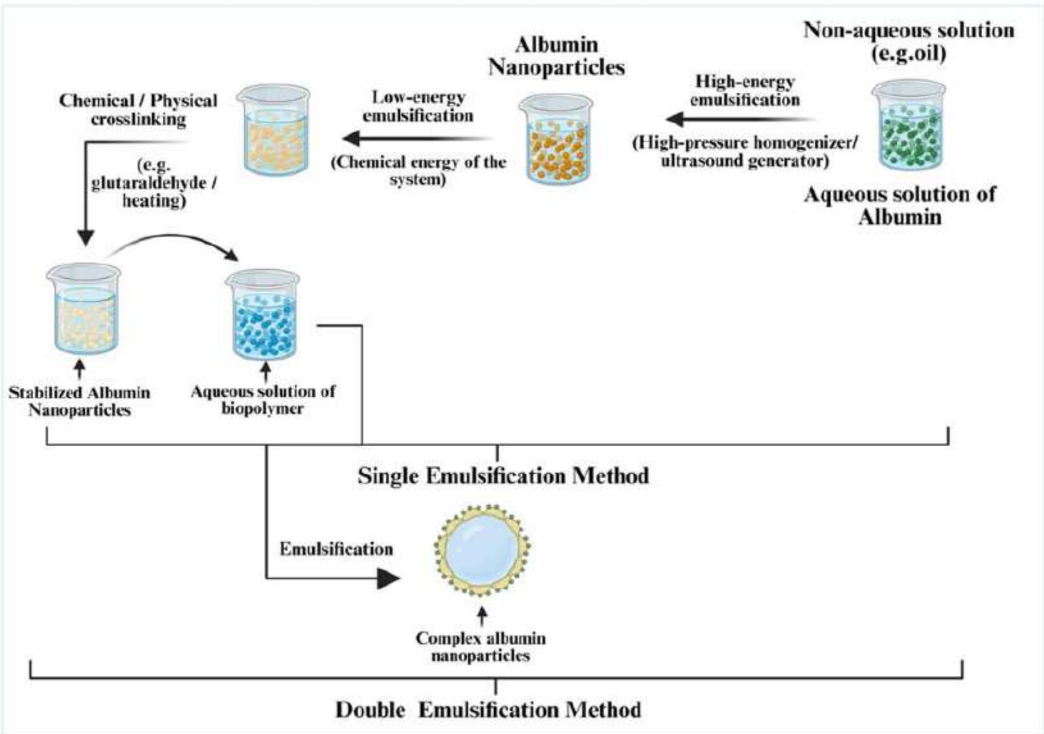

Fig. 4: Schematic representation of the emulsification method (single and double) used to prepare albumin-based nanoparticles (Loureiro et al., 2016).

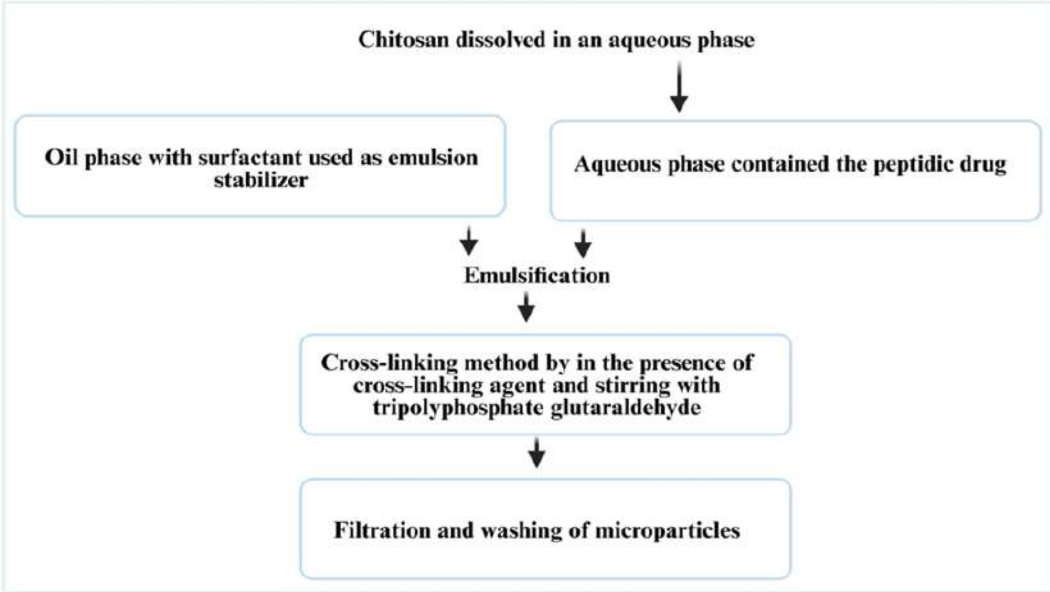

Fig. 5: Emulsion cross-linking method (Hussain et al., 2018).

Precipitation Method

In this method, the reaction between the precursors leads to the formation of insoluble nanoparticles, which precipitate out of the solution. This can occur through various chemical reactions such as reduction, hydrolysis, and complexation (Dudchenko et al., 2022).

Coacervation Method

Coacervation is when a solution splits into two parts: one rich in polymer and a solvent-rich phase. The nanoparticles form within the polymer-rich phase due to interactions between the polymer chains and the precursor compounds (Fig. 4). This method is often used for the synthesis of polymer-encapsulated nanoparticles (Schröder et al., 2022).

Selection of Precursor Compounds

The process begins with selecting suitable precursor compounds, which will form the nanoparticles upon reaction.

Preparation of Solutions

Separate solutions containing the precursor compounds are prepared. These solutions typically contain metal salts or organic compounds that will react to form the desired nanoparticles.

Mixing of Solutions

The precursor solutions are mixed under controlled conditions. The mixing can be done gradually to ensure uniformity and control over the reaction kinetics.

Precipitation or Coacervation

The mixing of the precursor solutions leads to nanoparticle formation through precipitation or coacervation:

Nanoparticle Collection

After the nanoparticles have developed, they are usually removed from the solution. This can be achieved through techniques such as centrifugation, filtration, or precipitation by adding a non-solvent.

Washing and Drying

The collected nanoparticles may undergo washing steps to remove any impurities or residual reactants. After washing, they are usually dried to obtain a powdered form suitable for further characterization and applications.

Characterization

Lastly, the created nanoparticles undergo analysis using different methods to assess their size, shape, composition, and other traits. Common techniques for this characterization include dynamic light scattering (DLS) transmission electron microscopy (TEM), X-ray diffraction (XRD), and scanning electron microscope (SEM) (Baig et al., 2021).

Spray-drying

Spray drying is a method that's been around for a long time and is used in many different areas like food and chemicals. It first started in the pharmaceutical industry back in the early 1900s when it was used to dry blood. Over time, it became really popular in pharmaceuticals for lots of things like making solid mixtures, putting drugs and oils into capsules, and drying out things like proteins, vaccines, DNA, and antibodies (Vehring et al., 2020).

In making medicine, spray drying is super helpful because it helps to create powders with tiny particles, from really small ones to a bit bigger ones. This method is particularly effective for producing particles that can be inhaled into the lungs, allowing us to control various critical aspects of the particles, such as their size, shape, density, flowability, moisture content, crystallinity, and dispersibility. Plus, it's like a two-in-one deal because it works for both making particles and shaping crystals. (Vehring, 2008).

This single-step manufacturing process operates on the fundamental principles of atomizing liquid into fine droplets and subsequently evaporating the solvent using drying hot gas. The process unfolds through four key stages: preparation of the liquid feedstock, atomization of the feed via a nozzle into a spray that interfaces with the drying hot gas, formation of particles through evaporative mass transfer, and finally, the separation of the dried product from the gas stream. Fig. 7 demonstrates the overall working of a small-scale spray dryer. (Ishwarya et al., 2015).

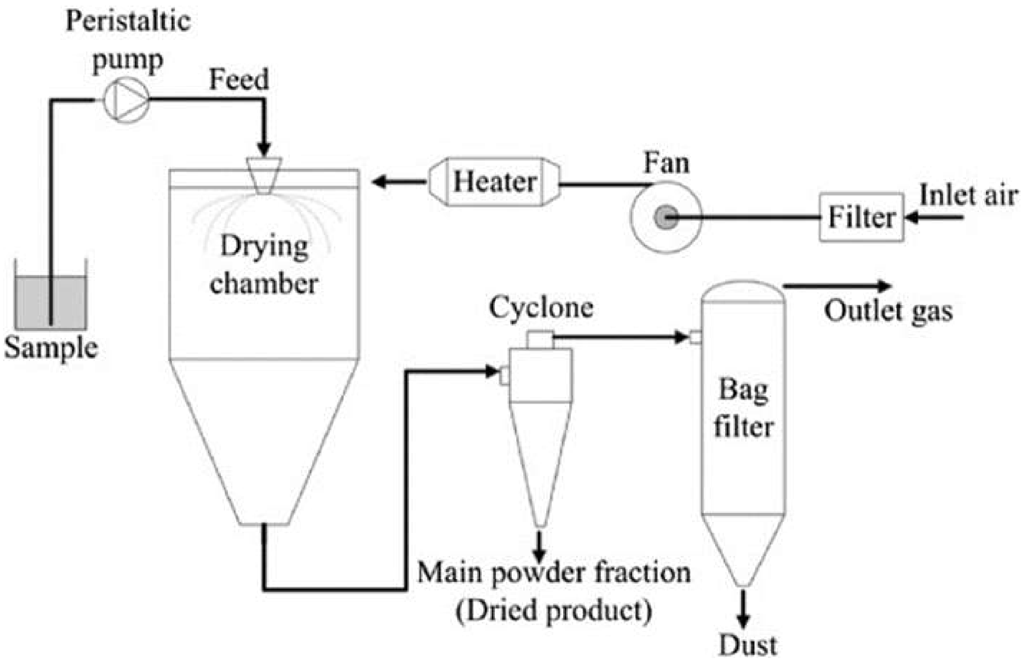

Fig. 7: Schematic diagram of the small-scale spray dryer (Khuenpet et al., 2016).

Future Challenges and Perspectives

The future challenges for nano-feed additives include long-term safety assurance, regulatory framework enhancement, cost reduction and scalability, enhanced stability and efficacy, and ethical considerations. Ensuring the long-term safety of nano-feed additives is crucial, as it could impact human health throughout the food chain. Further research is needed to assess the potential risks associated with their consumption by animals. Regulatory framework enhancement is necessary to address emerging concerns effectively. Comprehensive testing protocols and regulations are essential for safe and responsible use in the industry. Cost reduction and scalability are also crucial, as high production costs and scalability issues need to be overcome. Research should focus on strategies to prevent agglomeration and enhance the dispersion of nanoparticles within feed-matrices.

Ethical considerations regarding the ethical implications of nanotechnology in animal agriculture must be addressed, with stakeholders engaging in dialogue and setting ethical guidelines. The way forward for nano-feed additives involves continued investment in research and development, collaborative regulatory efforts, technological innovation, education and awareness, and sustainable practices. Investment in research and development is essential to address safety concerns, improve production techniques, and enhance the efficacy of nano-feed additives. Collaborative regulatory efforts should involve regulatory agencies, industry stakeholders, and scientific experts to develop robust regulatory frameworks. Technological innovation is key to overcoming cost and scalability challenges, while education and awareness can raise awareness among farmers, consumers, and policymakers.

Research institutions and industry partners should focus on developing cost-effective production methods, novel delivery systems, and advanced nanomaterials to improve animal agriculture efficiency and sustainability. Education and awareness about nano-feed additives' benefits, risks, and ethical considerations are crucial for their acceptance and responsible use. Outreach programs, workshops, and educational materials can raise awareness among farmers, consumers, and policymakers. Emphasizing sustainable practices in nano-feed additive development and deployment, such as circular economy, resource efficiency, and environmental stewardship, can minimize environmental impact and maximize nanotechnology benefits.

Conclusions

Nanotechnology involves manipulating atomic and molecular structures to create functional materials, devices, and systems at a nano-scale. These materials have significant applications in medicine, livestock systems, and veterinary medicine, enhancing drug bioavailability, enabling targeted delivery, and facilitating deeper tissue penetration. Nanoparticles are grouped into dispersions, organic, inorganic, emulsions, and nano clays based on their chemical characteristics. Inorganic nanoparticles like titanium dioxide are used as UV protection barriers in feed packaging, while organic nano-capsules enhance feed nutritional value. Nanotechnology holds immense potential in fields like medicine, veterinary medicine, and livestock systems. Smaller particles have faster diffusion through the gastrointestinal tract, and lignocellulosic nanovesicles are used in the food industry. Despite technology getting better all the time and being used in many different ways, there is not enough research happening in this particular area. The production of nanoparticles by using eco-friendly techniques, known as green synthesis, could be a good alternative to using chemicals. But we need to do a lot more research to make sure it works well and is safe for animals, people, and the environment.

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Chapter 14

Use of Natural Feed Additives as a Remedy for Diseases in Veterinary Medicine

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ABSTRACT

This chapter describes the efficiency and implementation of some common feed additives used as a treatment in veterinary medicine. With the recent inflation and increasing costs of treatments, there is a need to use natural feed products to combat diseases. The knowledge of medicinal feed additives is helpful in some livestock farming plans like organic farming where the farmers are not allowed to use the allopathic way of treatment. Also, in recent years, the concern for antibiotic resistance has significantly increased because these antibiotics leave their residue in the animal body tissues leading to the appearance of subsequent resilient ancestors of microorganisms. This situation desires an urge to use natural feed additives in the treatment of diseases. The knowledge of herbal medicine is now at a threatened stage because it was verbally communicated to only locals and family members. As a consequence, this knowledge is confined to a limited number of people. Nowadays, as the situation described above, there is a need to utilize ethno-veterinary knowledge for the benefit of humanity. The phytochemical screening of these feed additives has shown that they contain some bioactive compounds such as anthraquinone, lectins, alkaloids, essential oils, thymol, tannins, thymoquinone, flavonoids, limonene, saponins, steroids/triterpenes, polypeptides, and some other compounds. These compounds are present in different parts of plants such as seeds, leaves, bark, roots, and fruits. The different parts of plants and their mixtures/preparations are used for antibacterial, anti-venom, antifungal, wound healing, and some other pharmacological purposes. There is a need to further investigate the safety, dosage, mode of use, and efficacy of these feed additives by undertaking certain antimicrobial and phytochemical experiments. In conclusion, these feed additives when undergoing certain procedures like purification, extraction, or isolation could be used in new drug development.

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INTRODUCTION

In most developing countries, the principal hindering element to the animal production is the poor health of animals. The reason is limited funding of health services for animals in these countries. In these circumstances, traditional knowledge of the remedies is more readily available than allopathic veterinary treatments (Alawa et al., 2002). A greater number of communities exist in the world that is still dependent on the medicinal knowledge of plants for the treatment of common diseases (Güler et al., 2021). The knowledge of medicinal plants has been used greatly in African countries such as Uganda and South Africa and many other Asian countries like Iran, India, Pakistan, Bangladesh, Afghanistan, and Nepal (Abdalla and McGaw, 2020). Even in developed countries, currently, about 25% of all the available medicines/drugs have ingredients derived from plants having medicinal properties (Güler et al., 2021). Global researchers have been attracted to the secondary metabolites of plants to be used as complementary or alternative medicine. In the past, investigation in the domain of ethno-veterinary science is comparatively ignored compared to the other related fields (Abdalla and McGaw, 2020).

Natural Feed Additives VS. Synthetic Drugs to Treat Diseases in Veterinary Medicine

Synthetic antibiotics usage in medicine was begun in 1940s to increase livestock productivity. With time, nowadays, the microbes have developed resistance against many of these antibiotics. In the past, these antibiotics successfully kill or attenuate pathogens, but now become mostly ineffective (Elliott, 2015). Moreover, the use of these antibiotics in livestock used for human consumption also produces drug-resistant strains to treat human infections. One report of the USA-FDA (2016) stated that only in the United States of America, about 17,000 tons of synthetic antibiotic drugs were used in livestock. This equaled four times the antibiotics amount used for human consumption in the year 2015 (USA-FDA, 2016).

Spellberg et al. (Spellberg et al., 2016) demonstrated that farm animals become resistant to tetracycline antibiotics in just 14 days and it can spread to the farm workers. They proved this statement by showing the existence of tetracycline-resistant microbes in their stool samples. This production of resistant strains of pathogens and their transfer to the human food chain is unavoidable. Many healthcare organizations mainly the European Medicines Agency and World Health Organization have laid their concerns on this issue. The US Centers for Disease Control and Prevention and the Institute of Medicine are also included in this list.

To combat this issue, there is a need to develop new antibiotics or to use other strategies to tackle microbial resistance. In this picture, when we look into natural resources, our mother nature has provided a complete range of equipment to combat this issue. The usage of natural feed resources made from plants in treating health problems is an old and worthwhile approach. The usage of single or multiple medicinal plants extracts or combining the plant extract with synthetic antimicrobial drugs to treat infections can open up new strategies in the war against pathogens.

Nowadays, natural bioactive compounds derived from plants are becoming popular in animal feeds due to their antimicrobial properties because the European Union has banned antibiotic growth promoters. The reason is because these compounds reside in animal body tissues and pathogens have developed resistance against them. The aromatic compounds and oils deduced from plants contain several positive properties like being anti-inflammatory, increased feed intake, antiviral, digestion enhancers, coccidiostatical, immunity enhancer, and antibacterial. In comparison to inorganic substances or synthetic antibiotics, the plant-extracted compounds are proven to be ideal as feed additives, and natural, residue-free, and less toxic for animal nutrition (Hajati et al., 2014).

Effects of Natural Feed Additives on the Performance of Animals

In animal nutrition, natural feed additives are gaining importance and high acceptability as an alternative disease remedy source. The flavonoids present in alfalfa (*Medicago sativa L.*) produce oxidation stability muscles by decreasing the value of thiobarbturic acid reactive substance. This experiment was tested on rabbits to check their production and meat quality. This experiment suggested that alfalfa addition to the feed will improve meat quality (Dabbou et al., 2018).

The three main natural compounds present in herbal feed additives that have been shown to decrease methane gas production are tannins, essential oils, and saponins. It is reported that the antimicrobial properties of plant bioactive metabolites can alter the rumen ecosystem and thus reduce methane gas production (Samal et al., 2016). Some grazing forages have gained importance due to their properties as effective anthelmintics (Githiori et al., 2006). Some forages like *Cichorium intybus* have gained attention due to their property to control parasites in ruminant animals. They contain tannins and some other herbal secondary metabolites. One study on sheep showed that the tannins extracted from *Hedysarum coronarium, Lotus corniculatus,* and *Lotus pedunculatus* have reduced the transformation of L1 to L3 larvae of *Trichostrongylus colubriformis* nematode (Molan et al. 1999).

Role of Feed Additives used to Treat Bacterial and Fungal Infections of Animals

Anthrax is a very deadly and infectious disease of livestock. *Bacillus anthracis* is the causative agent of Anthrax (Mwakapeje et al. 2018). This disease has a zoonotic importance because humans can get the disease directly from the infected animal (Fasanella et al. 2014).

One study proved that an extract of medicinal plants showed a great antibacterial effect against the *Bacillus anthracis*. The surprising thing was the lowest values that can restrict the growth of the pathogen had a starting value of 0.02 mg/ml and ending value of 0.31 mg/ml. the medicinal plants used in this study were *Bolusanthus specious*, *Pittosporum viridiflorum*, *Hypericum roeperianum*, *Bolusanthus speciosus* and *Maesa lanceolata* (Elisha et al., 2015).

The poultry industry suffers huge economic losses due to the mycotoxins produced by the fungi (Dhama et al., 2013). The brooder's pneumonia in poultry or commonly called Aspergillosis caused by fungi known as *Aspergillus fumigatus* is the largest devastating pathogen. Normally the fungal infections require an extended planning of administration of drugs which will result in high cost. Topically available preparation of drugs extracted from naturally available feed materials might prove valuable alternatives (Arné et al., 2011).

Role of Feed Additives used to Treat Viral Diseases of Animals

Research has shown that many compounds extracted from natural feed sources contain antiviral properties. These antiviral agents have been used to treat viral infections for decades. It was estimated that about 20% to 30% of natural feeding resources from plants in temperate and tropical areas had antiviral properties (Pérez, 2003).

In India, many nutritionally important plants are used to treat the foot-and-mouth disease of animals. The plants used for such purposes are *Andrographis paniculata*, and *Colocasia esculenta*. The crude extract from the seeds of *Nyctanthes arbortristis* having alcoholic properties had antiviral properties. The glucosides extracted from the same plant were shown to be active against the Semliki Forest viruses (SFV) (Mishra et al., 2015).

Role of Feed Additives used to Treat Inflammatory Diseases of Animals

Many secondary metabolites of natural feed additives possess the properties of being scavengers of free radicals and antioxidants. There are also a lot of molecules present in natural feed additives that can inhibit the inflammatory cytokines and inhibit the liberation of factor κB. This procedure is required for the production of inflammation in inflammatory bowel disease. One study on rats showed that 32 alkaloids were having the effect of destruction of epithelial barrier in experimental models.

Piper longum is the plant used to extract piperine. It had anti-inflammatory properties. This alkaloid was proven to increase the pharmacological action and absorption of a feed additive curcumin from *Curcuma longa* (Diwan et al., 2011). (Hu et al., 2015) studied the effect of piperine on some rats that were experimentally induced with colitis. They showed better results in weight loss, manifestation of inflammatory mediators, injury, and diarrhea.

Another common feed additive berberine extracted from *Coptis* was found to have a strong effect on inflammatory models on intestines (Mokhber-Dezfuli et al., 2014). Another alkaloid sinomenine demonstrates its pain-killing properties on inflammatory and neuropathic pain models (Hu et al., 2015).

Role of Feed Additives used to Treat Parasitic Diseases of Animals

(Koné et al., 2011) stated that there are several compounds extracted from natural feed additives that showed a striking activity against parasites. Their examples include atanine extracted from *Evodia rutaecarpa*, eugenol that is a component of clove oil, cinnamon and bay leaf, palasonin extracted from *Butea monosperma*, alantalactone extracted from *Inula helenium*, tetra-hydroharmine extracted from *Banisteriopsis caapi*, azadirachtin, extracted from the garlic.

(Mansur et al., 2014) studied in vitro experiments on rodent cestodes that the naturally available stem bromelain, cysteine proteinase, and papain which are present in *Papaya* latex showed an anthelmintic property.

Commonly, for the control of ticks, some chemicals are used on the animals and/or to their housing. With time, frequent use of these chemicals led to the evolution of resistant species of parasites (Adenubi et al., 2018). To tackle this situation, (Rosado-Aguilar et al., 2017) studied the acaricidal properties of some naturally occurring plant species including Asteraceae, Poaceae, Fabaceae, Verbenaceae, Lamiaceae, and Piperaceae. They have found that the secondary metabolites of these plant species specially n-hexanal, thymol, 1,8-cineol, and, carvacrol exhibited acaricidal activity against different tick species including *Amblyomma*, *Argas*, *Dermacentor,* and *Hyalomma* ticks.

Common Feed Additives used in Veterinary Medicine Derived from Medicinal Plants

The use of traditional knowledge of commonly available feed additive is now gaining its importance in modern communities as well. In (Table 1) are described some of the feed additives, their medicinal use, mode of administration and the part(s) of the plant used (Suroowan and Mahomoodally, 2020).

Table 1: List of some commonly available natural feed additives used in daily life health problems of animals.

Sr. No	Plant Scientific Name	Portion Used	Ailment(s) Treated	Usage Guide	Reference
1	*Fumaria indica*	Whole plant	Diarrhea	Orally	Abbasi et al., (2013)
2	*Eucalyptus camaldulensis*	Flowers and Leaves	Cold and fever	Topically	Abbasi et al., (2013)
3	*Fumaria officinalis*	Leaves and Seeds	Diarrhea and fever	Orally	Abbasi et al., (2013)
4	*Fagopyrum esculentum*	aerial	Antimicrobial, diuretic and bactericidal	Orally	Ahmed and Murtaza (2015)
5	*Ficus palmata Forssk.*	Leaves	Anti-parasitic	Orally	Ahmed and Murtaza (2015)
6	*Isodon rugosus*	aerial	Against fleas	Topically	Ahmed and Murtaza (2015)
7	*Leptopus cordifolius*	Rootss and Leaves	Anti-parasitic	Orally	Ahmed and Murtaza (2015)
8	*Melia azedarach*	Seedss	Anti-parasitic	Orally	Ahmed and Murtaza (2015)
9	*Primula denticulata*	Whole plant decoction	Hepatic fever	Orally	Ahmed and Murtaza (2015)
10	*Senecio chrysanthemoides*	aerial	Anti-parasitic	Orally	Ahmed and Murtaza (2015)
11	*Skimmia laureola*	Leaves	Cold and shivering	Orally	Ahmed and Murtaza (2015)
12	*Aquilegia pubiflora*	Aerial	Anti-parasitic	Orally	Ahmed and Murtaza (2015)
13	*Arisaema jacquemontii*	Whole plant	Cholera, dyspepsia and snake bite	Orally	Ahmed and Murtaza (2015)
14	*Arisaema flavum*	Leaves	Foot and mouth disease	Orally	Ahmed and Murtaza (2015)
15	*Lavandula lanata*	Flowers	Cold	Orally	Benítez et al. (2012)
16	*Marrubium vulgare*	Flowersing stems	Cold	Orally	Benítez et al. (2012)

17	*Marrubium supinum*	Flowersing stems	Cold	Orally	Benítez et al. (2012)
18	*Stipa tenacissima*	Leaves	Cold	Orally	Benítez et al. (2012)
19	*Berberis vulgaris*	Roots and bark	Gastroparasites of intestines and Coughing	Orally	Davis et al. (1995)
20	*Pinus wallichiana*	Resins	Coughing and endo-parasites	Orally	Davis et al. (1995)
21	*Sophora mollis*	Leaves and Flowers	Liver flukes	Orally	Davis et al. (1995)
22	*Cuminum cyminum*	Seeds	Mastitis	Orally	Dilshad et al. (2010)
23	*Galium aparine*	Leaves and Seeds	Mastitis	Orally	Dilshad et al. (2010)
24	*Acacia karroo*	Bark and Leaf	Diarrhea and parasites of intestines	Orally	Dold and Cocks (2001)
25	*Agapanthus praecox*	Roots	Diarrhea	Orally	Dold and Cocks (2001)
26	*Bulbine alooides*	Roots	Red water	Orally	Dold and Cocks (2001)
27	*Curtisia dentata*	Bark	Heart water disease	Orally	Dold and Cocks (2001)
28	*Gnidia capitata*	Roots	Heart water disease in cows and anthrax	Orally	Dold and Cocks (2001)
29	*Hippobromus*	Bark	Bark used for Heart water disease and Diarrhea	Orally	Dold and Cocks (2001)
30	*Indigofera sessilifolia*	Roots	Diarrhea	Orally	Dold and Cocks (2001)
31	*Mystroxylon aethiopicum*	Bark	Heart water disease	Orally	Dold and Cocks (2001)
32	*Pelargonium reniforme*	Roots decoction	Diarrhea, Heart water disease	Orally	Dold and Cocks (2001)
33	*Stangeria eriopus*	Roots	Internal parasites in livestock	Orally	Dold and Cocks (2001)
34	*Strychnos decussata*	Bark infusion	Roundworm in cows	Orally	Dold and Cocks (2001)
35	*Strychnos henningsii*	Bark infusion	Heart water disease and diarrhea in cattle	Orally	Dold and Cocks (2001)
36	*Capsicum annuum*	Fruits	Helminthiasis, Blood parasites	Orally	Farooq et al. (2008)
37	*Pinus roxburghii*	Oil	Parasitic mites	Topically	Farooq et al. (2008)
38	*Jatropha curcas*	Roots and Leaves	Mastitis and Anti-parasitic	Orally	Ganesan et al. (2008)
39	*Acacia nilotica*	Bark	Pneumonia problem	Orally	Gradé et al. (2009)
40	*Acalypha fruticosa*	Roots	Pneumonia problem	Orally	Gradé et al. (2009)
41	*Acacia oerfota*	Bark	Pneumonia problem	Orally	Gradé et al. (2009)
42	*Acmella caulirhiza*	Roots	Pneumonia problem	Orally	Gradé et al. (2009)
43	*Acacia sp.*	Fruits	pox	Orally	Gradé et al. (2009)
44	*Aeollanthus sp.*	Roots	Blood parasites	Orally	Gradé et al. (2009)
45	*Balanites aegyptiacus*	Exudate	Heart water disease	Orally	Gradé et al. (2009)
46	*Aspilia mossambicensis*	Fruits and Roots	Blood parasites	Orally	Gradé et al. (2009)
47	*Calotropis procera*	Whole plant	Blood parasites	Orally	Gradé et al. (2009)
48	*Butyrospermum paradoxum*	Seeds oil	Parasitic mites	Orally	Gradé et al. (2009)
49	*Capparis fascicularis*	Bark	Heart water disease	Orally	Gradé et al. (2009)
50	*Capparis tomentosa*	Roots	Blood parasites	Orally	Gradé et al. (2009)
51	*Commiphora habessinica*	Exudate	Parasitic mites	Orally	Gradé et al. (2009)
52	*Capparis sp.*	Bark	Blood parasites	Orally	Gradé et al. (2009)
53	*Carica papaya*	Seeds	parasites of intestines	Orally	Gradé et al. (2009)
54	*Cucumis sp.*	Fruits	Blood parasites	Orally	Gradé et al. (2009)
55	*Dombeya rotundifolia*	Leaves and Flowerss	Newcastle disease	Orally	Luseba and Van der Merwe (2006)
56	*Euphorbia cooperi*	aerial	Blackquarter	Orally	Luseba and Van der Merwe (2006)
57	*Synadenium cupulare*	Latex	Eye infection and black quarter	Topically	Luseba and Van der Merwe (2006)
58	*Cynoglossum zeylanicum*	Whole plant	Eyes problem	Topically	Malla and Chhetri (1970)
59	*Dioscorea deltoidea*	Tuber	Constipation	Orally	Malla and Chhetri (1970)
60	*Maesa chisia*	Bark	Ringworm	Topically	Malla and Chhetri (1970)
61	*Solanum indicum*	Leaves	Ringworm	Topically	Malla and Chhetri (1970)
62	*Combretum caffrum*	Leaves	Eyes problem	Topically	Masika et al. (2002)
63	*Hibiscus malacospermus*	Roots	Retained placenta and intestinal worms	Orally	Masika et al. (2002)
64	*Tephrosia macropoda*	Roots, Seeds and Leaves	Anti-parasitic for cattle	Orally	McGaw and Eloff (2008)

65	*Piper betle*	Leaves	Constipation and end parasites	Orally	Nair and Chanda (2008)
66	*Jasminum humile*	Roots and Flowers	Fever and pain	Orally	Pande et al. (2007)
67	*Aconitum heterophyllum*	Unspecified	Intestinal worm and fever	Orally	Pande et al. (2007)
68	*Lantana camara*	Leaves	Measles	Orally	Pande et al. (2007)
69	*Nicotiana tabacum*	Leaves	Intestinal worms	Orally	Pande et al. (2007)
70	*Ocimum basilicum*	Leaves and Seeds	Skin infection	Topically	Pande et al. (2007)
71	*Ocimum tenuiflorum*	Leaves and Seeds	Coughing and fever	Orally	Pande et al. (2007)
72	*Abutilon indicum*	Leaves and Fruits	Dysentery and diarrhea	Orally	Parthiban et al. (2016)
73	*Adhatoda vasica*	Leaves and bark	Coughing, Diarrhea and dysentery	Orally	Parthiban et al. (2016)
74	*Datura metel*	Fruits and Leaves and Roots	Dysentery and skin diseases	Orally, Topically	Parthiban et al. (2016)
75	*Euphorbia hirta*	Latex	Wound	Topically	Parthiban et al. (2016)
76	*Ficus benghalensis*	Latex and Roots	Maggot wound and stomach ache	Topically, Orally	Parthiban et al. (2016)
77	*Gymnema sylvestre*	Leaves	Fever	Orally	Parthiban et al. (2016)
78	*Madhuca indica*	Flowers	Fever	Orally	Parthiban et al. (2016)
79	*Tribulus terrestris*	Leaves	Diarrhea	Orally	Parthiban et al. (2016)
80	*Sida acuta Burm*	Leaves	Diarrhea	Orally	Pragada and Rao (2012)
81	*Musa paradisiaca*	Fruits	Measles	Topically	Phondani et al. (2010)
82	*Artemisia kermanensis*	Aerial part	Anti-fungal	Orally	Pirbalouti et al. (2009)
83	*Quercus brantii*	Fruits	Anti-fungal	Topically	Pirbalouti et al. (2009)
84	*Artemisia herba*	aerial	Anti-parasitic	Orally	Pirbalouti et al. (2009)
85	*Scrophularia striata*	aerial	Anti-fungal	Topically	Pirbalouti et al. (2009)
86	*Tanacetum polycephalum*	Flowers	Anti-fungal	Topically	Pirbalouti et al. (2009)
87	*Thymbra spicata*	aerial	Anti-fungal	Topically	Pirbalouti et al. (2009)
88	*Thymus daenensis*	aerial	Anti-fungal	Topically	Pirbalouti et al. (2009)
89	*Annona mucosa*	Exudate	Anti-parasitic	Orally	Ritter et al. (2012)
90	*Bactris gasipaes*	Leaves	Anti-parasitic	Orally	Ritter et al. (2012)
91	*Bixa orellana*	Leaves	Parasitic mites	Orally	Ritter et al. (2012)
92	*Cymbopogon citratus*	Leaves	Anti-parasitic	Orally	Ritter et al. (2012)
93	*Derris spruceana*	Roots	Parasitic mites	Orally	Ritter et al. (2012)
94	*Eleutherine bulbosa*	Roots	Parasitic mites	Orally	Ritter et al. (2012)
95	*Gossypium barbadense L.*	Leaves	Anti-parasitic	Orally	Ritter et al. (2012)
96	*Lecythis pisonis*	Leaves	Parasitic mites	Orally	Ritter et al. (2012)
97	*Lippia alba*	Roots	Anti-parasitic	Orally	Ritter et al. (2012)
98	*Ouratea aquatica*	Bark	Parasitic mites	Orally	Ritter et al. (2012)
99	*Quassia amara*	Leaves	Anti-parasitic	Orally	Ritter et al. (2012)
100	*Tithonia diversifolia*	Leaves	Parasitic mites	Orally	Ritter et al. (2012)
101	*Adiantum capillus*	Leaves and stem	Coughing	Orally	Sehgal (2013)
102	*Brassica campestris*	Leaves and Seeds	Injuries and mastitis	Topically	Sehgal (2013)
103	*Brassica juncea*	Leaves and Seeds	Intestinal worms	Orally	Sehgal (2013)
104	*Emblica officinalis*	Fruits	Coughing and cold	Orally	Sehgal (2013)
105	*Eucalyptus umbellata*	Leaves	Cold and fever	Orally	Sehgal (2013)
106	*Jasminum multiflorum*	Roots and Flowers	Fever and pain	Orally	Sehgal (2013)
107	*Senna occidentalis*	Leaves	Diarrhea	Orally	Sehgal (2013)
108	*Artemisia nilagirica*	Leaves	Anti-parasitic and lice	Orally, Topically	Sharma et al. (2012)
109	*Bambusa arundinacea*	Leaves and stem	Anti-parasitic	Orally	Sharma et al. (2012)
110	*Cedrus deodara*	Stem	Foot and mouth disease	Topically	Sharma et al. (2012)
111	*Eruca sativa*	Seeds oil	Parasitic mites and small pox	Topically	Sharma et al. (2012)
112	*Grewia optiva*	Leaves	Remove parasites	Orally	Sharma et al. (2012)
113	*Pyrus pashia*	Roots and Leaves	Parasitic mites and appetite stimulant	Topically, Orally	Sharma et al. (2012)
114	*Pyrus pashia*	Fruits	Eye infection	Topically	Sharma et al. (2012)
115	*Mangifera indica*	Leaves	Gastroparasites of intestines	Orally	Sujon et al. (1970)
116	*Momordica charantia*	Leaves	Gastroparasites of intestines	Orally	Sujon et al. (1970)
117	*Harrisonia abyssinica*	Fruits	Endoparasites	Orally	Ulhaq et al. (2011)
118	*Cassytha filiformis*	Twigs	Liver fluke	Orally	Upadhyay et al. (2011)

119	*Crateva magna*	Bark	Anthrax	Orally	Upadhyay et al. (2011)
120	*Diospyros buxifolia*	Fruits	Foot and mouth disease	Orally	Upadhyay et al. (2011)
121	*Diospyros montana*	Bark	Dysentery	Orally	Upadhyay et al. (2011)
122	*Enicostemma hyssopifolium*	Whole plant	Intestinal worms	Orally	Upadhyay et al. (2011)
123	*Ficus racemosa*	Fruits	Diarrhea	Orally	Upadhyay et al. (2011)
124	*Launaea procumbens*	Roots	Diarrhea	Orally	Upadhyay et al. (2011)
125	*Ocimum canum*	Seeds and Leaves	Diarrhea	Orally, Topically	Upadhyay et al. (2011)
126	*Sesbania sesban*	Seeds	Diarrhea	Orally	Upadhyay et al. (2011)
127	*Acacia tortilis*	tips of branches	Diarrhea	Orally	Van der Merwe et al. (2001)
128	*Phyllanthus burchellii.*	aerial	Eye infections	Topically	Van der Merwe et al. (2001)
129	*Hypoxis hemerocallidea*	Corms	Fertility enhancement	Orally	Van der Merwe et al. (2001)
130	*Peltophorum africanum*	Bark and Roots bark	Tonic and Diarrhea	Orally	Van der Merwe et al. (2001)
131	*Croton gratissimus*	Leaves and Roots	Pneumonia problem, tonic and fertility enhancement	Orally	Van der Merwe et al. (2001)
132	*Solanum panduriforme*	Fruits	Diarrhea	Orally	Van der Merwe et al. (2001)
133	*Indigofera frutescens*	Roots bark decoctions	Anti-parasitic	Orally	Watt and Breyer- Brandwijk (1962)
134	*Lantana rugosa*	Leaves	Pastes	Topically	Watt and Breyer- Brandwijk (1962)
135	*Pelargonium sidoides*	Decoction of unspecified parts	Anti-parasitic for calves	Orally	Watt and Breyer- Brandwijk (1962)

Conclusion and Future Prospects

A lot of research is ongoing in the field of determining the effects of natural herbal extracts having the potential to control and treat animal infections. This becomes an emerging and interesting major in Veterinary Medicine, Veterinary Pharmacology, Veterinary Reproduction, Veterinary Parasitology, and other related fields. The use of Natural Feed additives to treat health problems of livestock is increasing day by day and they are becoming an integral part of veterinary medicine. Therefore, expanding the growth of plant feed additives having functional secondary metabolites will boost animal production and health due to having nutritional combinations of antioxidants, fatty acids, and important vitamins. Because of the growing antibiotic resistance and knowledge of ethno-veterinary medicine, natural feed additive products are attracting global researchers as an alternative medicine to synthetic drugs. In this respect, experimental research is needed on animals and in vivo to approve the usefulness of bioactive products extracted from plant feed additives. This is also to discover new medicinal remedies.

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Chapter 15

Improving Fillet Quality Traits in Cultured Fish with Natural Feed Additives

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ABSTRACT

The use of natural feed additives has emerged as a promising strategy to enhance fillet quality traits in cultured fish while meeting consumer demands for sustainable and health-promoting aquaculture products. This chapter provides a comprehensive overview of the effects of various natural feed additives including plant-derived compounds, algal products, probiotics, prebiotics, enzymes and organic acids on critical fillet quality parameters. The findings demonstrate that these additives can modulate nutritional composition, improve textural properties, enhance color and appearance and positively influence flavor and odor characteristics. Moreover, natural feed additives exhibit potent antioxidant and antimicrobial properties, contributing to extended shelf-life and improved oxidative stability of fish fillets. The mechanisms underlying these effects such as pigmentation, antioxidant activity, muscle protein interactions, gut microbiota modulation and nutrient metabolism. Emerging trends such as the exploration of novel sources, combination strategies and omics-based approaches are identified as future research directions. It has been concluded that the strategic incorporation of natural feed additives in aquaculture production systems can significantly enhance the fillet quality traits, contributing to the sustainable growth and competitiveness of the aquaculture industry while meeting evolving consumer expectations for premium, nutritious and eco-friendly seafood products.

KEYWORDS		
Cultured fish, Consumer acceptance, Fillet quality, Natural feed additives, Sustainable aquaculture	Received: 13-May-2024 Revised: 16-July-2024 Accepted: 11-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Fillet quality traits play a pivotal role in the success and sustainability of the aquaculture industry. Consumers are increasingly discerning, demanding high-quality fish products that not only meet their sensory expectations but also provide nutritional benefits and assurance of safety and environmental responsibility. The traits such as texture, color, flavor and nutrient composition significantly influence the consumer acceptance, purchasing decisions and ultimately the marketability and profitability of aquaculture products. Poor fillet quality can lead to product rejection, shorter shelf-life and reduced market value, thus, undermining the economic viability of aquaculture operations (Lohita and Srijaya, 2024). The use of natural feed additives presents a promising approach to enhancing fillet quality traits in cultured fish while addressing consumer concerns and promoting sustainable aquaculture practices. Conventional aquaculture feeds often lack essential nutrients and compounds necessary for optimal fillet quality and the use of synthetic additives has raised concerns regarding food safety, environmental impacts and antimicrobial resistance (Hossain et al., 2024). Natural feed additives derived from plants, animals or microbial sources offer a potential solution by providing bioactive compounds that can improve the fillet texture, color, flavor and nutritional composition. Furthermore, the use of natural additives aligns with consumer preferences for sustainable and environmentally friendly aquaculture practices, potentially increasing the marketability and consumer acceptance of aquaculture products (Xie et al., 2024).

Fillet quality traits such as texture, color and nutritional composition directly influence the consumer acceptance and purchasing decisions. A poor fillet quality can lead to reduced shelf-life, lower market value and potential consumer rejection. Ensuring consistent and desirable fillet quality is crucial for the aquaculture industry to remain competitive and meet consumer demands. Consumers are becoming increasingly health-conscious and demand products that are nutritious, safe and environmentally sustainable. The growing awareness of the health benefits associated with consuming fish and seafood has driven the demand for high-quality aquaculture products. Meeting consumer preferences and market demands for premium aquaculture products can lead to higher profit margins and increased market shares (Calanche et al., 2020).

Conventional aquaculture feeds often lack essential nutrients such as polyunsaturated fatty acids (PUFAs), vitamins and pigments which are crucial for enhancing the fillet quality traits (Kandathi et al., 2020). The use of synthetic feed additives like antibiotics and growth hormones have raised concerns about potential risks to human health, environmental contamination and antimicrobial resistance (Ogunkalu 2019). There is a growing demand for sustainable and natural alternatives to conventional feed ingredients and additives to improve fillet quality while addressing consumer concerns. The nutritional composition of fish fillets is a critical factor influencing their quality, consumer acceptance and health benefits. Proteins, lipids, minerals and vitamins play significant roles in determining the nutritional value and sensory properties of the fish fillets (Sobczak et al., 2021).

Fillet Quality Traits

Nutritional Composition (protein, lipids, minerals, vitamins)

The protein contents and quality are crucial for the nutritional value and textural properties of fish fillets. High-quality proteins with a balanced amino acid profile contribute to the firmness and desirable mouth-feel of fish flesh. Additionally, protein content influences water-holding capacity, which impacts juiciness and tenderness (Sampels 2015; Khalili and Sampels, 2018). Lipid composition, particularly the levels of omega-3 polyunsaturated fatty acids (PUFAs) has a significant impact on human health benefits and flavor. Omega-3 PUFAs, such as Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA) are known for their cardiovascular and neurological benefits. Additionally, lipids contribute to the characteristic flavor and aroma to the fish fillets (Xie et al., 2023).

Mineral content, such as calcium, iron, zinc and selenium, contributes to the overall nutritional profile of fish fillets. These minerals play the essential roles in various physiological processes and can impact fillet quality through their involvement in enzymatic reactions and structural integrity (Kiczorowska et al., 2019). The vitamins like vitamin A, D and E are also important components of fish fillets. Vitamin A contributes to vision, immune function and growth (Saheli et al., 2021), vitamin D is essential for calcium absorption and bone health while vitamin E functions as an antioxidant, protecting lipids from oxidation and contributing to the shelf-life (Rahimnejad et al., 2021).

Textural Properties (firmness and gaping)

Textural properties including firmness and gaping are crucial determinants of fillet quality and consumer acceptance. Firmness and flesh texture are among the most important attributes considered by consumers when evaluating fish products. A firm, dense texture is generally preferred, as it contributes to a desirable mouth-feel and overall eating experience (Kotzamanis et al., 2020). Gaping or the separation of muscle fibers can leads to an unappealing appearance and decreased product quality. Gaping can occur during various stages of processing such as filleting, skinning and storage and can be exacerbated by factors like handling stress, temperature fluctuations and nutritional deficiencies. Gaping can also results from the degradation of connective tissue proteins such as collagen which provides structural support to the muscle fibers. Proper handling, processing techniques and nutritional strategies aimed at maintaining the integrity of connective tissue and thus can help minimize the gaping and to improve the fillet quality ((Zhang et al., 2023).

Color and Appearance

Color and visual appearance are crucial attributes that significantly influence the consumer perception and purchase decisions in the fish industry (Proi et al., 2023). The desirable reddish-orange color of red tilapia fillets, for example, is primarily attributed to the presence of carotenoid pigments such as astaxanthin. Carotenoids are naturally synthesized by microalgae and accumulate in the flesh of fish through their diet. However, the inability of fish to synthesize carotenoids de-novo necessitates the inclusion of these pigments in aquaculture feeds to achieve the desired color intensity. In addition to pigments, factors such as feed composition, processing methods and storage conditions can affect the fillet color and appearance (Harith et al., 2024). For instance, the presence of lipid oxidation products can lead to discoloration and an unappealing appearance and ultimately reducing the marketability of fish products (Samarajeewa 2024).

Flavor and Odor Characteristics

Flavor and odor are crucial sensory attributes that determine consumer acceptance and enjoyment of fish products (Chen et al., 2022). These characteristics are influenced by a complex interplay of various volatile and non-volatile compounds present in the fish flesh (Martin et al., 2023). Lipid composition particularly the levels of volatile compounds and fatty acids significantly influence the flavor and odor. Fatty acids such as EPA and DHA can contribute to desirable flavors, while the breakdown of lipids during storage or processing can leads to the formation of off-flavors and undesirable odors. Additionally other factors such as feed composition, handling practices and microbial activity can impact flavor and odor characteristics. For example, the presence of certain amino acids or nucleotides can contribute to desirable umami flavors, while microbial spoilage can result in unpleasant odors and flavors (Cheng et al., 2024).

Shelf-life and Oxidative Stability

Shelf-life and oxidative stability are essential factors that determine the quality and marketability of fish fillets during storage and distribution. Lipid oxidation, a major cause of quality deterioration, can lead to off-flavors, discoloration and a decrease in nutritional value. Oxidative processes are influenced by various factors, including the fatty acid composition of the fish, exposure to oxygen, light and temperature as well as the presence of pro-oxidants and antioxidants. Fish species with high levels of polyunsaturated fatty acids (PUFAs) are more susceptible to oxidation due to the higher degree of unsaturation in their lipids (Messina et al., 2021).

To extend the shelf-life and to prevent oxidative changes various strategies can be employed, such as inclusion of antioxidants in feeds or packaging materials, proper handling and storage conditions e.g. temperature control, modified atmosphere packaging and the use of processing techniques that minimize the oxidation (Petcu et al., 2023). Antioxidants both natural and synthetic, can effectively inhibit lipid oxidation by scavenging free radicals or chelating metal ions that catalyze oxidation reactions. Natural antioxidants such as Tocopherols, vitamin E, carotenoids and plant extracts are gaining increasing attention due to their potential health benefits and consumer acceptance (Blasi and Cossignani 2020).

Fillet quality traits including nutritional composition, textural properties, color and appearance, flavor and odor characteristics and shelf-life and oxidative stability are critical factors influencing the success and sustainability of the aquaculture industry. Addressing these quality traits through appropriate feed formulations, handling practices and processing techniques are essential for meeting consumer demands and ensuring the marketability of cultured fish products (Abd El-Fatah et al., 2023).

Factors Influencing Fillet Quality

Fish Species and Genetic Factors

Different fish species have inherent variations in muscle structure, lipid composition and other factors that can significantly impact fillet quality traits (Duart et al., 2021). For example salmonids like trout and salmon generally have higher levels of beneficial omega-3 fatty acids compared to other species (Lutfi et al., 2022). Within a species, genetic factors play a crucial role in determining the fillet quality characteristics like flesh color, texture and fatty acid profiles (Moroni et al., 2024). These genetic variations can be exploited through selective breeding programs to improve desirable traits. Selective breeding has been successful in enhancing traits like muscle yield, flesh firmness and pigmentation in various cultured fish species (Johnson 2021).

Diet Composition and Feed Additives

The composition of the aquaculture diet including protein sources, lipid sources and the inclusion of specific nutrients or additives can significantly influence the fillet quality traits. Protein sources affect the amino acid profiles of fish fillets, which in turn influence textural properties like firmness and water-holding capacity. Plant-based proteins may result in softer textures compared to animal-based proteins. Lipid sources rich in long-chain polyunsaturated fatty acids (LC-PUFAs), such as fish oil can improve the nutritional composition, flavor and oxidative stability of fish fillets. Feed additives like carotenoid pigments e.g. astaxanthin, vitamins e.g. vitamin E and minerals can enhance fillet color, nutritional value and oxidative stability (Webb 2021).

Environmental Conditions (water quality, temperature, etc.)

Water quality parameters such as dissolved oxygen levels, pH and ammonia concentrations can significantly affect the fish health and consequently the fillet quality. Poor water quality can induce stress and affect muscle metabolism, leading to textural defects and reduced shelf-life. Temperature fluctuations can cause stress and influence muscle metabolism, affecting textural properties like firmness, gaping and drip loss. Optimal temperature ranges are species-specific and crucial for maintaining fillet quality. Seasonal variations in environmental conditions such as temperature and photoperiod can also impact fillet quality traits like color, lipid composition and texture (Gisbert et al., 2021).

Stress and Handling Practices

Stress during handling, transport and slaughter can lead to physiological changes in fish that negatively impact fillet quality. Stress can deplete muscle energy reserves, affecting post-mortem pH changes and textural properties. Improper handling practices such as rough treatment or exposure to extreme temperatures can cause physical damage to the muscle tissue and accelerate quality deterioration. Pre-slaughter stress can result in the depletion of muscle energy reserves, affecting post-mortem pH changes and textural properties like gaping and drip loss. Proper handling and slaughter techniques are crucial to minimize the stress and to maintain the fillet quality (Dong et al., 2023).

By understanding and addressing these key factors that influence the fillet quality, aquaculture producers can implement appropriate management strategies, selective breeding programs, optimized feed formulations and improved handling and processing techniques to consistently produce high-quality cultured fish products that meet consumer demands and market expectations (Little et al., 2018).

Natural Feed Additives for Improving the Fillet Quality

Plant-derived Compounds (essential oils, polyphenols, carotenoids)

Plant-derived compounds such as essential oils, polyphenols and carotenoids have gained significant attention as natural feed additives for improving the fillet quality in cultured fish. Essential oils extracted from aromatic plants possess antioxidant and antimicrobial properties that can enhance shelf-life and improve the sensory characteristics of fish fillets. Polyphenols, found in various plant sources like fruits, vegetables and herbs can also contribute in oxidative stability and potentially improve the textural properties through their interactions with muscle proteins. Carotenoid pigments particularly astaxanthin and canthaxanthin play a crucial role in enhancing the desirable reddish-orange color of salmonid fillets, improving their marketability and consumer acceptance (Biswas et al., 2023). Algal products including microalgae and seaweeds are rich sources of bioactive compounds with potential benefits for fillet quality. Microalgae such as Chlorella and Spirulina are valuable sources of proteins, pigments and polyunsaturated fatty acids (PUFAs) and can improve the nutritional composition and color of fish fillets (López-Pedrouso et al., 2020). Seaweeds like brown algae (*Ascophyllum nodosum*), contain polyphenols, minerals and other compounds that can enhance the antioxidant capacity, texture and flavor characteristics (Peñalver et al., 2020; Tagliapietra and Clerici, 2023).

Table 1: Different factors affecting the fillet quality of a fish

Factor	Description
Genetics	The genetic background of the fish plays a crucial role in determining fillet quality. Different fish species and even different strains within a species can have varying fillet characteristics such as texture, color and fat content. Selective breeding programs can be used to improve fillet quality by focusing on desirable traits.
Nutrition	The diet of the fish significantly influences the fillet quality. Proper nutrition is essential for optimal growth, health and fillet composition. Factors such as type and quality of feed ingredients, feed formulation and feeding practices can affect fillet quality. For example, the inclusion of high-quality protein sources, essential fatty acids and micronutrients in the diet can enhance fillet texture, flavor and nutritional value.
Rearing conditions	The environmental conditions in which fish are reared can impact the fillet quality. Water quality parameters, such as temperature, oxygen levels, pH and dissolved solids should be maintained within the optimal ranges to ensure fish health and fillet quality. Stocking density, water flow rates and other management practices also influence fillet quality by affecting fish stress levels and growth performance.
Harvest and processing	The methods used for harvesting and processing fish can significantly affect the fillet quality. Proper handling practices, such as minimizing stress during harvest, rapid chilling and maintaining hygiene are crucial to preserve fillet quality. The time between harvest and processing should be minimized to prevent deterioration. Appropriate processing techniques, such as filleting, trimming and packaging should be employed to ensure consistent quality and extend shelf life.
Storage conditions	Post-harvest storage conditions play a vital role in maintaining the fillet quality. Factors such as temperature, humidity and storage duration can impact fillet freshness, texture and flavor. Proper cold chain management, including rapid cooling and maintaining the appropriate storage temperatures are essential to prevent the spoilage and to maintain the quality. Modified atmosphere packaging and other advanced storage technologies can further extend the shelf life of fish fillets.
Seasonal variations	Fillet quality can vary depending on the season, particularly in wild-caught fish. Factors such as water temperature, food availability and reproductive cycles can influence fillet composition and quality. For example, fish caught during the spawning season may have lower fillet quality due to changes in body composition and energy allocation. Understanding seasonal variations in fillet quality is important for optimizing the harvest strategies and meeting market demands.
Pre-slaughter factors	The pre-slaughter conditions and practices can impact the fillet quality. Factors such as duration of fasting before harvest, transportation conditions and handling stress can affect the fillet quality. Proper pre-slaughter management like minimizing the stress, providing adequate fasting periods and ensuring humane handling help to maintain the fillet quality and to improve animal welfare.
Post-mortem changes	Fillet quality can deteriorate over time due to post-mortem changes in the fish muscle. Factors such as enzymatic activity, oxidation and microbial growth can lead to quality degradation. Proper post-mortem handling such as rapid chilling and appropriate storage conditions can slow down these changes and extend the shelf life of fish fillets. Understanding the biochemical and microbiological processes involved in the post-mortem changes can help to develop the strategies to maintain fillet quality.

Probiotics which are live beneficial microorganisms and pre-biotics, are non-digestible food ingredients that selectively promote the growth of beneficial gut bacteria have shown promise in improving the fillet quality in aquaculture. Probiotics can modulate the gut microbiota, improve nutrient utilization and enhance immune function, thus potentially leading to improved growth performance and fillet quality (Wang et al., 2020). Prebiotics such as inulin and fructo-oligosaccharides can selectively stimulate the growth of beneficial gut bacteria, contributing to improved gut health and nutrient absorption, which can positively impact the fillet quality. Enzymes and organic acids can be incorporated into aquaculture feeds to improve nutrient digestibility and absorption, potentially enhancing fillet quality. Exogenous enzymes such as phytases and proteases can improve the utilization of plant-based feed ingredients, leading to better growth performance and fillet yield. Organic acids like citric acid and butyric acid can modulate gut pH, inhibit pathogenic bacteria and improve nutrient absorption, potentially benefiting the fillet quality (Busti et al., 2020).

Table 2: Role of feed additives in enhancing the performances in aquaculture

Natural feed additives	Instance	Mode of actions	References
Essential fatty acids	Arachidonic acid, eicosapentaenoic acid, linolenicacid and linoleic acid	Omega-3 polyunsaturated fatty acids are among the most frequently used ingredients in aquaculture feed, conclude that differences in EFA requirement for metabolic adaptation to different habits in aquaculture	Monroig et al. (2022) and Lu et al. (2021)
Essential oils	*Oreganum heracleoticum*, *Sparusaurata*, estergole and oleoresin	Increase the growth performance and antioxidant effects and enhance the muscle protein activity	Malheiros et al. (2020) and Tran et al. (2018)
Probiotics	*Baciiluspumlis B16*, *B. mojavensis J7*, *Streptomyces panacagri* and *Streptomyces flocculus*, *Lactobacillus salivarius UCC118* and *Lactobacillus* spp. *MSU3IR*	Protective against foodborne pathogens and is an alternative to antibiotics and improves the bacteriocin level of biomolecules	X. F. Liu et al. (2015)
Prebiotics	Mannan-oligosaccharides (MOS), fructoligosaccharides and galactoligosaccharides	Promote innate immune response, increase fish growth and improve heath	Carbone and Faggio (2016) and Mugwanya et al. (2022)
Synbiotics	*Bacillus subtilis WB60* and MOS	Control lysozyme activity during digestion in the gut	S. Lee et al. (2018)
Organic acids	Acetic acid, formic acid, fumaric acid, lactic acid, propionic acid and citric acid	Act as anesthetics for fish, causes immunosuppression, promotes growth and induces weight gain	Davies et al. (2020), Hoseinifar et al. (2017) and Omosowone et al. (2015)
Exogenous enzymes	Protease, amylase, phytase, lipase and carbohydrase enzymes	Unique ability to grow and increase nutritional value	Khieokhajonkhet et al. (2014) and Rodriguez et al. (2018)

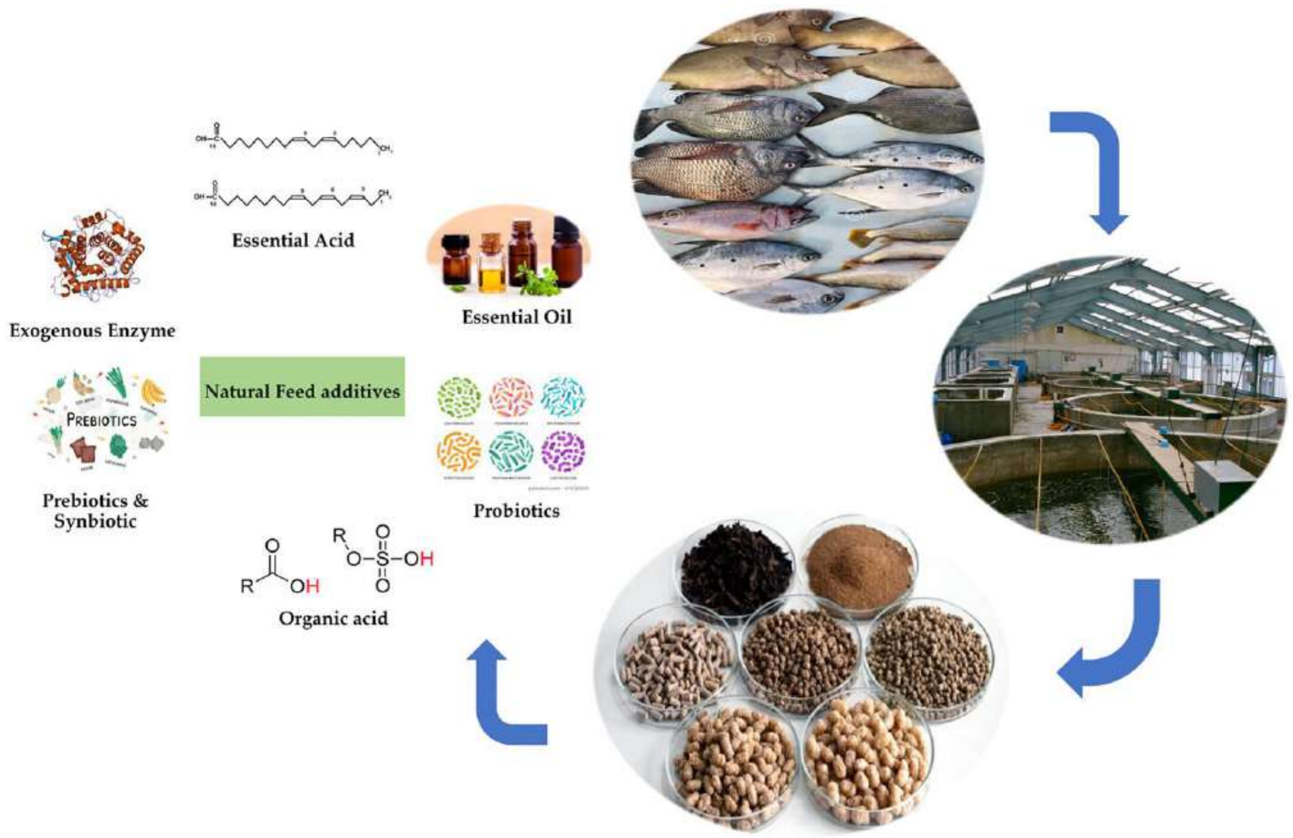

Fig. 1: Feed additives in aquaculture (Marimuthu et al., 2022).

Natural feed additives can modulate the protein, lipid and mineral content of fish fillets, thereby influencing their nutritional profile. For instance, the inclusion of plant-derived protein sources, such as soybean meal or pea protein concentrate can affect the amino acid composition and digestibility of fillet proteins. Similarly, the use of alternative lipid sources like vegetable oils or algal oils can impact the fatty acid profiles and lipid content of fillets. Mineral-rich additives, such as seaweeds and clay minerals can enhance the mineral composition of fillets, providing essential micronutrients like selenium, iodine and zinc (El-Sayed et al., 2023).

One of the primary goals of using natural feed additives is to enrich fish fillets with beneficial fatty acids, particularly omega-3 polyunsaturated fatty acids (PUFAs). Microalgae like Schizochytrium and Nannochloropsis are rich sources of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), respectively and their inclusion in aquaculture feeds can effectively increase the levels of these essential fatty acids in fish fillets. Marine-derived oils and fish by-products can also contribute to the enrichment of omega-3 PUFAs in fillets (Naghdiet al., 2024).

Natural feed additives can also fortify fish fillets with antioxidants and vitamins, enhancing their nutritional value and shelf-life. Plant-derived polyphenols, carotenoids and tocopherols (vitamin E) possess potent antioxidant activities that can protect lipids from oxidation and extend the shelf-life of fish products. Additionally, microalgae and seaweeds are rich sources of vitamins, such as vitamin A, C and E, which can be transferred to fish fillets through dietary supplementation (Ali et al., 2022).

By modulating the nutritional composition of fish fillets, natural feed additives can enhance their nutritional value, promote human health benefits and potentially improve the consumer acceptance and marketability. However, it is crucial to consider the potential trade-offs and interactions between different nutritional components, as well as the impact on sensory attributes and overall fillet quality. Careful formulation and optimization of feed additives are necessary to achieve the desired nutritional profile while maintaining other desirable fillet quality traits. Improving flesh firmness and water-holding capacity: Natural feed additives can contribute to improving the flesh firmness and water-holding capacity of fish fillets, which are crucial attributes influencing consumer acceptance and product quality. Plant-derived polyphenols and dietary fibers have been shown to interact with muscle proteins, potentially enhancing their structural integrity and water-binding capacity. For example, the inclusion of grape seed extract or citrus fiber in aquaculture feeds has been reported to improve the firmness and texture of fish fillets (Gulzar et al., 2023).

It is important to note that the effects of natural feed additives on textural properties may vary depending on the specific compounds, their inclusion levels and the fish species involved. Additionally, the interactions between different feed additives and their potential synergistic effects should be considered when formulating aquaculture diets. Careful evaluation and optimization are necessary to achieve the desired textural properties while maintaining other important fillet quality traits such as nutritional composition, color and flavor (Huang et al., 2021).

Effects on Color and Appearance

Pigmentation and Carotenoid Deposition

One of the primary effects of natural feed additives on fillet color and appearance is through pigmentation and carotenoid deposition. Carotenoid pigments such as astaxanthin and canthaxanthin are essential for imparting the desirable reddish-orange color to salmonid fillets and improving their marketability. These pigments can be sourced from natural sources like microalgae e.g. *Haematococcus pluvialis* or yeast e.g. *Phaffia rhodozyma* and incorporated into aquaculture feeds. The inclusion of these natural carotenoid sources has been shown to effectively enhance the pigmentation and color intensity of fish fillets, meeting consumer preferences and market demands (Pulcini et al., 2020).

Preventing Discoloration and Melanosis

Natural feed additives can also help to prevent the discoloration and melanosis, which are common quality defects affecting the appearance of fish fillets. Melanosis characterized by brownish-black spots, is caused by the enzymatic oxidation of phenolic compounds and can be a significant issue for certain fish species. Plant-derived polyphenols and natural antioxidants like tocopherols and carotenoids have been shown to inhibit melanosis by scavenging free radicals and chelating metal ions involved in the oxidation process. Additionally, certain plant extracts and essential oils possess anti-microbial properties that can help prevent microbial spoilage and discoloration (Zhang et al., 2023).

Influence on Fillet Surface and Muscle Structure

Natural feed additives can also influence the surface appearance and muscle structure of fish fillets, which can impact their visual appeal and acceptability. Plant-derived dietary fibers and polysaccharides have been reported to modulate the water-holding capacity and structural integrity of muscle fibers, potentially influencing the surface texture and appearance of fillets (Gao et al., 2023). Additionally, certain seaweed extracts and probiotic bacteria have been shown to influence the expression and activity of enzymes involved in muscle fiber organization and development, potentially affecting the overall muscle structure and appearance (Peng et al., 2024). It is important to note that the effects of natural feed additives on fillet color and appearance may vary depending on the specific compounds, inclusion levels and the fish species involved. Factors such as processing methods, storage conditions and lighting can also influence the perceived color and appearance of fish products. Therefore, careful evaluation and optimization of natural feed additive formulations are necessary to achieve the desired color and appearance while maintaining other important fillet quality traits (Das et al., 2020).

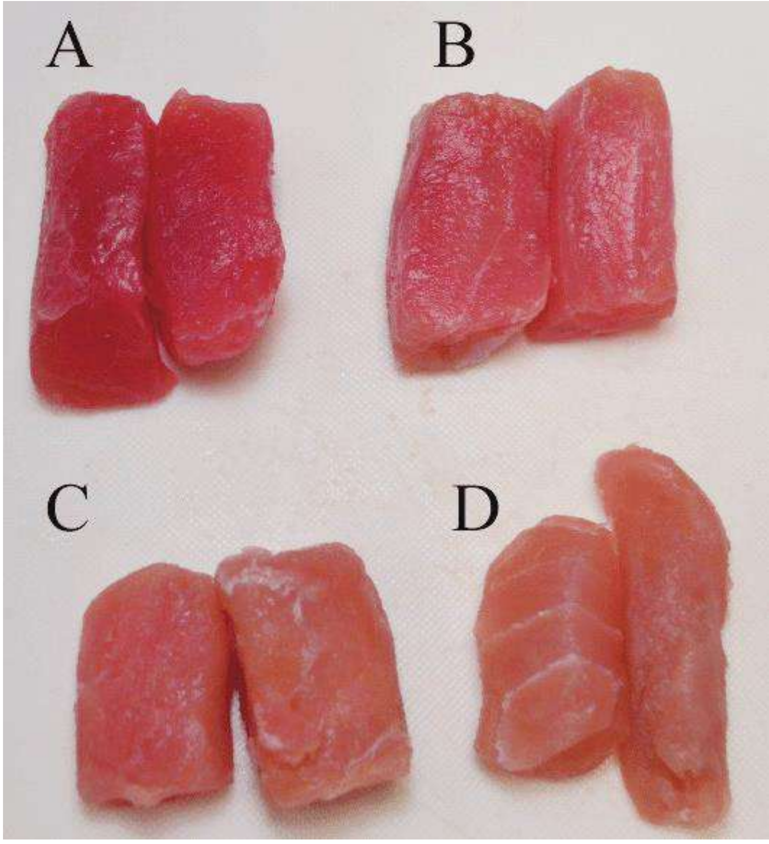

Fig. 2: Appearance of the tuna meat slice of each grade. A, excellent; B, good; C, acceptable; D, " not acceptable ”. Note that the redness is more enhanced in the higher quality meat (Mala et al., 2013)

Effects on Flavor and Odor

Modulating Volatile Compounds and Aroma Profiles

Natural feed additives can modulate the volatile compounds and aroma profiles of fish fillets, contributing to their characteristic flavors and aromas. Plant-derived essential oils and extracts, rich in terpenes, phenolic compounds and other volatile components, can impart distinct flavors and aromas to fish fillets (Resende et al., 2024). For example, the inclusion of rosemary or thyme essential oils in aquaculture feeds has been reported to influence the aroma profiles and sensory characteristics of fish products (Kunová et al., 2021).

Additionally, certain microalgae and seaweed extracts contain unique volatile compounds that can contribute to the flavor and aroma of fish fillets. For instance, the inclusion of the microalga Schizochytrium in fish diets has been shown to influence the volatile profile and impart a desirable "sea weedy" aroma to the fillets (Samuelsen et al., 2018). Reducing off-flavors and lipid oxidation: off-flavors and odors resulting from lipid oxidation are significant quality issues in fish products, affecting their sensory acceptability and shelf-life. Natural feed additives with antioxidant properties, such as plant-derived polyphenols, carotenoids and tocopherols can help reduce lipid oxidation and prevent the formation of off-flavors. For example, the inclusion of grape seed extract or green tea extract in aquaculture feeds has been shown to improve the oxidative stability and reduce the development of off-flavors in fish fillets (Ardhraet al., 2021).

The flavor and odor of fish fillets can also be influenced by the metabolites produced by gut microbiota or probiotic bacteria supplemented in aquaculture feeds. Certain probiotic strains, such as lactic acid bacteria can produce metabolites like organic acids, diacetyl and other compounds that can contribute to the flavor and aroma of fish products. Additionally, the modulation of gut microbiota by probiotics or prebiotics can influence nutrient absorption, metabolism and the production of volatile compounds, potentially affecting the overall flavor and odor profiles of fish fillets (Pongsetkul et al., 2022).

It is crucial to consider the potential interactions and synergistic effects among different natural feed additives, as well as their compatibility with other feed ingredients and processing conditions. Careful evaluation and optimization are necessary to achieve the desired flavor and odor profiles while maintaining other important fillet quality traits, such as nutritional composition, texture and shelf-life (Huang et al., 2021).

Effects of Natural Feed Additives on the Shelf-life and Oxidative Stability of Fish Fillets

Many natural feed additives possess potent antioxidant and antimicrobial properties that can contribute to extending the shelf-life and improving the oxidative stability of fish fillets. Plant-derived polyphenols, carotenoids and tocopherols (vitamin E) are known for their strong antioxidant activities, capable of scavenging free radicals and chelating metal ions involved in lipid oxidation processes. Natural feed additives like essential oils and plant extracts can exhibit antimicrobial properties, inhibiting the growth of spoilage microorganisms and extending the microbial shelf-life of fish products. For instance, the inclusion of thyme or oregano essential oils in aquaculture feeds has been reported to reduce the microbial counts and to improve the microbiological quality of fish fillets during storage (Dolea et al., 2018).

By harnessing the anti-oxidant and antimicrobial properties of natural feed additives, the freshness and overall shelf-life of fish fillets can be extended. This not only improves product quality and consumer acceptance but also reduces economic losses associated with spoilage and waste (Racioppoet al., 2021). Natural anti-oxidants can prevent lipid oxidation, discoloration and the development of off-flavors, while antimicrobial compounds can inhibit microbial growth and spoilage, prolonging the shelf-life of fish products (Mei et al., 2019).

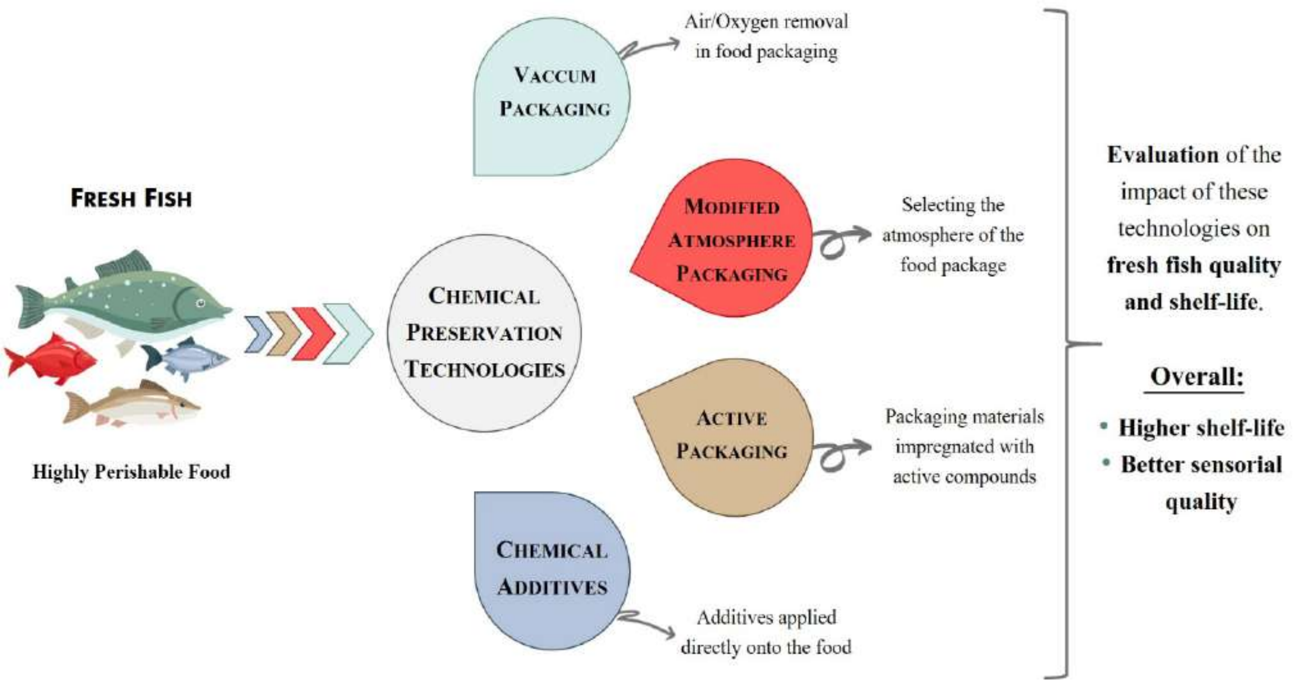

Fig. 3: Different strategies to extend the shelf life of a fish (Amaral et al., 2021)

Lipid and protein oxidation are major contributors to quality deterioration and reduced shelf-life in fish products. Natural feed additives with antioxidant properties can effectively inhibit the lipid oxidation by scavenging free radicals and chelating pro-oxidant metals. This helps to preserve the nutritional value, flavor and color of fish fillets during storage. Additionally, some natural antioxidants, such as polyphenols and carotenoids can also inhibit protein oxidation, preventing the formation of protein carbonyls and maintaining the structural integrity of muscle proteins (Zhang et al., 2024).

Determining the optimal dosages and administration methods for natural feed additives is a critical challenge. The efficacy and potential side effects of these additives can vary depending on the inclusion levels, administration routes e.g. dietary, injection or immersion and the specific compounds involved. Over- or under-dosing can lead to ineffective results or potential toxicity issues, respectively. The bioavailability and stability of natural feed additives can be influenced by factors such as feed processing conditions, interactions with other feed ingredients and the physiological state of the fish. Thus, careful dose-response studies and optimization of administration methods are essential to ensure the desired effects on fillet quality while minimizing potential adverse effects or economic inefficiencies (Nie et al., 2022).

The use of natural feed additives in aquaculture is subject to regulatory oversight and consumer acceptance considerations. In many countries, the use of feed additives in animal production, including aquaculture is regulated by governmental agencies to ensure the food safety, efficacy and environmental sustainability. Natural feed additives may be subject to regulatory approval processes, requiring extensive safety evaluations, efficacy studies and documentation. Additionally, consumer acceptance is a critical factor, as many consumers demand transparency, traceability and assurances of sustainable and environmentally-friendly production practices (Deconinck and Hobeika 2023).

Proper labeling, communication and education campaigns may be necessary to address consumer concerns and promote the acceptance of natural feed additives in aquaculture products. Furthermore, ongoing research and development efforts are needed to identify and develop new, safe and effective natural feed additives that meet regulatory requirements and consumer expectations. Addressing these practical considerations and challenges is crucial for the successful implementation and widespread adoption of natural feed additives in aquaculture production systems aimed at improving the fillet quality and meeting consumer demands for high-quality, sustainable and environmentally-friendly seafood products (Sethi et al., 2023).

The use of Natural Feed Additives for Improving Fillet Quality in Cultured Fish

Novel Natural Feed Additives and Sources

The search for novel natural feed additives and sources is an ongoing pursuit in aquaculture research and development. Unexplored plant species, marine organisms and microbial sources offer potential for identifying new bioactive compounds with beneficial effects on fillet quality traits. For example, the exploration of under-utilized seaweed species, marine sponges and extremophilic microorganisms may yield novel compounds with antioxidant, pigmenting or other desirable properties (Senadheera et al., 2023).

Additionally, the application of advanced extraction techniques such as supercritical fluid extraction, enzyme-assisted extraction and ultrasound-assisted extraction may facilitate the recovery of bioactive compounds from natural sources with enhanced efficiency and selectivity. These novel natural feed additives and sources could potentially address emerging consumer demands, regulatory requirements and sustainability concerns in the aquaculture industry (Saha 2024).

Combination Strategies and Synergistic Effects

Combining multiple natural feed additives with complementary or synergistic effects is an emerging trend in the pursuit of optimizing fillet quality traits. By leveraging the synergistic interactions between different bioactive compounds, such as plant-derived polyphenols, carotenoids and essential oils, it may be possible to achieve improved anti-oxidant, antimicrobial and sensory-enhancing effects (Basavegowda and Baek 2021). Furthermore, the combination of natural feed additives with other strategies such as selective breeding, advanced feed formulations and optimized environmental conditions, could yield synergistic benefits for fillet quality improvement. However, careful evaluation of potential interactions, dosages and compatibility is necessary to ensure the safety, efficacy and economic viability of these combination strategies (Puvanasundram et al., 2021).

Omics-based Approaches for Quality Trait Optimization

Advances in omics technologies such as genomics, transcriptomics, proteomics and metabolomics are opening new avenues for optimizing fillet quality traits in cultured fish through the use of natural feed additives. These approaches can provide insights into the molecular mechanisms underlying the effects of natural feed additives on muscle physiology, nutrient metabolism and fillet quality traits (Guppy et al., 2018). By integrating omics data with traditional phenotypic and performance data, it may be possible to identify genetic markers, gene expression patterns and metabolic pathways associated with desirable fillet quality traits. This information can inform selective breeding programs, feed formulation strategies and the targeted application of natural feed additives to modulate specific quality traits. Omics-based approaches can facilitate the discovery and characterization of novel bioactive compounds from natural sources, accelerating the development of new natural feed additives tailored for specific fillet quality objectives (Rise et al., 2019). As aquaculture continues to evolve and consumer demands for high-quality, sustainable and health-promoting seafood products grow, the integration of natural feed additives, combination strategies and omics-based approaches will play a pivotal role in optimizing fillet quality traits and ensuring the long-term success of the industry. The utilization of natural feed additives presents a promising approach to enhancing the fillet quality traits in cultured fish, while addressing consumer demands for sustainable and environmentally-friendly aquaculture practices.

This chapter has comprehensively explored the various effects of natural feed additives, such as plant-derived compounds, algal products, probiotics and enzymes on critical fillet quality parameters including nutritional composition, textural properties, color and appearance, flavor and odor and shelf-life and oxidative stability. The key findings highlight the potential of these natural additives to modulate fillet quality traits through mechanisms such as pigmentation, anti-oxidant activity, modulation of muscle structure and influence on gut microbiota and metabolism (Lohita and Srijaya 2024). The applications of natural feed additives in sustainable aquaculture extend beyond the fillet quality improvement, contributing to the overall sustainability, environmental stewardship and economic viability of the industry. By reducing reliance on synthetic additives and promoting the use of natural, renewable and often locally-sourced ingredients, natural feed additives align with the principles of circular economy and responsible resource utilization (Fritsche et al., 2020).

Future Perspectives and Emerging Trends

Future research opportunities in this field include the exploration of novel natural feed additive sources such as underutilized plant species, marine organisms and extremophilic microorganisms. Additionally, the investigation of combination strategies and synergistic effects among different natural additives, as well as the integration of omics-based approaches, holds promise for optimizing fillet quality traits and advancing our understanding of the underlying molecular mechanisms. Interdisciplinary collaborations among researchers, aquaculture producers, feed manufacturers and regulatory bodies will be crucial in translating the findings from this chapter into practical applications, ensuring the safety, efficacy and commercial viability of natural feed additives. Ultimately, the adoption of natural feed additives has the potential to contribute to the sustainable growth of the aquaculture industry, meet evolving consumer demands and promote the production of high-quality, nutritious and environmentally-responsible seafood products.

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Chapter 16

Mitigation of Enteric Pathogens and Modulation of Gut Microbiota in Livestock by Natural Feed Additives

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ABSTRACT

The pursuit of sustainable strategies for enhancing the livestock health and productivity has driven the exploration of natural feed additives. The use of natural feed additives has been considered as a sustainable strategy to enhance the livestock health and productivity and have pivotal role in mitigating the enteric pathogens and modulating gut microbiota, which are crucial for animal health, welfare and food safety. The chapter analyzes cutting-edge research on plant, animal and microbial-derived additives, revealing their antimicrobial, immune-modulatory and prebiotic effects on the gut ecosystem. It addresses challenges such as variability and inconsistency, exploring factors like source, composition, dosage, species and environment that influence outcomes. The strategies for optimizing the use of additives including improved dosage, delivery, bioavailability, targeted release and palatability should be considered for effective results. The synergistic potential on combining additives with probiotics, prebiotics and different dietary interventions should be properly utilized along with regulatory considerations for an improved consumer acceptance. Future research directions encompasses novel source identification, mechanistic studies, large-scale trials and sustainability assessments. This exploration provides valuable insights for stakeholders, policymakers and consumers, advancing the convergence of animal health, food safety and environmental sustainability in livestock management.

KEYWORDS Enteric pathogens, Gut microbiota, Livestock health, Natural feed additives, Sustainable aquaculture	Received: 24-May-2024 Revised: 18-July-2024 Accepted: 14-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Importance of Gut Health in Livestock Production

Maintaining a healthy gut is crucial for efficient nutrient absorption, growth performance and overall productivity in livestock animals. A well-balanced gut microbiota plays a vital role in various physiological processes including digestion, immune modulation and disease resistance (Hemmati et al., 2023).

Challenges Posed by Enteric Pathogens and Dysbiosis

Enteric pathogens such as *Salmonella*, *Escherichia coli* and *Campylobacter* can cause severe gastrointestinal infections, leading to economic losses in livestock production due to reduced growth, mortality and food safety concerns (Callaway et al., 2008). Additionally, dysbiosis, an imbalance in the gut microbial community, can compromise gut health, leading to decreased feed efficiency, increased susceptibility to infections and impaired immune function (Obayomi et al., 2024).

Need for Alternative Strategies to Antibiotics

The widespread use of antibiotics in livestock production has led to the emergence of antibiotic-resistant bacteria, posing a significant threat to the public health. Furthermore, concerns over antibiotic residues in animal products and the potential impact on human gut microbiota have prompted the need for alternative strategies to maintain gut health and control enteric pathogens (Pandey et al., 2024).

Common enteric bacterial pathogens:

- ***Escherichia coli*:** Certain strains such as enterotoxigenic *E. coli* (ETEC) and Shiga toxin-producing *E. coli* (STEC) can cause severe diarrhea, dehydration and even death in livestock, particularly in young animals (Balestracci et al., 2023).
- ***Salmonella*:** Various serovars like *Salmonella Typhimurium* and *Salmonella Enteritidis*, can lead to salmonellosis, a foodborne zoonotic disease characterized by diarrhea, fever and abdominal cramps in livestock (Lamichhane et al., 2024).
- ***Campylobacter*:** Species like *Campylobacter jejuni* and *Campylobacter coli* can cause campylobacteriosis, a bacterial infection resulting in diarrhea, abortion and infertility in cattle, sheep and other livestock (Nobi et al., 2024).

Viral pathogens:

- **Rotavirus:** A major cause of viral gastroenteritis in young livestock, leading to severe diarrhea, dehydration and even death in calves and other neonatal animals.
- **Coronavirus:** Coronaviruses like porcine epidemic diarrhea virus (PEDV) and bovine coronavirus (BCoV) can cause acute diarrhea, dehydration and weight loss in pigs and cattle, respectively.

Parasitic pathogens:

- ***Cryptosporidium*:** *Cryptosporidium parvum* and *Cryptosporidium andersoni* are common protozoan parasites that cause cryptosporidiosis, a diarrheal disease in calves, lambs and other young livestock.
- ***Giardia*:** *Giardia duodenalis* is a flagellated protozoan that can lead to giardiasis, a condition characterized by diarrhea, malabsorptionand weight loss in livestock.

Impacts on animal health and productivity: Enteric pathogens can have severe impacts on livestock health and productivity, including:

- Reduced growth rates and feed conversion efficiency due to malabsorption and diarrhea.
- Increased mortality rates, especially in young animals, leading to economic losses.
- Increased veterinary costs and treatment expenses.
- Potential for zoonotic transmission to humans through contaminated food products.

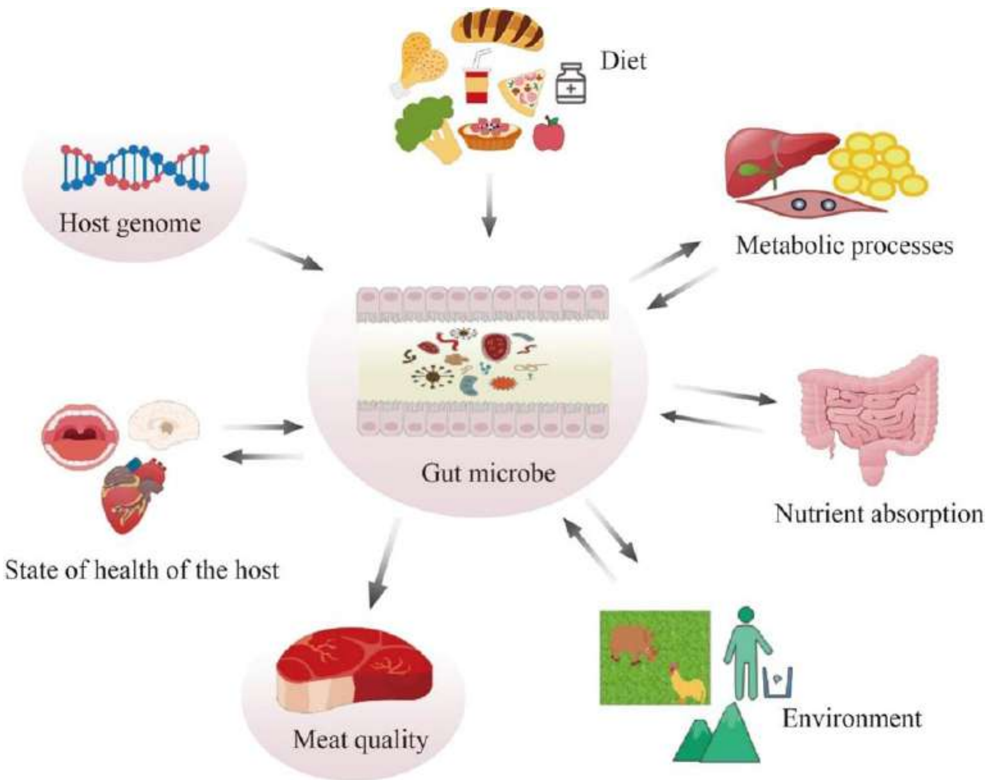

Fig. 1: Functions of gut microbiota (Chen et al., 2022).

Gut Microbiota and Its Role in Livestock Health

The gut microbiota, a diverse and complex community of microorganisms residing in the gastrointestinal tract plays a crucial role in the overall health and productivity of livestock animals. This intricate ecosystem consists of bacteria, archaea, fungi and viruses with bacteria being the most abundant and well-studied component. The gut microbiome is a dynamic and highly diverse ecosystem that varies among different animal species, breeds and even individuals. It is estimated to harbor trillions of microorganisms with the majority belonging to the phyla Firmicutes, Bacteroidetes, Proteobacteria and Actinobacteria. The composition and diversity of the gut microbiota are influenced by various factors including diet, age, environmental conditions and host genetics (Maritan et al., 2024).

A well-balanced and diverse gut microbiota contributes to numerous physiological processes and plays a vital role in maintaining the overall health and performance of livestock animals. Some of the key functions of a healthy gut microbiota include:

1. Nutrient digestion and metabolism: The gut microbiota produces a wide range of enzymes that aid in the digestion of complex carbohydrates, proteins and lipids enhancing nutrient absorption and energy utilization (Baky et al., 2024).
2. Immune system modulation: The gut microbiota plays a crucial role in the development and regulation of the host's immune system, contributing to the prevention of pathogenic infections and maintaining intestinal homeostasis (Wardman et al., 2022).
3. Vitamin and metabolite production: Certain gut microbes are capable of synthesizing essential vitamins such as vitamins K, B12 and folate, as well as producing beneficial metabolites like short-chain fatty acids (SCFAs) that can be absorbed and utilized by the host (Alrubaye and Kohl, 2021).
4. Pathogen exclusion: A diverse and balanced gut microbiota can outcompete and inhibit the growth of potential pathogens through various mechanisms, including the production of antimicrobial compounds, competition for nutrients and adhesion sitesand modulation of the host immune response (Khan et al., 2021).
5. Growth and feed efficiency: A healthy gut microbiota contributes to improved feed conversion efficiency, weight gainand overall growth performance in livestock animals by enhancing nutrient utilization and modulating metabolic pathways (Bergamasch et al., 2020).

The composition and diversity of the gut microbiota are influenced by various factors including:

1. Diet: The type and composition of the diet play a significant role in shaping the gut microbiota. Diets rich in fiber, prebiotics and specific feed additives can promote the growth of beneficial bacteria, while diets high in protein or fat may favor the proliferation of different microbial populations (Carmody and Bisanz, 2023).
2. Age: The gut microbiota undergoes significant changes throughout the lifespan of an animal, with the initial colonization occurring during birth and early life stages. The composition and diversity of the microbiota tends to stabilize as the animal matures (Warne and Dallas, 2022).
3. Environmental factors: Factors such as housing conditions, hygiene practices and exposure to environmental microbes can influence the gut microbiota composition. For example, animals raised in clean and controlled environments may have a less diverse microbiota compared to those raised in more natural settings (Anwar et al., 2021).
4. Antimicrobial use: The use of antibiotics and other antimicrobial agents can significantly disrupt the gut microbiota, leading to a decrease in diversity and an imbalance in microbial populations, a condition known as dysbiosis (Ramirez et al., 2020).
5. Host genetics: The host's genetic background can influence the gut microbiota composition, as certain genes are involved in regulating the immune response, intestinal barrier functionand metabolic pathways that interact with the gut microbes (Bubier et al., 2021).
6. Stress and health status: Stress factors such as transportation, harsh environmental conditionsand disease states, can alter the gut microbiota composition and contribute to dysbiosis, potentially leading to decreased performance and increased susceptibility to infections (Gomaa, 2020).

Understanding the intricate relationship between the gut microbiota and livestock health is crucial for developing effective strategies to promote animal health, productivity and overall welfare. Through dietary interventions, prebiotics, probiotics and other management practices, it is possible to modulate the gut microbiota and harness its beneficial effects for improved livestock production (Barathan et al., 2024).

Natural Feed Additives for Pathogen Mitigation and Gut Modulation

The use of natural feed additives has gained significant attention as a sustainable alternative to antibiotics in livestock production. These additives offer various benefits, including the potential to mitigate enteric pathogens, modulate the gut microbiota and improve overall animal health and performance (Emami et al., 2020). Several classes of natural feed additives have been explored for their potential applications in livestock production.

Plant-derived Compounds

Plant-derived compounds, such as essential oils, tannins and saponins, have been extensively studied for their antimicrobial, anti-inflammatory and immuno-modulatory properties.

Essential oils

Essential oils are volatile, aromatic compounds extracted from plants. They possess antimicrobial activities against various enteric pathogens, including *Salmonella*, *Escherichia coli* and *Campylobacter*. The mechanisms of action involve disruption of bacterial cell membranes, inhibition of quorum sensing and interference with bacterial metabolic pathways. Essential oils such as thymol, carvacrol and cinnamaldehyde have been shown to modulate the gut microbiota, promoting the growth of beneficial bacteria and reducing the abundance of potential pathogens (de Sousa et al., 2023).

Tannins

Tannins are polyphenolic compounds found in various plants including legumes, fruitsand cereals. They possess antimicrobial and anti-inflammatory properties, making them potential candidates for pathogen mitigation and gut health modulation (de Melo et al., 2023). Tannins can inhibit the growth of pathogenic bacteria like *Salmonella* and *E. coli* by disrupting their cell membranes and interfering with essential metabolic processes. Additionally, tannins can modulate the gut microbiota by selectively promoting the growth of beneficial bacteria and inhibiting the proliferation of harmful microbes (Molino et al., 2021).

Saponins

Saponins are glycosidic compounds found in various plants such as quinoa, soybeans and certain herbs. They exhibit antimicrobial, immuno-modulatory and anti-inflammatory properties. Saponins can disrupt bacterial cell membranes, inhibit virulence factors and modulate the immune response making them potential candidates for pathogen control and gut health improvement in livestock (Otterbach et al., 2021).

Probiotics and Prebiotics

Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host. Prebiotics are non-digestible food ingredients that selectively promote the growth and activity of beneficial bacteria in the gut (Mishra and Acharya, 2021). The use of probiotics in livestock production aims to restore and maintain a balanced gut microbiota, enhance the immune response and inhibit the growth of pathogens. Common probiotic strains used in livestock include *Lactobacillus, Bifidobacterium, Bacillus* and *Saccharomyces*. Probiotics can compete with pathogens for adhesion sites and nutrients, produce antimicrobial compounds and modulate the host's immune system, thereby mitigating the effects of enteric pathogens and promoting gut health (Raheem et al., 2021). Prebiotics, such as inulin, fructo-oligosaccharides (FOS) and galacto-oligosaccharides (GOS), selectively promote the growth of beneficial gut bacteria like *Bifidobacterium* and *Lactobacillus* species. Prebiotics can modulate the gut microbiota, enhance the production of short-chain fatty acids (SCFAs) and exert immuno-modulatory effects contributing to improved gut health and pathogen control in livestock (Kaewarsar et al., 2023).

Enzymes and Organic acids

Enzymes and organic acids have been explored as feed additives for their potential to improve nutrient digestibility, control pathogens and modulate the gut microbiota. Exogenous enzymes such as phytases, proteases and carbohydrases can improve the digestibility of feed components, leading to better nutrient utilization and reduced substrate availability for pathogenic bacteria. Additionally, some enzymes, like xylanases and glucanases, can degrade non-starch polysaccharides, potentially modulating the gut microbiota and reducing the risk of dysbiosis (Velázquez-De et al., 2021). Organic acids such as formic, acetic, propionic and butyric acids can exert antimicrobial effects by disrupting the pH gradient and metabolic processes of bacteria. Organic acids can inhibit the growth of enteric pathogens like *Salmonella*, *E. coli* and *Campylobacter* while promoting the growth of beneficial gut bacteria like *Lactobacillus* species (Taylor and Doores, 2020).

Mechanisms of Action

Natural feed additives employ various mechanisms to mitigate the enteric pathogens and modulate the gut microbiota, including:

a. **Anti-microbial Activity**

Many plant-derived chemicals such as essential oils, tannins and saponins have antibacterial effects that directly inhibit or disrupt the metabolic processes of enteric pathogens (Jubair et al., 2021).

b. **Modulation of Gut Microbiota**

Probiotics, prebiotics and certain plant-derived compounds can selectively promote the growth of beneficial gut bacteria like *Lactobacillus* and *Bifidobacterium* species, while inhibiting the proliferation of harmful microbes (Liu et al., 2022).

c. **Immunomodulation**

Some natural feed additives such as probiotics and plant-derived compounds can modulate the host's immune response, enhancing the production of cytokines, immunoglobulins and other immune mediators, thereby improving resistance against enteric pathogens (Torres-Maravilla et al., 2024).

d. **Improved Nutrient Utilization**

Enzymes and organic acids can enhance nutrient digestibility and reduce the availability of substrates for pathogenic bacteria potentially modulating the gut microbiota and promoting the growth of beneficial microbes (Rathnayake et al., 2021).

e. **Quorum Sensing Inhibition**

Some plant-derived compounds like essential oils can interfere with the quorum sensing mechanisms of pathogenic bacteria disrupting their ability to regulate virulence factors and biofilm formation (Prazdnova et al., 2022).

Natural feed additives can modulate the ability of enteric pathogens to adhere and colonize the intestinal epithelium which is a crucial step in the pathogenesis of infectious diseases. Certain probiotic strainssuch as *Lactobacillus* and *Bifidobacterium* species can compete with enteric pathogens for adhesion sites on the intestinal epithelium, thereby limiting their ability to colonize the gut (Campana et al., 2017). Additionally, probiotics can produce antimicrobial compounds, like bacteriocins that can inhibit the growth and adhesion of pathogens (Begum et al., 2021). *Lactobacillus* salivarius could inhibit the adhesion and invasion of *Salmonella enteritidis* in intestinal epithelial cells by producing bacteriocins and modulating the expression of virulence genes (Kanmani and Kim, 2020).

Some plant-derived compounds such as tannins and saponins can interfere with the adhesion of enteric pathogens to the intestinal epithelium. These compounds can bind to bacterial adhesins or modify the surface properties of the intestinal epithelium thereby limiting the ability of pathogens to colonize the gut. Saponins from *Yucca schidigera* could inhibit the adhesion of *Escherichia coli* O157:H7 to intestinal epithelial cells by modifying the bacterial cell surface properties (Jackson, 2021).

Natural feed additives can modulate the host's immune systemenhancing the defense mechanismagainst enteric pathogens and promoting a more effective immune response. Promotion of beneficial bacterial populations: Natural feed additives can selectively promote the growth and activity of beneficial bacterial populations within the gut microbiota leading to improved gut health and functionality (Begum et al., 2021).

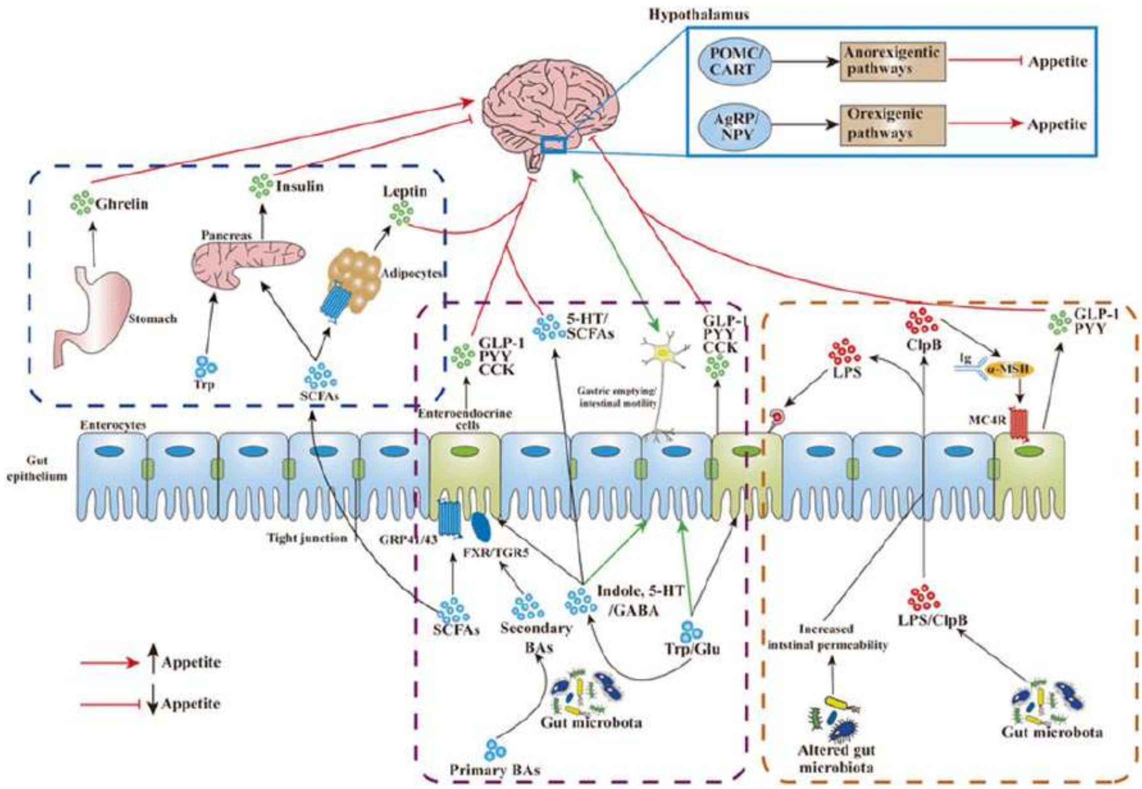

Fig. 2: Gut microbiota-associated mechanisms involved in host appetite control. Firstly, gut microbial metabolites can stimulate entero-endocrine cells to release anorexigenic hormones (PYY, GLP-1 and CCK) and neurotransmitter (5-HT) and promote the secretion of peripheral hormones (leptin, ghrelin and insulin). Secondly, Igs are involved in modulating the biological activity of appetite-regulating hormones such as leptin and ghrelin. In addition, gut microbiota produce identical protein sequences with appetite-regulating peptides such as ClpB that might directly act on anorexigenic neurons or bind to Igs to modulates the secretion of anorexigenic hormones from enteroendocrine L cells (Han et al., 2021).

Impacts on Gut Barrier Function and Nutrient Utilization

The modulation of the gut microbiota by natural feed additives can have significant impacts on gut barrier function and nutrient utilization ultimately influencing animal health and productivity (Yadav and Jha, 2019).

Gut Barrier Function

The gut microbiota plays a crucial role in maintaining the integrity of the intestinal barrier which is essential for preventing the translocation of harmful substances and pathogens (Panwar et al., 2021). Natural feed additives such as probiotics and prebioticscan modulate the gut microbiota and contribute to the maintenance of a healthy gut barrier by promoting the production of SCFAs modulating tight junction proteins and regulating the immune response. Supplementing the diet of weaned piglets with a probiotic mixture containing Lactobacillus and Bifido bacterium strains improved the intestinal barrier function by increasing the production of SCFAs and modulating the expression of tight junction proteins (Wu et al., 2020).

Nutrient Utilization

The gut microbiota is involved in various metabolic processes including the breakdown of complex carbohydrates, proteins and lipids as well as the synthesis of vitamins and other essential nutrients (Rowland et al., 2018). Natural feed additives can modulate the gut microbiota leading to changes in the metabolic capabilities of the microbial community and potentially improving the nutrient utilization and energy extraction from the diet. Supplementing the diet of broiler chickens with a combination of prebiotics and probiotics improved the digestibility of protein and energy leading to improved growth performance and feed efficiency (Khalid et al., 2021).

The use of natural feed additives for mitigating enteric pathogens and modulating the gut microbiota in livestock has been met with varying degrees of efficacy and inconsistent results across different studies (Cameron and McAllister, 2019; Honan et al., 2021; Wang et al., 2024). This variability can be attributed to several factors: (a) Natural additives are derived from various plant, animal or microbial sources and their composition can differ based on factors such as geographical location cultivation conditions and extraction methods. These variations in composition can influence their biological activities and efficacy (Faustino et al., 2019). (b) Dosage: The dosage of natural additives plays a crucial role in determining their effects. Insufficient dosages may not produce the desired outcomeswhile excessive dosages can lead to adverse effects or toxicity (Zang et al., 2023). Identifying the optimal dosage range is essential for consistent and reliable results. (c) Livestock species and breed: Different livestock species and breeds may respond differently to the same natural additives due to variations in their physiological characteristics gut microbiota composition and metabolic processes. (d) Environmental factors: Environmental conditions such as housing, temperature, humidity and feed composition can influence the gut microbiota and the efficacy of natural additives (de Bruin et al., 2024). (e) Experimental design and methodologies: Inconsistencies in experimental designsampling techniques and analytical methods across studies can contribute to variable results. Addressing these sources of variability and standardizing experimental protocols is crucial for obtaining consistent and reproducible results with natural feed additives (Sandner et al., 2022).

Optimization of Dosage and Delivery Methods

Optimizing the dosage and delivery methods for natural feed additives is essential for maximizing their efficacy and minimizing potential adverse effects. Determining the optimal dosage range for each natural additive is crucial. This can be achieved through dose-response studies considering factors such as the target livestock species, desired effects and potential side effects (Wu et al., 2022). Various delivery methods such as direct feeding, encapsulation or incorporation into feed pellets can influence the bioavailability, stability and release profile of the active compounds in natural additives. Choosing the appropriate delivery method can enhances the efficacy and minimize degradation or loss of active compounds (Rostamabadi et al., 2021). Some delivery systems such as encapsulation or coatings can be designed to release the active compounds in specific regions of the gastrointestinal tract ensuring targeted delivery and improved bioavailability (Chai et al., 2018). Optimizing formulations and storage conditions can improve the stability and shelf-life of natural additives ensuring consistent potency and efficacy over time. The delivery method and formulation should also consider the palatability and feed acceptance by the livestock as poor palatability can lead to reduced feed intake and consequently a lower efficacy (Tona, 2018). Optimizing both the dosage and delivery methods can enhance the consistency and reliability of natural feed additives in mitigating enteric pathogens and modulating the gut microbiota.

Combination Strategies and Synergistic Effects

Using combinations of different natural feed additives or combining them with other interventions can potentially lead to synergistic effects and enhanced efficacy. Different natural additives may target different mechanisms or pathways in mitigating enteric pathogens or modulating the gut microbiota and combining them can provide a broader range of activities and potentially synergistic effects. Combining natural additives with probiotics (beneficial live microorganisms) or prebiotics (substrates that selectively stimulate the growth of beneficial gut bacteria) can create a synergistic effect by promoting the growth of beneficial gut microbiota while mitigating pathogens. Incorporating the natural additives into specific dietary regimens or feeding strategies can enhance their effects on gut health and pathogen mitigation. Combining the natural additives with other interventions such as vaccines antimicrobials or management practicescan create a multi-pronged approach for improving livestock health and productivity (Callaway et al., 2021). Exploring these combination strategies requires a thorough understanding of the modes of action and potential interactions between the different components. Careful experimental design and evaluation of potential synergies antagonisms or adverse effects are necessary to develop effective and safe combination strategies (Carrasson et al., 2021)

Regulatory Considerations and Consumer Acceptance

The use of natural feed additives in livestock production is subject to regulatory oversight and consumer acceptance that are important considerations for their successful implementation:

a. Regulatory frameworks: Most countries have regulatory bodies that oversee the approval and use of feed additives, including natural additives in livestock production. These regulatory frameworks aim to ensure the safety and efficacy of the additives for both the animals and consumers of animal-derived products (Sen et al., 2025).
b. Safety assessments: Natural feed additives may need to undergo rigorous safety assessments to evaluate their potential toxicity environmental impact and potential for residues in animal-derived products. These assessments are crucial for obtaining the regulatory approval and ensuring the consumer safety (Zeiner et al., 2024).
c. Labeling and claims: Regulations may also govern the labeling and claims associated with natural feed additives ensuring transparency and preventing misleading or unsubstantiated claims (Bayır et al., 2024).
d. Approval processes: The approval processes for natural feed additives can vary across different countries or regions potentially creating barriers to their widespread adoption and commercialization (Smith et al., 2021).
e. Consumer perception and acceptance: Consumer attitudes and perceptions towards the use of natural additives in livestock production can influence their acceptance and demand in the market. Addressing consumer concerns providing educationand ensuring transparency in the production process can facilitate consumer acceptance (de Araújo et al., 2022).
f. Organic and sustainable production: The use of natural feed additives aligns with the growing consumer demand for organic and sustainable livestock production practices which can drive their adoption and acceptance (Schmid et al., 2017).

Future Research Directions

The conclusion will likely identify areas that require further research and exploration to advance the understanding and practical implementation of natural feed additives in livestock production. Some potential future research directions may include: a. Identification and characterization of new natural sources: Continuous exploration and screening of novel plant, animalor microbial sources for bioactive compounds with beneficial effects on gut health and pathogen mitigation. b. Elucidation of modes of action: Further investigation into the mechanisms by which natural additives exert their effects on enteric pathogens gut microbiota and host physiology enabling more targeted and effective applications. c. Optimization of dosage delivery and formulations: Continued research on optimizing dosages, developing targeted delivery systems and improving formulations to enhance bioavailability stability and efficacy of natural additives. d. Combination strategies and synergistic effects: Exploring potential synergies between different natural additives as well as their combination with probiotics prebiotics dietary interventions or other management practices to develop integrated and holistic approaches. e. Large-scale field trials and validation: Conducting large-scale field trials and validation studies to assess the practical implementation, scalability and economic feasibility of using natural feed additives in diverse livestock production systems. f. Regulatory and consumer acceptance studies: Investigating consumer perceptions, preferences and concerns regarding the use of natural feed additives and collaborating with regulatory bodies to establish appropriate guidelines and policies. g. Sustainability and environmental impact assessments: Evaluating the long-term sustainability and potential environmental impacts of using natural feed additives, considering factors such as resource utilization, waste management and carbon footprint.

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Chapter 17

Revolutionizing Animal Nutrition: The Promise of Next-Generation Feed Additives

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ABSTRACT

Sustainable production practices must be used to address a variety of challenges, including those related to animal health and the environment. Amidst the growing challenges faced by traditional animal husbandry techniques, the global demand for animal products is on the rise due to population increase, rising incomes, and evolving dietary preferences. Innovative approaches including probiotics, prebiotics, enzymes, and phytogenic have become crucial for improving feed efficiency, intestinal health, and immunity in poultry and livestock. As a result, there is a growing focus on revolutionizing feed additives to improve animal performance, health, and nutrition while reducing environmental effects. However, certain issues and concerns come with the revolutionization of feed additives. Factors include maintaining public perceptions, carrying out thorough safety evaluations, dealing with the moral ramifications of modern technology and managing legal and regulatory conditions.

KEYWORDS
Revolution, Innovative, Probiotics, Phytogenic, Enzymes, Vitamins, Technology

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INTRODUCTION

Livestock producers face the dual challenges of providing for the nutritional needs of their animals and balancing sustainability objectives with economic restraints. In this instance, feed additives play a key role in tackling these complex issues. The dynamic landscape of animal nutrition today is characterized by the confluence of improving animal health, optimizing feed efficiency, and reducing environmental effects (Baishya et al., 2022).

Feed additives have a role in animal nutrition that goes beyond standard supplementation since they provide several benefits, such as increased feed efficiency, improved animal health, and reduced environmental impact. Feed additives are essential supplements that improve digestibility, contribute vital minerals to animal diets, as well as promote general health (Velazquez-De Lucio et al., 2021). These supplements provide long-term answers to prevalent issues in animal husbandry by encouraging better digestion, food absorption, and animal immunological function. They are essential for optimizing feed conversion efficiency, reducing feed waste, and minimizing the need for antibiotics in livestock production. The latest innovations in next-generation additives, probiotics, and prebiotics are essential for sustaining a healthy gut microbiota (Su and Chen, 2020).

By disintegrating complex feed components, enzymes improve nutrient use, increasing feed efficiency and diminishing environmental impact. Their significance in contemporary livestock rearing is highlighted by their ability to promote holistic well-being and reduced dependence on antibiotics (Han et al., 2024). The feed additives have the power to improve animal welfare and performance while simultaneously encouraging ecologically friendly agricultural methods. Moreover, developments in other fields, such as enzymes, plant extracts, and essential oils, have also been made in feed additives (Giannenas et al., 2020). The botanical additives, on the other hand, provide natural substitutes with antibacterial and anti-inflammatory qualities, enhancing animal health and satisfying customer demands for environmentally responsible goods. Through the reduction of waste, and mitigation of antibiotic usage, these additives help to create a livestock industry that is more durable and sustainable (Brevik et al., 2020).

The functional feed ingredients are crucial components of contemporary feed additives that guarantee animals' nutritional demands are satisfied at different phases of their lives. These ingredients include vitamins (vitamin E), minerals, and amino acids (Shastak et al., 2023). Throughout the livestock value chain, the use of next-generation feed additives announces several advantages, such as increased animal welfare, decreased environmental impact, better animal performance, and leading to the development of healthier food products. However, the organizations must work together to overcome obstacles including cost-effectiveness, regulatory impediments, disseminating information, and socioeconomic consequences (Graham and Ledesma-Amaro, 2023).

Traditional Feed Additives Commonly used in Animal Nutrition

Animal nutrition is defined as “the study of the material and the composition of the feed consumed by the animals, how that materials are a breakdown in the digestive tract of animals”.

The demand for seafood has led to a spectacular expansion in the worldwide aquaculture business in recent years. But along with this expansion and development comes the difficulty of ensuring aquatic species' growth and well-being in a way that is both environmentally benign and sustainable. There are several reasons for the increase in demand for herbal feed additives, one of which is the increased knowledge of the hazards to human health and the environment posed by the overuse of artificial chemicals in aquaculture.

The use of herbal feed additives has emerged as a viable approach to these problems by providing an organic boost to the growth and health of aquatic life. The herbal feed additives are an alternative to conventional methods used in aquaculture to "promote growth and fight against diseases," which rely on artificial chemicals and antibiotics. Through the use of botanical extracts, herbs, and plants, these additions harness the power of nature to improve the general health of aquatic animals.

One of the significant advantages of herbal feed additives numerous herbs contain abundant bioactive chemicals that have been shown to have antibacterial and anti-inflammatory characteristics. The potential of herbal feed additives to enhance "disease resistance and boost the immune system" in aquatic species. Lowering the likelihood of antibiotic resistance may result in the creation of marine goods that are safer and healthier.

These compounds can aid aquatic species in combating common illnesses and pathogens without the need for medications.

They could:

- Improve feed conversion ratios
- Optimize digestion
- More efficient feed utilization, and
- Faster growth rates.

Importance of Feed Additives

The feed additives are increasingly used to improve ruminant nutrition by;

- ❖ Enhancing feed digestibility
- ❖ Nutrient utilization; and
- ❖ Animal Health

Sustainable feed refers to alternative ingredients and manufacturing techniques that encourage resources, minimize environmental effects, and lessen dependency on wild fish stocks. These include reduced dependency on wild fish as feed sources and substituting plant-based elements like algae and soybean meal. All the suitable techniques are mentioned as sustainable methods in the feed additives (Alfiko et al., 2022).

The additional protein sources that can provide effective and environmentally friendly feed options are being investigated by researchers and farmers. Although insects may not immediately come to mind when thinking about fish feed, they provide some special benefits. These sources include insects, microbes, and single-cell proteins. The issue of sustainable feed in aquaculture has been tackled through insects, which show great potential (Rothig et al., 2023).

The phytochemicals have been discovered as one of the many feed additives that may be used to improve ruminant nutrition. The term "phytochemicals" refers to plant-based substances with bioactive characteristics that may be advantageous for ruminant nutrition. Plant metabolites known as essential oils are typically composed of terpenes and phenylpropenes that are derived from plant sources (Aziz et al., 2018).

Importance and Advantages of Insects

Raising insects from organic waste streams eliminates the negative environmental effects associated with producing feed. Furthermore, fish require insects for growth and development since they are incredibly nutrient-dense and abundant in proteins, vital amino acids, and minerals.

Recently, the insects have drawn a lot of interest as a feasible and sustainable substitute for fish meal in aquaculture. The insects are now more widely recognized as an eco-friendly and sustainable feed substitute for aquaculture. The protein level of many insect species is either higher than or equal to that of conventional feed sources like fishmeal. These microscopic animals are a desirable alternative for sustainable feed production because of their many advantages (Bingqian et al., 2023).

Limitations and Challenges

Conventional fish feed sources, like fishmeal and soybean meal, present serious environmental problems.

- ➢ The fishmeal production is largely dependent on the global fishery industry, which contributes to overfishing

- The depletion of wild fish stocks.
- Large-scale deforestation is frequently involved in the production of soybean meal, which results in habitat loss, a decline in biodiversity, and an increase in greenhouse gas emissions.

The aquaculture's use of sustainable feed for its farmed organisms is one important feature of the industry.

- First of all, it causes marine ecosystems to be disrupted, wild fish populations to decline, and overfishing to occur.
- Second, industrial fishing techniques that cause harm to non-target species and degrade marine environments are frequently used to produce fishmeal and oil.
- Lastly, using wild fish for feed depletes global fish stocks and jeopardizes attempts to preserve robust ocean ecosystems (Freccia et al., 2020).

Evolution of Next-Generation Feed Additives

Evolution is the process by which a rewarding, complex, or unpleasant condition gradually changes over several generations into a rewarding, more intricate, or pleasant state.

The evolution in terms of feed additives encompasses all the gradual modifications made to their use to enhance animal performance as well as the efficiency of all internal processes in the animal's body.

Historically, nutritionists and farmers have favored using natural feed additives containing minerals, plant matter, and valuable materials to enhance and fortify animal diets and meat quality.

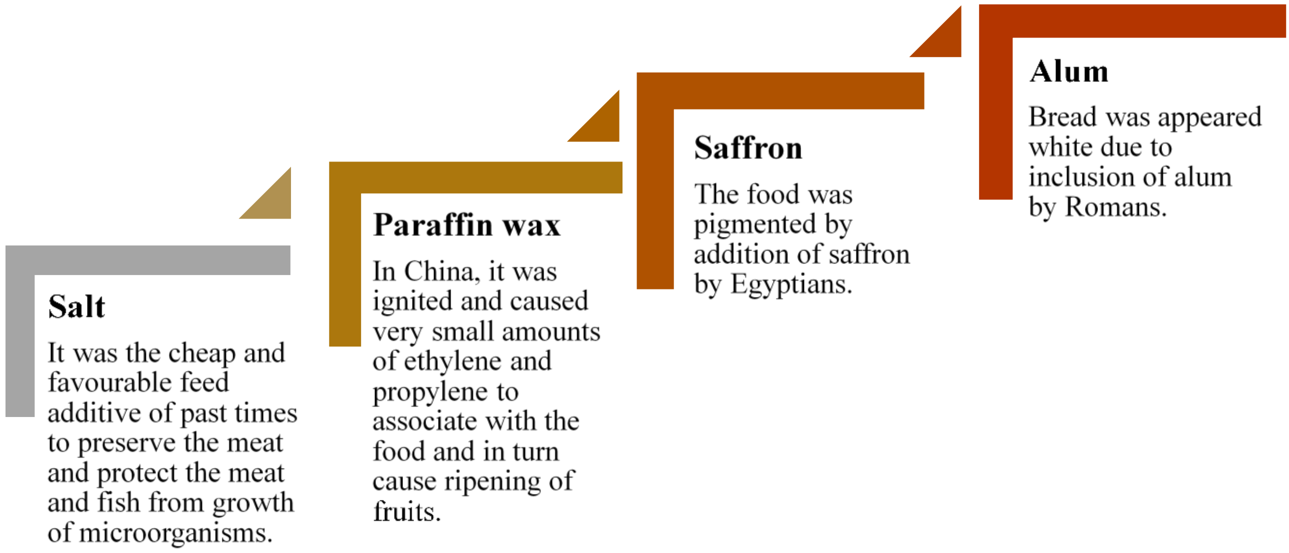

Fig. 1: Feed additives used in ancient times to improve the quality of meat and food

Yet, as time passed, changes in scientific study and mechanization brought about the introduction of nutritional supplements like synthetic vitamins and minerals, growth enhancers, and modified feed additives like antibiotics (Ilias et al., 2023).

Advances in Technology and Research Driving the Development

1) Precision feeding which is the use of data analytics, automation, sensors, and personalized feed ratios, has significantly changed animal husbandry as a result of technological modernization.
2) Nutrigenomics is the ascending aspect to ascertain the association between an animal's nutrition and genes. The scientists created altered diets to increase the animal's genetic capacity for growth and production after observing how different genes responded to different nutrients.

Examples of Innovative Approaches The feed additives that were most commonly established and utilized in the late twentieth century were:

- Antioxidants
- Enzyme
- Antibiotics

The prebiotics, probiotics, organic acids, and essential oils were the only feed additives that were currently employed in place of antibiotics to keep animals disease-free, and physically active, and having an undeniable impact on animal functioning.

Role of Feed Additives in Improving Nutrient Absorption and Utilization Of Animals

The nutrients were ingested, digested, and absorbed more effectively by the addition of feed additives in the feed of animals to keep the animal physically healthy and ensure the growth of animals.

Feed attractants are the feed additives that enhance the process of feed ingestion in animals in the gut of fish and shrimp, microbes are present, and for efficient working of these microbes, the feed additives like the prebiotics, probiotics,

volatile oils, acidifiers or antibiotics were added in their feed and positive results were evaluated in the process of:
- Digestion
- Absorption

The additives that ameliorate the process of digestion in animals are yucca, yeasts, and probiotics. The addition of yeasts in the feed of animals facilitates the activities of microbes in the gut of animals for attaining victorious outcomes in terms of growth performance and control of diseases.

Feed Formulation

Feed formulation is the process of creating compound feed by combining different amounts of feed ingredients and additives to nourish desirable animals and improve their development, health, and product quality at a reasonable cost. The following lists the feed formulation for a few ingredients:

Table 1: Feed formulation

Reported species	Feed ingredients	DM (%)	CP (%)	CF (%)	Ash (%)	P (%)	Fiber (%)	References
Gilthead sea bream	Soybean meal	84.2	38.7	3.5	6.7		4.7	(Nengas et al., 1955)
	Cottonseed meal	87.4	33.6	2.9	6.7		4.7	
	Blood meal	92.1	61.0	3.2	5.1		2.8	
	Skimmed milk	89.2	29.8	3.1	8.5		2.6	
European sea bass	Fishmeal, Norway	92.5	74.9	13.7	11.4	1.8		(da Silva and Oliva-Teles, 1998)
	Fishmeal, Portugal	89.5	70.1	11.5	18.3	3.1		
	Soybean meal (toasted, solvent extracted, and dehulled)	87.7	51.6	2.5	7.5	0.6		
	Blood meal	90.4	97.1	1.0	1.9			

Mechanism of Action

It explains the modifications in the activities and structure of organisms as a result of subjection to any substance and that substance is the feed additive.

Probiotics like yeasts have a specific mode of action in terms of nutrient digestion because they have a rich content of fiber that aids in ameliorating the process of nutrient consumption which causes enhancement in the yield of animal products and survival. The oxygen-lacking microbes of the ruminal portion progressively grow after the absorption of oxygen by yeast insertion and then perform their activities in elevating growth and curbing diseases (Pang et al., 2022).

Key Benefits of Feed Additives

The diversified feed additives with their beneficial roles are given below.

1) Prebiotics were the most prominent and act as food for intestinal microbes to ameliorate their performance.
2) Probiotics have advantages like ameliorating the yield of milk and elevating the ruminal pH.
3) By merging prebiotics and probiotics, symbiotics were composed. These feed additives are beneficial to ameliorate the health of animals by enhancing the well-being of microorganisms and fixing useful microbes firmly in the digestive tract of animals.
4) Essential oils were known to cause a decline in the performance of microbes, oxygen-deficient fungi, and methane formation by methanogens and these reductions were presumed to alter the segmental motion of protein disintegration.
5) Organic acids are most renowned for enhancing the population of useful microbes in the intestinal portion of animals.

Importance of Gut Health and Immunity in Animal Nutrition

Immunity is defined as the "state of defense against infectious disease conferred either through an immune response triggered by immunization or previous infection or by other non-immunological factors".

Types of Immunity

Two types of immuni ty are as follows;

1. Active immunity refers to "the process of exposing the body to an antigen to generate an adaptive immune response: the response takes days or weeks to develop but can also last a lifetime".
2. Passive immunity refers to "the process of producing IgG antibodies to fend off infection is known as passive immunity; it offers quick but brief, protection that lasts for no more than a few weeks to four months".

Role of Herbs

The herbs have an impact on how aquatic organisms respond to immunological responses; aside from their direct antibacterial properties, herbs strengthen the immune system of the host, making it more resilient to infections. This immune-stimulatory property is crucial for encouraging a more environmentally friendly and sustainable method of aquaculture while minimizing the need for traditional antibiotics. It has been shown that fish immunity is stimulated by glucose polymers, which are present in the cell walls of bacteria, fungi, and plants.

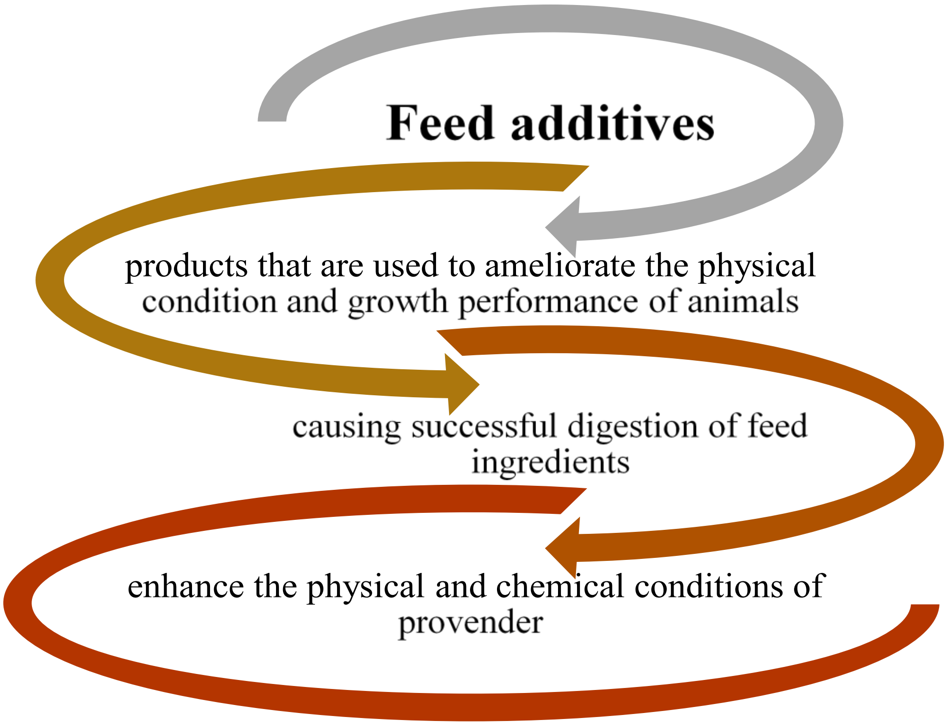

Fig. 2: Importance of feed additives

Significance of Herbal Feed Additives

In aquaculture, herbal feed additives help to regulate the gut microbiota, which supports a healthy microbial community that facilitates effective digestion and nutrient absorption. A healthy microbial community is fostered by the prebiotic actions of certain herbal substances, which stimulate the growth of beneficial microbes in the gut. The gut serves as an absorber of nutrients, a barrier against pathogenic pathogens, and a secretory source of some immune response components (Lalles et al., 2004).

How next next-generation feed additives contribute to its health and bolster immune function?

One such approach to reduce the amount of infections is stimulating the innate immune system. Limiting the use of antibiotics in animal agriculture requires the implementation of alternative preventive measures. Recent research has shown that green algae are a rich source of "bioactive natural compounds," which can be utilized to create a new class of growth enhancers that can "strengthen immune systems and boost animal health".

Secondary metabolites are a diverse group of chemicals that are produced by plants and act as defences against a range of physiological and environmental stressors. Some of these secondary metabolites can be helpful when added to feed for farmed animals, but some are detrimental (Huyghebaert et al., 2011), making them suitable for human consumption. Furthermore, none of these metabolites release any residues that can harm the environment. The plant-derived products known as phytogenic are added to feed to improve the "health and growth" of animals.

Sustainability Solutions for Animal Agriculture

Sustainability has become the concept used by individuals, organizations, and nations to assess and monitor human impacts on the natural environment. The sustainable development can be defined as "development which meets the needs of current generations without jeopardizing the ability of future generations to meet their own needs" (Michalk, 2015).

There are three goals in enhancing animal sustainability, including reducing their environmental impact (Hume et al., 2011):

- To optimize the number of productive progenies per breeding male and female
- To maximize the efficiency of turning feed and water into valuable animal product
- To reduce waste and losses due to infectious and metabolic diseases and stress

Raising livestock output and lowering environmental effects are the two goals that must be met to attain sustainability. The adaptation in an agricultural context can come from either human or ecological change.

The animals adapt to environmental conditions through a variety of methods, which lead to natural adaptation. The strategies for human adaptation and animal response include activities and methods that could aid animals in adjusting to climate change and improve livestock performance (Cheng et al., 2022).

The researchers have been investigating the way to manipulate gas emission in the next generation of animals using various feed additives, such as dietary enzymes (like protease and lipase) and blends of multiple enzymes (like glucoamylase from *Aspergillus niger*, and cellulase), probiotics (like *Bacillus amyloliquefaciens*, and *Levilactobacillus brevis*), prebiotics (like cyclodextrin, and oligosaccharide), and prebiotics (like *Bacillus amyloliquefaciens*, and *Bacillus reuter*), etc. (Hossain et al., 2024).

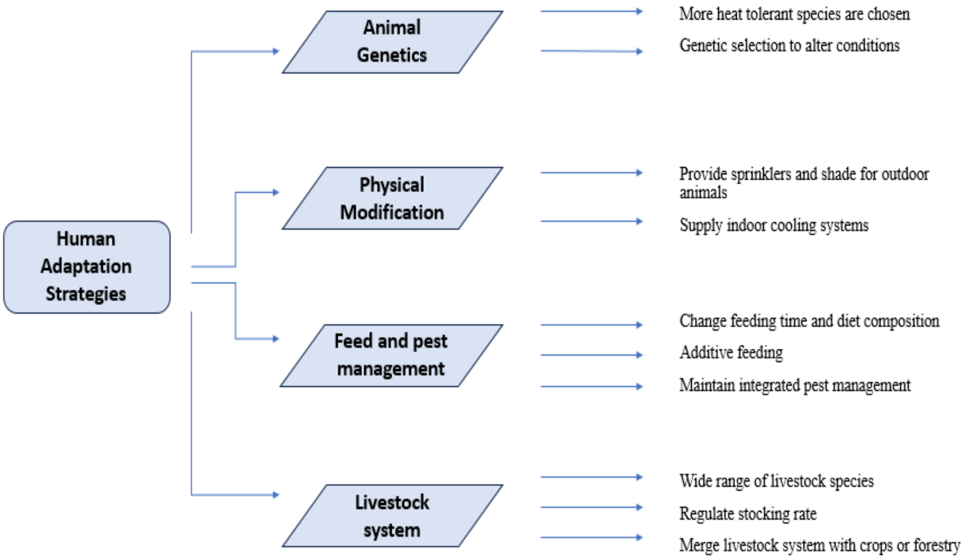

Fig. 4: Human Adaptation Strategies against Changing Environment

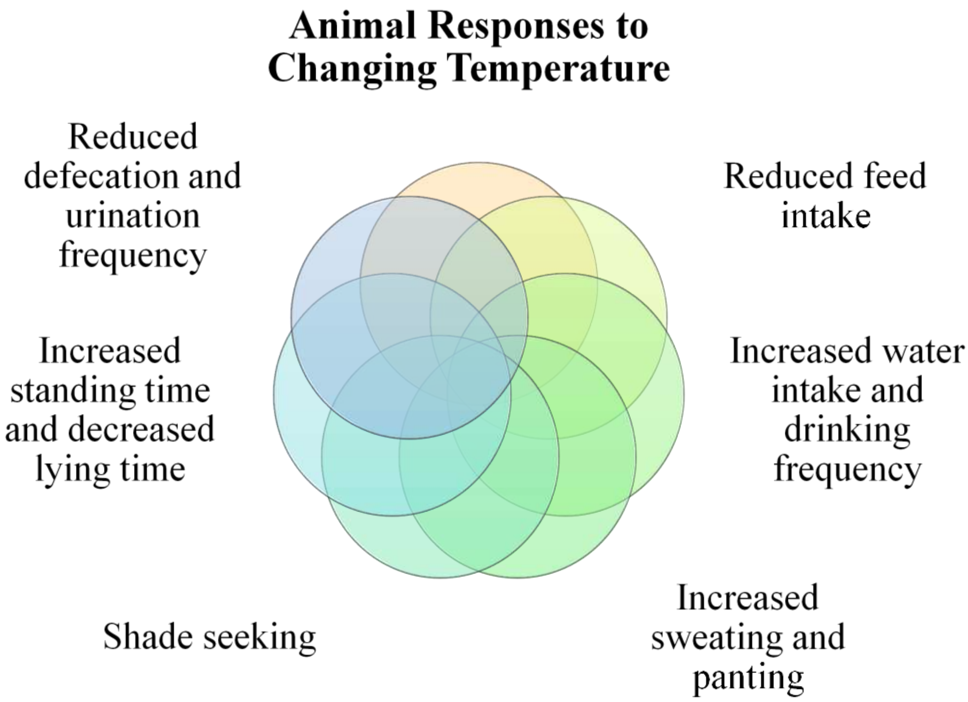

Fig. 5: Adaptations against Changing Environmental Temperature

Case Studies and Success Stories

Rare Earth Elements

The rare earth elements (REEs) are a class of metals that includes yttrium, scandium, and lanthanoids ranging from lanthanum to lutetium. Animals have consumed REEs as feed additives (Tommasi et al., 2023).

Table 2: Effects of selected REEs on animals

Animal	REEs	Authors	Result
Sows	REE mixture (200 mg/kg BW)	Xiong et al., (2019)	Improved antioxidant activity, reproduction of sows, and growth of piglets.
Fattening bulls	Citrates (100 to 300 mg/kg dry matter)	Renner et al., (2011)	Affect dry matter intake and clinical chemical parameters.

Anaerobic Rumen Fungal (ARF) Enzymes

The additives containing live ARF increase the digestion of ruminal fiber. This implies that fungal enzymes may be quickly broken down by rumen microorganisms or that these enzymes may inhibit the development or activity of ruminal microbes. This highlights how crucial it is to supplement ruminant feed with viable cultures of ARF. The ARF has been effectively added to feed to promote rumen fiber digestion and the digestibility of lignocellulosic feeds, which has improved milk production, and daily body weight gain in animals (Jyothi et al., 2024).

Phytogenic Feed Additive

A case study of the performance of broilers was carried out. The results of the studies revealed no globally significant effects on ultimate body weight, feed intake, or mortality. Nonetheless, there was a worldwide favorable impact on the feed conversion ratio. Thus, this study showed that it increased the birds' ability to convert feed to body weight (Martinez et al., 2022).

Probiotics

The probiotics have been made available to non-human animals, directly benefiting them through the creation of fortified feed. Numerous research projects and studies have asserted the advantages of probiotic consumption for animals. These are enumerated in some order below (Zommiti et al., 2020):

Table 3: Probiotic Effects on the Performance of Poultry, Ruminants, and Aquaculture

Animal	Probiotic	Effects
Poultry	*Lactobacillus acidophilus*	Remarkable improvement in growth performances
	Lactobacillus fermentum	Increase in final body weight and improvement of feed intake
Ruminants	*Saccharomyces cerevisiae*	Increase in dry matter intake and milk production
	Lactobacillus acidophilus NP51	Daily administration decreases E. coli fecal shedding in beef cattle
Aquaculture	*Lactobacillus plantarum*	Improvement of growth performance and protection activity in Nile Tilapia
	Bacillus subtilis	Increase of growth and survival levels in Prawn (*Macrobrachium rosenbergii*)

Regulatory Considerations

From a One Health (OH) perspective, animal welfare and health are correlated with consumer safety, feed user safety, environmental sustainability, and consumer safety. The quality and sustainability of animal feed is a fundamental component of the efficacy of the entire food chain.

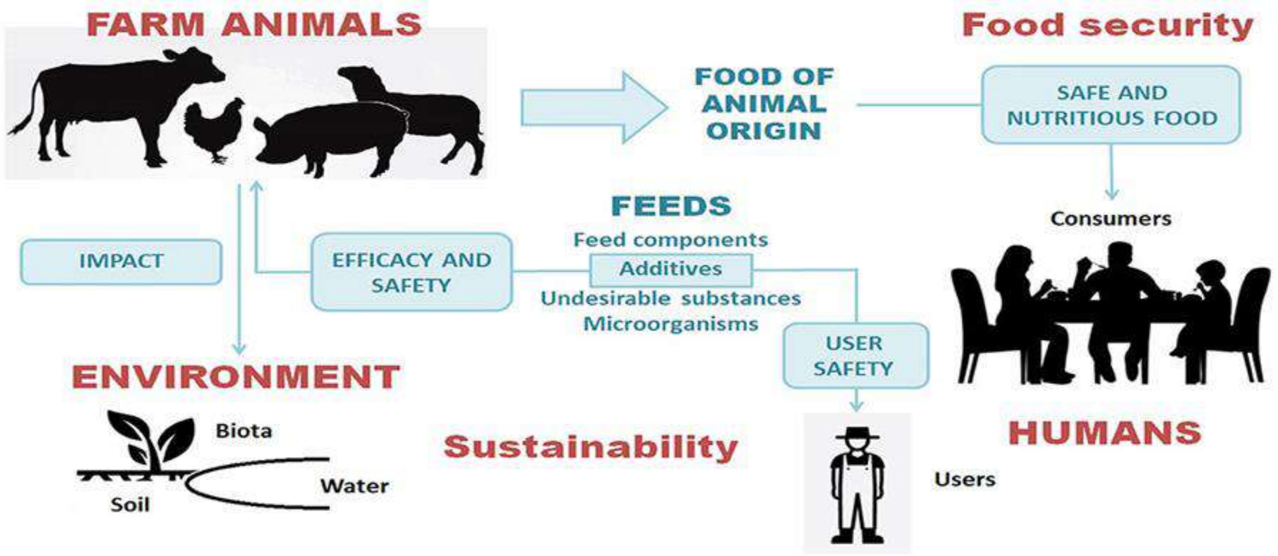

Fig. 6: Safety and sustainability of feed additives (Mantovani et al., 2022)

What does "safety" about a feed additive mean? The environment, animal health, and feed additives are at a crossroads. The One Health (OH) concept, which attempts to handle intricate problems in the human-animal-environment interact through cooperation, interaction, and cooperation across all relevant disciplines, is congruent with the scientific standards supporting regulatory requirements (Mantovani et al., 2022).

Guidelines for Feed Additives

Adding functional feed additives to an animal's diet can increase the quality of the feed, encourage growth, and boost the health and productivity of the animal. The goals of feed additive development and application should be to ensure product quality, adhere to safety regulations, and advance the health and welfare of animals. Additionally, the qualities and features of goods obtained from animals are greatly influenced by the types and caliber of feed and feed additives. (Ghavipanje et al., 2023).

Safety and Efficacy of Feed Additives

The FEEDAP Panel and other regulatory agencies are essential in evaluating the safety and effectiveness of different feed additives. The assessment procedure entails determining how chemicals affect consumer safety, the environment, and animal health. To guarantee the security and effectiveness of these products, regulatory considerations are crucial when making feed additives for animal nutrition. Research has shown that many feeds do not affect animals when used in authorized amounts. There are four essential parts of the feed quality-control program. The efficacy of feed additives is the main priority, with the environment's influence and customer safety coming first (Pandey et al., 2019).

- Quality of Ingredients
- Oversight of Processing
- Quality Assurance of Finished Feed
- Management of Hazardous Substances.

Evaluation Parameters and Product Quality

The evaluation parameters and product quality should follow the below-mentioned procedure (Rychen et al., 2017).

1. Thorough investigations should encompass clinical observations, body weight dynamics, and measurements of feed intake.
2. Additional factors specific to each animal species, such as the laying rate of hens and milk production in dairy cows, should also be considered.
3. Evaluations should include analysis of product composition, sensory attributes, and hygienic standards, preferably employing objective measurement techniques.

Regulatory Framework and Safety Assessment of Food Additives

The food additives now undergo regulatory scrutiny under the Food Additive Amendment (1958) to the Food, Drug, and Cosmetic Act. The FDA has the authority to demand proof from manufacturers that an additive is safe before it can be used in food. Two types of food ingredients are distinguished by the FDCA, each with its own set of regulations and technical requirements:

1. Chemicals that may unintentionally contaminate food
2. Chemicals deliberately introduced to food, either directly or indirectly

The preferred method for assessing the safety of food additives is outlined in a document commonly referred to as "the Redbook," which was first published in 1982 by the US FDA, called "Toxicological Principles for the Safety Assessment of Direct Food Additives and Color Additives" Used in Food. (Pressman et al., 2017).

Global Food Standards and Regulatory Frameworks

Along with the safety assessment efforts of global bodies like the CAC and JECFA, an overview and comparison of food additive regulations across various countries and jurisdictions can be done (Magnuson et al., 2013).

Certain are as follows:

1. It relies on scientific evidence from organizations like the Joint FAO/WHO Expert Committee on Food Additives (JECFA), established in 1956. The Codex Alimentarius Commission (CAC), formed in 1962 by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO), sets global food standards. These standards cover
   - Food additives
   - Contaminants
   - Veterinary drugs, and
   - Hygiene practices, ensuring food safety and quality worldwide.
2. In the European Union (EU), risk management is overseen by the Directorate General for Health and Consumers, while the European Food Safety Authority (EFSA) conducts independent risk assessments.
3. Australia and New Zealand harmonize their food standards under the Food Standards Australia New Zealand (FSANZ), with Australia's regulations managed by the Ministry for Primary Industries (MPI).
4. In South America, Mercosur, a common market, is gradually adopting regional standards, replacing national ones.

Concept of Traceability in Food Chain

The definition of traceability is necessarily broad because traceability is a tool for achieving many different objectives and food is a complex product. An independent food safety watchdog, the Food Standard Agency (FSA) identified three basic characteristics of traceability systems:

i. Identification of units/batches of all ingredients and products,
ii. Information on when and where they are moved and transformed, and
iii. A system linking these data. To enable traceability, an entity to trace has to be a Traceable Resource Unit (TRU) (Aung and Chang, 2014).

Evolution of Food Safety Regulations and Standards in Pakistan

We analyzed food safety issues, assessed food insecurity, and provided solutions for enforcing laws and policies at the national level in Pakistan (Khaliq et al., 2014).

Fig. 7: Global Food Standards

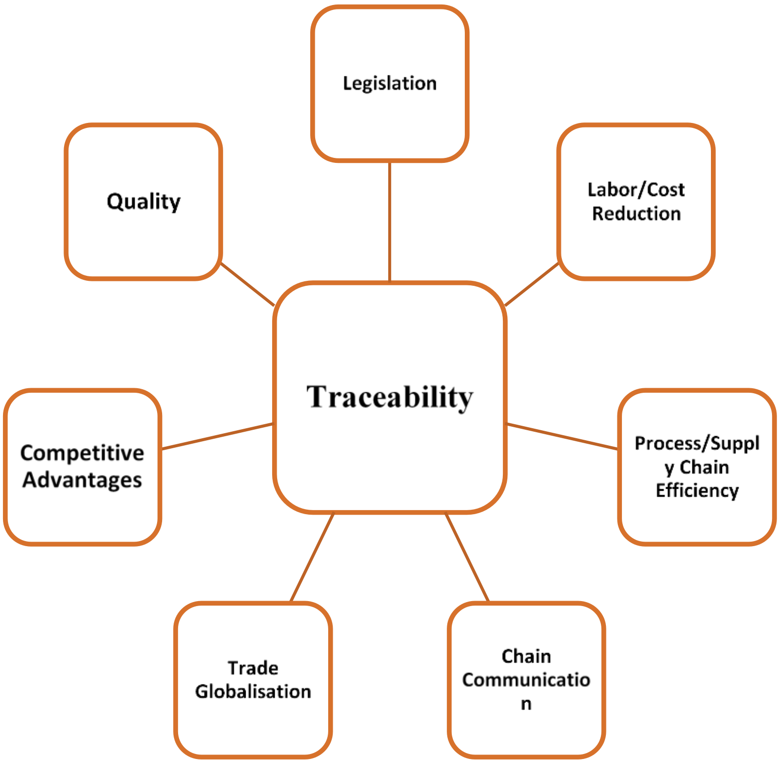

Fig. 8: Drivers for traceability of food supply chain

1. **The Pakistan Pure Food Laws (PFL):**
- Established in 1963, revised in 2007.
- Ensure the purity of raw food and regulate various aspects such as additives, preservatives, colors, antioxidants, and heavy metals.

2. **The Pure Food Ordinance of 1960:**
- Enacted to prevent food adulteration and maintain food quality in the market.

3. **The Ministry of Food Security and Research (MNFSR):**
- Established in 2011.
- Working on drafting the National Agriculture and Food Security Policy.
- Proposed a National Food Safety, Animal, and Plant Health Regulatory Act.

4. National Food Safety, Animal, and Plant Health Regulatory Authority (NAPHIS):

- Proposed to be formalized under the National Food Safety, Animal, and Plant Health Regulatory Act.

Future Challenges in the Feed Additives

The upcoming future hurdles involve gaining insight into the suitable integration of non-animal toxicology testing alternatives in safety evaluations, tackling emerging issues like potential impacts on the microbiome, persisting endeavors to align global regulations, and addressing consumer worries to encourage the efficient utilization of scarce food resources for an expanding global populace. The future challenges within the realm of feed additives for animal nutrition encompass the imperative for ongoing innovation to meet the changing demands for safe and naturally derived animal products (Kwon et al., 2023).

Technological Advancements

In the present day, numerous processes can be monitored in real-time through the utilization of cutting-edge technologies. While these technologies offer valuable data in their current state, additional benefits could be derived by integrating this information as inputs into nutrition simulation models. These models enable the prediction of unmeasurable variables in real time and forecast outcomes of interest. sensor data could be combined with advanced analytical techniques like data fusion, optimization methods, and machine learning to further enhance their utility in precision animal nutrition applications Moreover, the data generated by sensors can synergize with simulation models, thereby enhancing their capabilities and expanding their applications (Gonzalez et al., 2018).

Conclusion

Ultimately, the world of animal nutrition is greatly impacted by the use of feed additives to address various concerns such as animal health, feed effectiveness, and sustainability. These additives, including traditional supplements as well as modern innovations like probiotics, enzymes, and plant extracts, are crucial in enhancing nutrient absorption, strengthening the immune system, and promoting animal well-being. Regulations and advancements in technology play a key role in influencing the future of feed additives, emphasizing the importance of ensuring safety, efficacy, and sustainability in animal agriculture. To address upcoming challenges and opportunities, continuous innovation and teamwork are essential to meet the varied needs of animal nutrition while also protecting the health and welfare of animals and the environment.

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Chapter 18

Enzymatic Innovations: Maximizing Aquatic Nutrition Efficiency

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ABSTRACT

Enzymes are primarily a type of proteins in biological systems. They are commonly used as catalysts for catalyzing the rate of reactions. Feeding of these enzymes in the aquaculture field has some nutritional advancements. Maximum feed efficiency must be required for cost-effective operations. This chapter aimed to demonstrate the current status of knowledge on the influences of exogenous enzymes in aquaculture and explore the application of exogenous enzymes as a safe and effective additive for regulating productive performance, feed utilization, digestibility, carcass composition, immunological response of fish and reduce chemical pollution into the environment. The utilization of exogenous enzymes provides a holistic solution to the mortality of aquatic species. Additionally, enzymes perform significant roles in formulating cost-efficient, high-quality, and eco-sustainable aquafeeds. Currently, the utilization of enzymes in aquafeed can lower the utilization of fishmeal ingredients which ultimately reduces the expenses of fish production. This may help to reduce the demand for fishmeal ingredients from the aquaculture sector in the coming years.

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INTRODUCTION

Food security has become one of the major concerns of governments around the world as the population of human beings increases. Nutritional security is receiving higher preference in this era of revolutionary information technology. The United Nations Food and Agriculture Organization (FAO) projects that the global population will rise from the current estimated 7.5 billion to 9.1 billion by 2050. A substantial increase in the production of food will be demanded to fulfill the rising food demands of the growing population. In FAO report on "How to feed the world in 2050" assessed that the production of food in several countries will need to be doubled (FAO, 2020). Food choices of human beings are also changing toward more dairy as well as meat products. Therefore, FAO data explored that the rate of global per capita meat intake is rising only for fish and chicken. As feed conversion into edible meat from fish is the most effective for all reared species, aquafarming is potentially the most feasible source of protein production to fulfill worldwide requirements. Surrounding saturated agriculture and livestock production sectors are trying to fulfill the demands of an increasing population, particularly for higher quality and inexpensive protein sources (Chen et al., 2023).

In effect, aquaculture should share societal responsibilities with agri farming because it is a growing field in worldwide production of food. Flourishing global aquaculture sector can go hand in hand with agri farming for supporting the goal of attaining nutritional security. The aquafarming sector acts as a food production sector for needy nations because fish protein is a cheaper protein source instead of other animal-based protein sources. However, the dependence of aquaculture on expensive components of feed, lowers its economic feasibility and ultimately limits the demand from poor nations (Sampath et al., 2020). Furthermore, the growing percentage of the population that eats fish places greater demands on aquaculture than on nearly static catch fisheries. Aquafeed cost is the highest portion of operational expenses of aquaculture sectors and in this way, the price as well as accessibility of ingredients restrict the development of aquaculture. So, fish nutrition is a critical component for the development of worldwide aquaculture productivity (Naylor et al., 2021).

Challenges in Aquaculture Nutrition

There are multiple problems associated with the development of the aquafeed industry and nutritional research. Furthermore, the cost of fish meal ingredients appears to be increasing much more rapidly than its production rate, changing from 657USD per metric ton in Jul 2002 to 1,610USD per metric ton in Jul 2022 (Mundi, 2014). That's why, reducing the utilization of fishmeal in aquaculture feeds is imperative. Systematic as well as technical innovations are crucial for making aquaculture operations economical. The significant requirement for reducing fish meal utilization in aquafeed has led feed producers to apply two main nutritional strategies: low fish meal diets (LFD) as well as protein-saving diets (PSD). LFD involves replacing fishmeal with alternate protein sources like fish and other animal by-products, unicellular proteins, plant meals, and insect-based meals in the prepared feed to fulfill fish's basic protein needs (Yan et al., 2023).

An increasing quantity of fishmeal from fish by-products is being utilized and was assessed at over 27% of the worldwide fishmeal utilized in aquaculture in 2020 (FAO, 2020). Single-cell proteins as well as insects are promising alternatives to traditional fish meals because they have short life cycles, their production does not require a huge area, and they have highly digestible protein with amino acids content similar to fishmeal content. Plant-based components are the most efficient alternatives to fishmeal in aquafeed. At present, the aquaculture feed industry is trying to incorporate inexpensive plant-based ingredients to substitute expensive animal protein sources for preparing cost-efficient feeds (Wang et al., 2023). Plant-based protein sources, like soybean meal, cottonseed protein concentrate, and rapeseed meal have been broadly studied as a substitute for fish meal (Xie et al., 2023).

Protein-saving feeds on the other side feature a low protein content, supplemented with essential nutrients, like high lipids, amino acids, and high sugars (Yu et al., 2022). Although LFD as well as PSD have been known to offer cost-efficient benefits as well as lessen dependency on fish meal, studies have also associated to negative impacts on reared aquatic species (Willora et al., 2022). Presently, plant based protein sources dominate fishmeal replacement in aquafeed (Chen et al., 2022); but, these protein sources have various disadvantages like lower digestibility, poor bioavailability, antinutritional factors (ANFs), and palatability problems. Prior research has shown that feeds having plant protein sources may hinder digestive enzymes activities. This interruption is credited due to the existence of protease enzymes inhibitors in plant sources that fix to the active sites of endogenous proteases (Xu et al., 2022).

To tackle this problematic condition, investigators are incorporating exogenous enzymes into aquafeed as a verified nutritive strategy, which can enhance the quality of aquafeeds which include plant protein sources or other unwanted protein sources. This chapter discusses the application of exogenous enzymes in aquatic feed, encompassing its beneficial characteristics as well as inherent disadvantages. The aim is to provide a comprehensive understanding of the topic and to propose possible areas for further research to fully maximize all potential benefits (Liang et al., 2022).

Enzymes Currently Utilized in Fish Feed

Enzymes are proteins that catalyze multiple reactions, transforming compound materials into absorbable ones. They are found in all living organisms, from simplest to higher organisms. Enzymes are produced by various microorganisms, including fungi, bacteria, yeast, and rare gastric microbes. Enzymes are essential for nutrient advancements in aquaculture practices, reducing the negative effects of anti-nutritional factors and enhancing dietary energy. The addition of living microorganisms in aquafeed can stimulate enzyme production, and fermentation with microbes is widely used for large-scale commercial purposes. Enzymes are found in all living beings, from fungi to yeast, and are essential for the growth and health of aquatic species (Nathan et al., 2018).

Enzyme stability is essential for incorporating them into feed. Heat stability is a chief parameter to be considered. Granulated feed enzymes are a good option for the palletization process since they assist the enzymes stay active for extended periods. There are several classes of enzymes comprising lipase, xylanase, amylase, phytase, cellulase, protease, and several others as shown in Fig 1, which can enhance the bioavailability of nutrients, and absorption of nutrients during the digestion process; improve the fish growth performance, and also support the fish survival in early life stages. In this way, it prepares the feed more cost-effectively. Enzymatic usage may provide an answer to the mortality of larval forms of aquatic animals. Feeding larvae with exogenous enzymes would be a valuable practice (Islam et al., 2021).

Proteases

Exogenous protease is a crucial enzymatic player that optimizes the nutritional quality of alternative feed ingredients. It plays a vital role in controlling the negative effects of protein-based diets by exposing the bioavailability of essential dietary components. Protease enzymes, first recognized in 1903, can enhance the digestibility of protein and amino acids in animal and plant sources (Awad et al., 2020). Plant-based ingredients like rapeseed, soy, and canola contain trypsin inhibitors that prevent protein breakdown by trypsin in the intestinal tract. The apparent digestibility of protein-enhanced feeds can increase from 2 to 4% in feeds with 31% crude protein (CP) and from 3 to 8% for diets with 28 and 26% CP (Buchholz et al., 2020).

Protease has the potential to enhance the digestibility of protein components and aid in preparing aquafeeds that are more consumable and less contaminating. It can also help control feed preparation costs by selecting inexpensive components. Commercial proteases, such as papain, alcalase, neutrase, trypsin, and flavourzyme, can be categorized into three types based on their source: plant, animal, or microbes (Zheng et al., 2020). They can also be classified into neutral, acid, and alkaline proteases based on their working pH values. Temperature and pH influence protease activities and outcomes, which may vary depending on the animal's gastrointestinal tract pH and rearing temperature. Proteolytic enzymes can degrade proteins into peptides with trypsin and alcalase targeting peptide bonds at the C-terminal side of arginine and lysine residues and hydrolyzing hydrophobic bonds (Schneider and Lazzari, 2022).

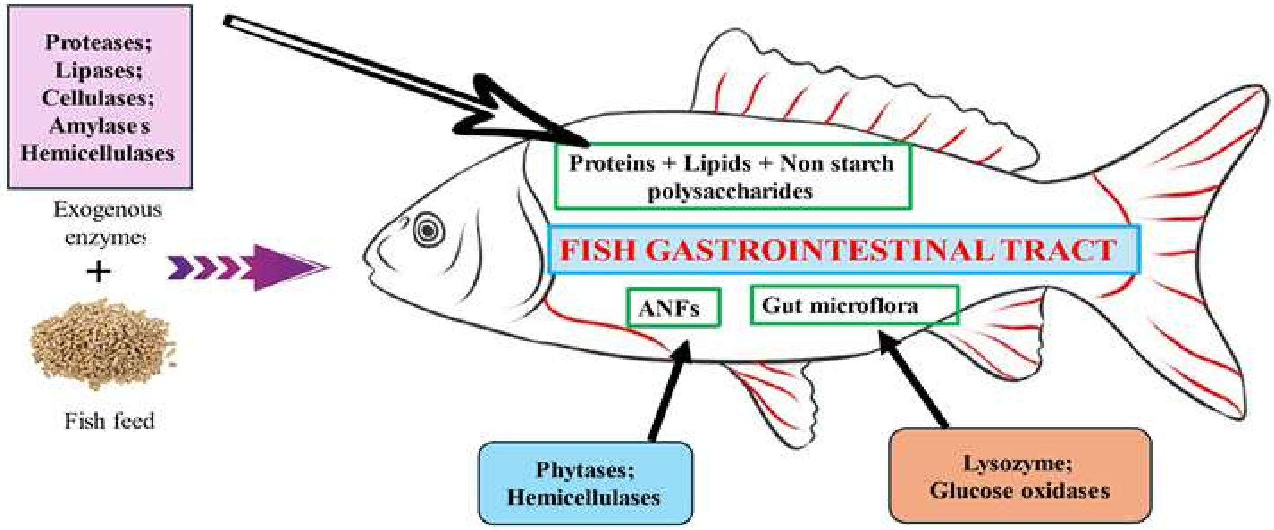

Fig. 1: Supplementation of different exogenous enzymes in fish feed (Liang et al., 2022)

Amylases

Amylase, which breaks down the starch, performs a vital role in the development of fish (Upreti et al., 2019). Starch is the prime digestible polysaccharide, present in plant-based aquafeed components that are widely utilized in the aqua farming sector. Fish growth is directly impacted by the starch degradation. Even while many fish species naturally have the digestive enzyme amylase, but the carnivorous fish may have poor expression of this enzyme, which would damage their capability to digest starch for energy (Ghosh et al., 2019). Furthermore, fish that are carnivorous may experience prolonged postprandial hyperglycemia, poor metabolic activities, and a lowered rate of nutrient utilization in aquatic feed that has a great quantity of carbohydrates (Petitjean et al., 2019). Consequently, feeding aquatic animals with feed containing exogenous amylase may make it easier for them to hydrolyze complex sugars and produce glucose for energy. The incorporation of exogenous α-amylase into aquafeed enhances Silver Perch's capability to digest starch (Hasan et al., 2023).

Lipases

Lipases are carboxylic ester hydrolytic enzymes that sequentially break down the ester bonds of triglycerides for forming glycerol as well as fatty acids. In the metabolism of fish, lipolytic enzymes have two classes: phospholipase A2 and lipases, that have been investigated mostly (Jacobsen et al., 2018). The main way to investigate the impacts of lipases on fish performance is to incorporate them into aqua feed lonely or with a combination of other enzymes. Their functions in regulating fish adipose tissues are crucial, as they eventually influence the quantity as well as the quality of meat produced by reared aquatic animals. Fish larvae have lipase enzymes in their mouths already but they demand typically to be activated by bile salts. The commercial multi-enzyme preparation that contains lipase enhances the development of fish (Upreti et al., 2019).

Phytases

Phytase enzyme has been utilized more frequently in aquafeed, revealing significant influences in multiple physiological processes that inhibit the action of phytate (Olugbenga et al., 2017). Phytate is an anti-nutritional factor usually present in plant-based feed components. This makes chemical complexes along with proteins, mineral elements (e.g., magnesium, zinc, and iron), and other nutrients, reducing the absorption as well as utilization of these ingredients. Particularly, phytate-bound phosphorus has a very lower level of bioavailability in mono-gastric species like fish, due to the lack of an intestinal phytase enzyme in these rearing species (Adeoye et al., 2016). Because of the rising number of phytase enzymes in the market, farmers are capable of degrading the anti-nutritional factors efficiently, so it is becoming a common strategy to incorporate phytase into aquafeed. Phosphorus is an essential mineral for fish development, but its discharge in the environment is becoming high day by day, and it may be accountable for pollution and eutrophication of coastal seawater as well as watersheds (Maas et al., 2018).

Enzymes Addition Procedures

Enzymes are essential in aquafeed for their capability to convert complex components into absorbable nutrients. They can be incorporated even during fermentation processes like the fermentation of soybean meal, which makes a delightful taste. Because lactic acid bacteria have a poor capability for the production of proteases that cause the breakdown of protein into smaller peptides. To tackle such issues, exogenous protease enzymes are generally incorporated during the fermentation of soybean meal. Nutritional exogenous enzymes are usually incorporated into aquafeed, whereas antibacterial enzymes (e.g., glucose oxidase) may also be incorporated into animals' protective products (Tsai et al., 2021). Pre-treatment of feed ingredients can enhance the utilization of nutrients and reduce nutrient discharge into the surrounding environment. However, the enzymatic pre-treatment of feed is infrequently utilized due to its high cost and potential adverse effects on feed properties and final pellet characteristics. So, techniques of addition must be chosen, according to their characteristics in aquafeed formulation. Various studies have shown that enzymes do not improve nutrient digestibility or fish growth performance, but another outcome was observed with similar enzymes utilized in salmonid aquafeeds (Jiang et al., 2021).

Exogenous enzymes in fish feed can have different effects depending on factors like ingredients, enzyme types, procedures, and rearing conditions. Acidic resistance of exogenous enzymes incorporated into aquafeed should be considered differently depending on development stages. Enzymes are necessary for most adult fish feed, and factors like pH, temperature, and moisture level significantly impact enzyme activity (Ye and Chi, 2018). Techniques like extrusion of conditioned hot mash and conditioning with steam under pressure are used to maintain enzyme activity during pelleting. Enzyme unfolding and inactivation can be explained by heat, moisture level, pressure, and time. Pelleting processes must ensure enzymatic activity retention (Sirisha et al., 2016).

Aquafeed can maintain enzyme activity through various procedures like pelleting, microencapsulation, and the use of lipids and natural polymers. Pellets can maintain the catalytic activity of multiple enzymes, even at high temperatures (Yao et al., 2019). Microencapsulation methods like alginate, chitosan, and xylans protect enzyme function during aquafeed production and protect against endogenous protease enzymes and water quality factors in the digestive tract. However, microencapsulation may not act in the proximal part of the intestine, where nutrient digestion and absorption occur. Encapsulation of microbial phytase in chitosan/alginate microcapsules enhances the digestibility and bio-availability of nutrients from plant-based proteinous feeds in Rainbow Trout (Guo et al., 2020).

The preparation, as well as methods of exogenous enzyme application to aquatic-reared species, is crucial for the optimum bio-processing of aquatic feed. Different processes for enzyme addition in feed vary according to the types of enzymes, biochemical characteristics of enzymes, target aquatic animals and their growth stages. Genetic engineering has been broadly utilized for enhancing the properties of enzymes and improving their use in the aquaculture sector (Gordeeva et al., 2019).

Advantages of Enzymes

Recently, supplementation of enzymes in aquafeed has become an efficient approach to enhance animal growth as well as gained massive attention from aquafeed manufacturers and aquaculture investigators. Different exogenous enzymes are broadly utilized as feed additives around the world due to their diverse benefits, as depicted in Fig 2.

Feed Utilization and Digestibility

Scientific studies have shown that enzymes can improve feed utilization and digestibility in fish feed. Non-starch polysaccharides found in walls of plants can increase the viscosity of digestive tract chyme, reducing the utilization of starches, proteins, and several other nutritional materials. Incorporating enzymes (like as carbohydrase) into aquafeed can enhance the utilization rate of feed by damaging the hydration membrane around the chyme and strengthening interactions between enzymes and chyme. Mostly plant-based aquafeeds and cereals carry phosphorus in the form of phytate, but finfish do not have these enzymes to hydrolyze such phosphorus forms. This leads to phosphorus pollution in the feed. Exogenous phytase enzyme can convert phytate phosphorus into the available phosphorus form, upgrading the utilization of phosphorus in aquafeed and consequently decreasing pollution (Pfeuti et al., 2019).

Growth Performance

Dietary regulation is a favorable approach for optimizing the growth of larval fish. Studies have shown that the growth response of larvae is poor when feeding formulated feed, possibly due to inadequate development of the gastric tract as well as inadequate enzymatic activities. The incorporation of external enzymes in the aquafeed can overwhelm the endogenous deficiency of these enzymes and enhance growth response. Dietary cellulase can raise the ether extract of body tissues by $99gkg^{-1}$, as well as the inclusion of phytase and cellulase can improve the lipid levels $499Ukg^{-1}$ and $2gkg^{-1}$ respectively. Consequently, dietary regulation is a beneficial approach for enhancing the whole growth performance of larval fish (Cao et al., 2022).

Promote Immune Response

Fish's immune system is influenced by various factors such as disease, pollutants, hormones, and feed. The inclusion of phytase up to 1,000 units per kg in feed can substantially enhance the immunity responses as well as the survival of *Oreochromis niloticus* after being challenged by *A. hydrophila*. In aquafeed having lower protein content and rich lipid content, dietary exogenous lipase enzymes can enhance fish intestinal immunological responses by increasing acid phosphatase activities, downregulating pro-inflammatory cytokines, as well as upregulating anti-inflammatory cytokine gene expression. This may be partly due to the regulation of nuclear factor-kB p65 protein inhibitors, κBα, IκB intestinal kinase, and rapamycin mark signaling pathways in aquatic species (Resende et al., 2022).

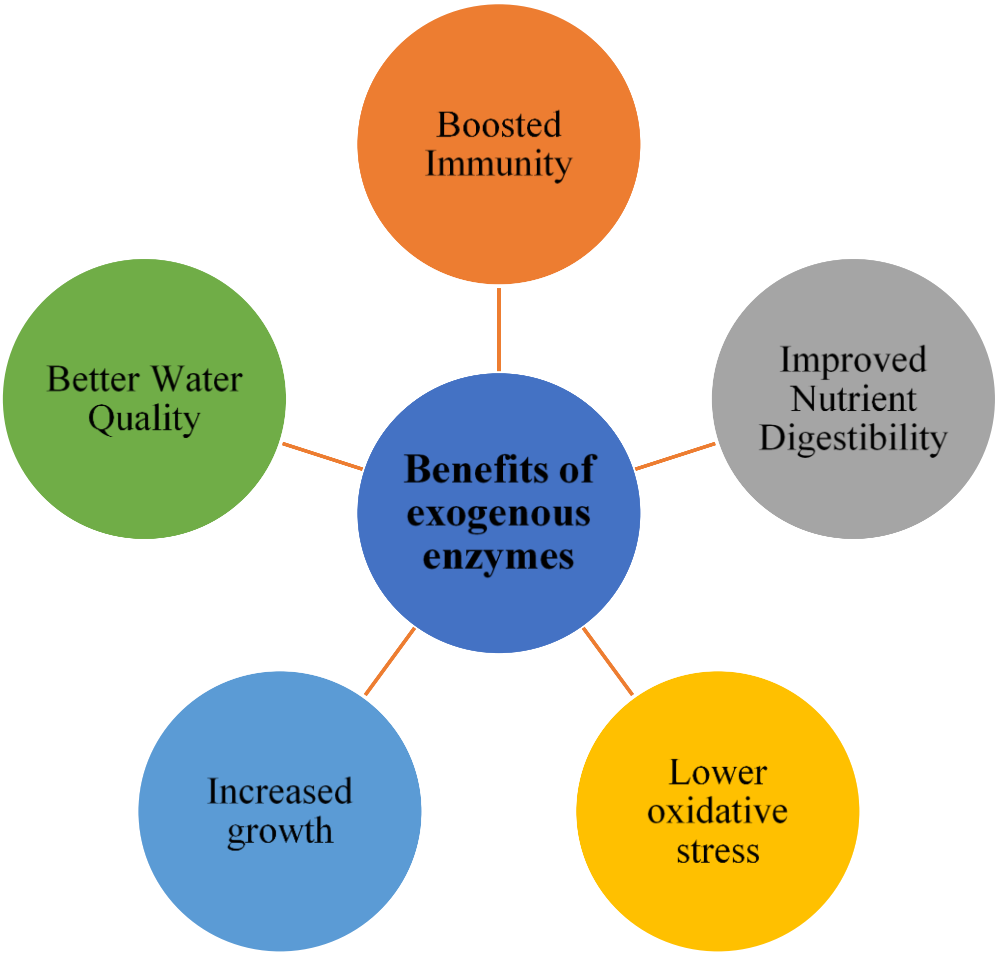

Fig. 2: Different benefits of exogenous enzymes in fish feed.

Addressing Challenges in Plant-Based Diet

Mostly critical issues with plant protein sources in aquafeeds for aquatic species, especially for flesh-eating species are high levels of carbohydrates, lower levels of proteins, poor amino acid profile, lower digestibility, and other nutritional substances and anti-nutritional factors. Poor amino acid profiles and unbalanced nutritional makeup can be balanced through the mixing of different ingredients of multiple origins as well as the utilization of feed supplements like vitamins, amino acids, minerals, etc (Song et al., 2020).

Impact on Fish Microbiota

Recent studies have explored the impacts of external enzymes on the microbiota of fish, revealing that dietary enzymes can significantly alter intestinal status. For example, Grass Carp fed cellulase-supplemented duckweed-based diets showed significant changes in bacterial species and density, while Tilapia fed carbohydrase-supplemented diets showed significant differences. Although the microbiota diversity parameters were not impacted by nutritional treatment, PERMANOVA analysis exposed differences in community profiles. A trend was shown for microbe's modifications, with the rise in intestinal bacterial diversity. Future research should focus on more detailed and massive studies utilizing high-throughput sequencing analysis to corroborate these hypotheses. This could help in understanding the impact of diet composition on fish microbiota (Wu et al., 2020).

So far, the investigation related to aquafeed supplemented with enzymes is trendy as well as non-systematic, and the present chapter is an effort to collect renewed research-based knowledge of exogenous enzymes to assess the impact of supplementation on growth, nutritional digestibility, feed consumption, immunological responses; challenges with plant based diet and disease vulnerability of finfish, also to strengthen more investigation on this concept and recommend further opportunities for upcoming research.

Characteristics of Enzymes and Delivery Efficiency

There are several strategies to enhance the economic feasibility of aquafeed supplementation with exogenous enzymes. In the preceding years, attention has been paid to the manufacturing of enzymes that are less susceptible to proteolysis during transportation in the digestive tract and thus survival is longer in the gastrointestinal tract. Nowadays, more investigations focus on the tolerance of acid-base, thermal stability, as well as substrate specification of external enzymes.

Enhancing Enzyme Thermal Stability and Encapsulation

To prevent the deactivation of enzymes in the high-temperature diets, a large number of enzymes with higher thermal stability have been discovered from thermophilic bacterial species or engineered by genetical engineering. Additionally, another practice, the fluidized bed technology, was used for coating the protease enzymes. This approach is becoming more popular in the food production sectors because encapsulated substances can be utilized under higher temperature ranges and other extreme conditions, thus strengthening their vitality as well as stability (Liu et al., 2018).

Species-specific Consideration

Additionally, supplemented enzymes will display varying efficacy in different aquatic animals due to the variety of their digestive tracts. The gastric environment of fish with the absence of a stomach is neutral (like Cyprinidae) or slightly alkaline. However, due to the synthesis of gastric juice in stomach-bearing fishes, the pH in the gastric system is very low, even reaching 1.3 in Tilapia. Therefore, the acid-base tolerant ability of supplemented enzymes also influences the fish species. Novel strategies involve genetic manipulation of the structure of the manufactured enzymes so, it is greatly intrinsically acid-base tolerant (Shi et al., 2017).

Enzyme Specificity

The specificity of an enzyme is the ability to pick up a specific substrate from a group of similar molecules. Specificity is a molecular identification method, and it works through the conformational as well as structural complementarity between substrate and enzyme. A single enzyme indicates varying levels of specificity regarding its substrates. Like, trypsin, a serine protease enzyme of the gastrointestinal tract, can hydrolyze a peptide linkage in which an amino group is donated by a basic amino acid like histidine, lysine, and arginine; lactase can only hydrolyze the β-1-4 glycosidic bonding of lactose to get glucose and galactose; similarly, maltase only acts on α-1-4 glycosidic bond of 2 glucose molecules in maltose. Hence, the effectiveness of external enzymes utilized in aquafeeds must be evaluated on the enzyme-substrate specification of individual ingredients (Vielma et al., 2004).

Overcoming Inhibitor

Instead of the multiple benefits, supplemented enzymes experience several inhibitors in the digestive system that could significantly inhibit the roles of supplemented enzymes. Like, hydrolysis of supplemented enzymes can happen by protease enzyme produced in fish bodies. To overwhelm this restricted factor, various polymeric complexes are being utilized in the medicinal sector to enhance the delivery effectiveness of supplemented enzymes and establish an effective chitosan nanoencapsulation delivery system for strengthening the effectiveness of supplemented trypsin in the digestive tract of Rohu. These findings show that a nanoencapsulated system for trypsin mimics zymogen proteolytic activities through a controlled delivery system, enhancing performance and intestinal security (Kumari et al., 2013).

Multienzyme Complexes

Aquafeed, a complex blend of crude lipids, carbohydrates, crude protein, and inorganic salt, may offer benefits by using a supplemented multienzyme instead of a single enzyme. However, some studies have shown that the addition of phytase and protease in diets has no significant impact on growth responses, feed conversion ratio, or nutritional digestibility of Trout (Yigit et al., 2018). The multi-enzyme complex (Superzyme CS: amylase, xylanase, protease, cellulase, and β-glucanase) in Trout aquafeed did not significantly influence growth performance. To improve the combination effectiveness of supplemented enzymes, it is crucial to understand how enzymes synergistically hydrolyze their substrates. Supplemented enzyme mixtures with practical adjustments can improve fish growth response and lower feed coefficients (Diogenes et al., 2018). Ghomi et al. (2012) stated that *Huso huso* fed with multienzyme complex 249mgkg^{-1}, which comprises lipase, protease, phytase, α-amylase, xylanase, hemicellulase, β-glucanase, cellulase, pectinase, and pentosanase; showed significant weight gain as well as specific growth rate, and also considerably enhanced FCR.

Correspondingly, it was also described that feed containing multienzyme Natuzyme50® (Bioproton) improved the digestibility of proteins in Tilapia fish, increased the activity of gastric enzymes, and boosted growth. Additionally, Diogenes et al. (2018) examined that feed containing Natugrain® TS, BASF (NAT) and endo-1,4 beta-xylanase (5,500TXU/g) in *Scophthalmus maximus* improved the digestibility and activity of digestive enzymes in the posterior part of the fish's intestine. Understanding substrates is crucial for developing multienzyme complexes that damage targeted substrates (Hlophe-Ginindza et al., 2016).

Economical Benefits of Enzymes

The application of exogenous enzymes must be appropriate, and show significant advancements in feed conversion or quality of product to fulfill modifications in formula cost ensuring great profit margin. Furthermore, they must somehow enhance the low-price formulation by reducing input expenditures and expanding outcomes like animals' growth, health status, or expenditures for making one unit of animals' protein (Su et al., 2022). The economic advantages of utilizing phytase are more straightforward than those of proteases and xylanases. Phytase offers a direct financial advantage by substituting the requirement for inorganic phosphate. The advantages of decreasing phosphorus load and aquafeed preparation expenditures are clear, and as a result, phytase enzyme is reflected as one of the standard feed additives (Boyd et al., 2020).

Conclusion and Future Opportunities

With the rising application of plant-based ingredients like wheat bran, wheat flour, and palm oil by-products in aquafeeds, there is a benefit in enhancing the digestibility of plant cell walls for exposing vital nutritional substances arrested in the plant cells through the incorporation of exogenous enzymes in diets. Cereals' cell walls (like rice, barley, wheat, and maize), are chiefly composed of β-glucans as well as arabinoxylans, while oil-based crops (like sunflower, soy, and canola) are chiefly pectins and xyloglucans. Exogenous enzymes that hydrolyze mannans, cellulose, xylans, etc, are broadly utilized in poultry or livestock diets, but they are also incorporated into aquafeed. The combined addition of xylanase and phytase along with proteases enzyme boosts the utilization of protein overall. Further study is focused on investigating the complexes of exogenous enzymes for boosting aquafeed effectiveness. Sustainable aquafarming relies on eco-friendly aquafeeds, as fishmeal is a costly component in aquafeed production. Researchers are exploring alternatives to fishmeal, such as plant protein sources supplemented with exogenous enzymes. This approach can produce economical, high-quality, and eco-sustainable aquafeeds. Currently, using these enzymes in aquafeeds can reduce fishmeal usage, thereby reducing fishmeal production costs. This approach could help reduce the need for fishmeal from aquaculture in the future.

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Chapter 19

Impact on Water Quality of Aquarium after Adding *Bacillus subtilis* in Aquarium

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ABSTRACT

Aquarium are used for raising ornamental fishes or aquatic animals. People usually keep aquariums at their home for their own fun and interest. But the poor water quality of the aquarium can cause the death of fishes and shrimps. While probiotics or beneficial bacteria can improve the water quality of the aquarium. These beneficial bacteria can be supplied with a regular feed of the host animal or it can be added in pond or aquarium to improve water quality. *Bacillus subtilis* is a beneficial bacterium to overcome water pollution and it provides a healthy environment or surrounding to aquatic animal. Healthy environment for aquatic animal is non polluted and contaminated free water so it's better to use *Bacillus subtilis* rather than facing problems of polluted water. Probiotics, specifically *Bacillus* species, are more effective in converting organic matter to CO2, it is recommended to keep probiotic levels high in aquaculture production systems or ponds in order to lower the load of organic carbon, it is beneficial to improve water quality and fish health.

KEYWORDS
Aquarium, Probiotics, *Bacillus* spp., *Bacillus subtilis*, Ornamental fishes, Water quality

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INTRODUCTION

Aquaculture

Rearing or culturing of aquatic animals is known as aquaculture. Fishes, shrimps, starfish, echinoderms and molluscs all these are aquatic animals (Hyuha et al., 2011)

Aquarium

In the aquatic ecosystem, there are two types of fishes are being cultured: 1) food fish 2) ornamental or colorful fishes. These ornamental fishes can be marine and freshwater. According to a research, ninety percent of these fishes belongs to freshwater that are kept in aquarium (Dawes, 1998). First wide aquatic animal's house or aquarium was placed in the zoological garden of London in eighteen fifty-three (1853) (Brunner, 2012). Ornamental fish raising in aquarium is considered as well-known hobby of European people. United States is famous for selling their ornamental aquatic animals all around the world (FAO 1996-2005; Chapman 2000).

Modern techniques are used for improving food fish culturing system but there are no new techniques that can bring improvements in fish house or aquarium (Chapman 2000). According to (Monticini, 2010), each year almost two billion colorful fishes are used for exporting purpose. Colorful aquarium fishes have gained the attraction of hobbyists because of their rising need these fishes are cultured more in number moreover their high exportation is considered as a major risk for their sustainability (Chao et al., 2001). Aquarium for raising ornamental fishes shown in Fig. 1.

Ornamental Fishes

Demand for ornamental fishes is increasing day by day, as these are used to increase the beauty of homes. People usually capture pictures of colorful fishes for their fun and joy. Because of increasing demand, their culturing rate has been increased all around the world (Kumar et al., 2015). According to research by (Chen et al., 2020) almost twenty million attractive fishes are captured from natural aquatic ecosystem and people buy two million of them for their own fun and enjoyment. That's the reason there is a need to increase the production rate of these colorful fishes.

(Novák et al., 2020) described that total seven thousand species of colorful fishes are existed all around the world and it is believed that out of them five thousand are those that live in fresh water while only eighteen hundred species are those that live in marine aquatic ecosystem. According to research, almost 120 countries are involved in selling, purchasing and trading of colorful fishes. Among these top trading countries are Asian like China and well-established countries like U.S. The culturing rate of colorful fishes in these countries is sixty percent (Evers et al., 2019).

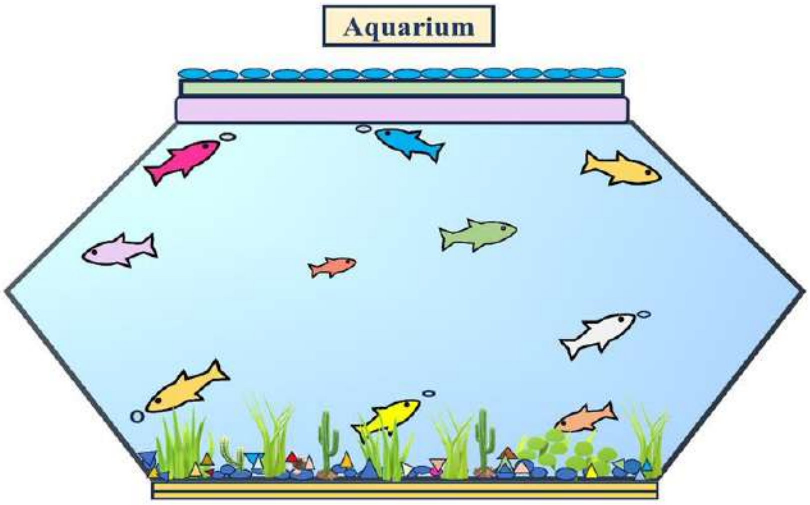

Fig. 1: Aquarium for raising ornamental fishes

Water Quality of Aquarium

Water is the environment of aquatic animals. Beautiful aquarium fishes that are raised in freshwater, their water quality must be beneficial for the survival of culturing animals (Ghufran and Kordi 2005). The quality of aquarium water is determined by temperature, oxygen, nitrogenous content, PH range, carbon and ammonium content of culturing water. For the best water quality, these factors must be according to the demand of fish (Lesmana and Daelami 2009).

Clean Water Aquarium

Purity of water can be determined by its biological, physical, and chemical factors (Eruola et al., 2011). Water plays a vital role in the growth of aquatic animals. All water parameters must be according to the demand of cultured animal, its quality must be good to get good production from aquaculture (Sofia, 2018). Fishes raised in clean water Aquarium is shown in Fig. 2.

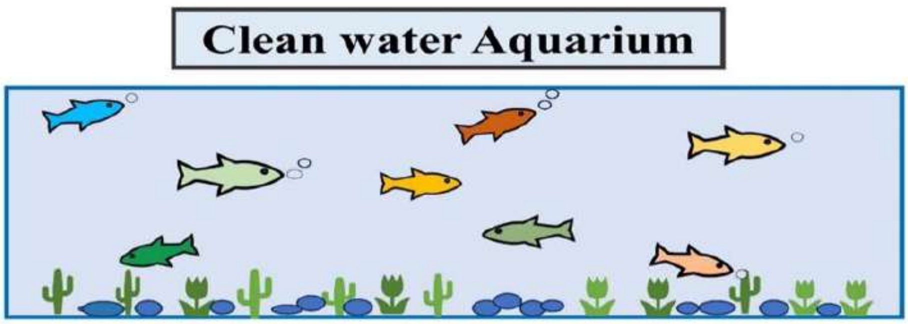

Fig .2: Fishes raised in clean water Aquarium

Polluted Water Aquarium

According to (Umesh et al., 2008) death rate among fishes has been increased while weight and production rate has been decreased due to poor water quality of the aquatic ecosystem. Disease-causing bacteria that are present inside culturing water can increase disease risk among aquatic animals. These harmful bacteria can also deteriorate water quality (Shakya et al., 2013; Wang et al., 2018). Fishes raised in polluted water aquarium is shown in Fig. 3.

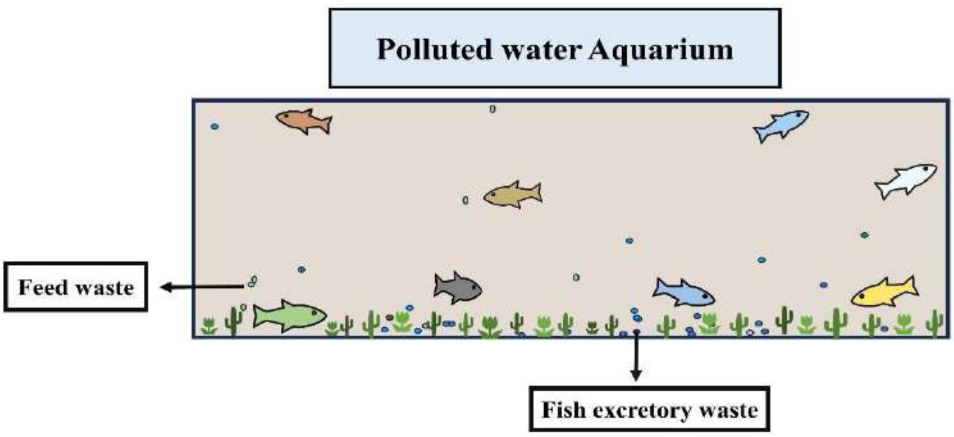

Fig. 3: Fishes raised in polluted water aquarium

Harmful Effects of Antibiotics

Antibiotics are considered to increase the development rate of aquatic animals. Tetracycline, beta-lactam and macrolides these are antibiotics that are widely used in the aquatic ecosystem (Chen et al. 2020). Antibiotics can be used by blending it with a regular diet of aquatic animals. It can also be added to the culturing water, can also be given to infected aquatic animal by injections (Liu et al., 2017).

People usually add antibiotics in culturing water without knowing the reason of disease (Rahman et al., 2022). Antibiotics are not digested by aquatic animal (Chen et al., 2020), according to another research it is released from the fish's body in its original form (Burridge et al., 2010).

From year 2010 to 2015, the use of antibiotics in the aquatic ecosystem was increased up to 14 billion, it was believed by researchers that use of antibiotics can increase up to 100 billion till year 2030. Mostly, these antibiotics are released in the aquatic ecosystem in their original form and these can be very harmful for environment (Wang et al., 2021).

Probiotics

According to Gismondo et al., (1999), the name "probiotic" comes from a Greek term which means "for life." According to Fuller's (1989), an ideal probiotic should possess the following qualities: (1) it should be effective (2) should be harmless and not hazardous; (3) should exist as viable cells, normally in large quantities; (4) probiotic should actively participate in the metabolism of the gut; and (5) it should have stability and viability over extended storage and field conditions.

A cost-effective method to overcome water pollution in aquatic ecosystem is to maintain it by pathogens or beneficial bacteria and it is the most reliable method to improve water quality (Verschuere et al., 2000; Liu et al., 2012).

***Bacillus* spp.**

High levels of nitrogenous chemicals, such as ammonia, nitrite, and nitrate, can be harmful for aquaculture animals and these nitrogenous wastes can increase their mortality rates. However, this susceptibility varies depending on the species. According to Verschuere et al. (2000), gram-positive *Bacillus* species are typically more effective in converting organic or decaying matter into CO_2 than gram-negative bacterial species. This leads to a higher conversion percentage of organic carbon to bacterial biomass or slime.

Probiotics have been added directly in the ponds in order to improve water quality (Boyd and Cross, 1998) and to increase the survival rate of aquatic animals (Moriarty, 1998). It has been determined that aerobic gram-positive endospore-forming bacteria, including *Bacillus* spp., can improve water quality by changing the overall composition and quantity of aquatic microbial communities that are associated with aquatic animals (Bandyopadhyay and Mohapatra, 2009). Some benefits of *Bacillus* species for aquatic ecosystem is shown in Fig 4.

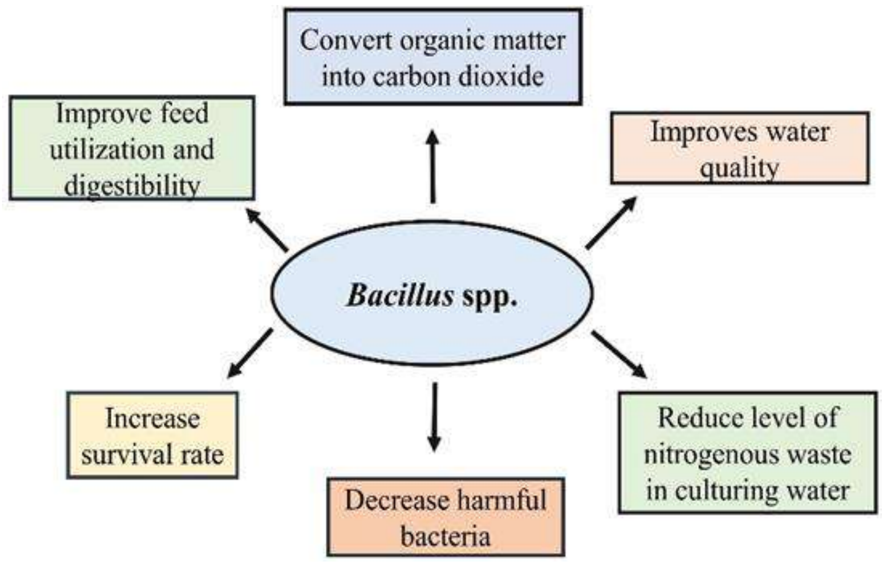

Fig 4. Benefits of *Bacillus* species for aquatic ecosystem

According to Boyd and Gross (1998), probiotics can also help to improve the quality of the soil and water. According to Mohapatra et al., (2012), different probiotics have different impacts on the development and nutrient intake of various aquatic animals. According to Martínez et al., (2012), the efficiency of probiotics in fish farming is dependent on some parameters, including the temperature of the body, enzyme level, host genetic resistance, and quality of water.

Bacillus species are used to improve water quality, these spp. can decrease harmful vibrios and are used to increase growth and survival rates of juvenile *Penaeus monodon* (Dalmin et al., 2001). According to Nandi et al., 2018 probiotics can be beneficial for aquaculture as they provide protection against harmful diseases and also provide contaminant free water.

Probiotics can take part in the aquaculture industry by recycling organic nutrient that's how they contribute to improve water quality (Wang and Wang 2008). The Food and Agriculture Organization (FAO) has now suggested probiotics to enhance the quality of the aquatic environment and probiotics are also used to decrease mortality (Subasinghe, 2005) or to boost host tolerance to harmful diseases (Irianto and Austin, 2002). Some other advantages of probiotics are that it stimulates immune system and provide protection to aquatic animal by controlling the risk of disease and by preventing the entry of disease-causing agents (Dawood and Koshio, 2016). According to some researches that in carp fishes these beneficial bacteria also used to improve immune system and to overcome disease (Wu et al., 2015).

Appropriate use of probiotics in fish diet has so many valuable effects for the aquaculture, including the best growth rate, better immune system, good survival rate and improved gut health (Van Hai, 2015). These beneficial bacteria are also important in overcoming algal bloom especially most harmful red tide phytoplankton (Qi et al., 2009). Canadian and USA farmers rarely use antibiotics for controlling disease in fish farming. They use beneficial bacteria to overcome disease-causing agents, so in these both countries probiotics are considered as one of the best treatment for aquaculture sector (Bandyopadhyay et al., 2015).

Probiotics was firstly used and explained by Lilly and Stillwell (1965). According to them, these are substance that are made by protozoans and these substances encourage the growth of other microbes. Later, it was explained that these beneficial bacteria can increase the growth of aquatic animals when these probiotics are supplied with their regular diet.

In fish culturing pond or aquarium water can be polluted by aquatic animal feces, excessive feed waste and dead fish. Harmful pathogens of soil in aquaculture or pond can be mixed with water and can cause water pollution (Wang et al., 2018). The solid waste in water that may include decomposed dead fish and broken fins is also the main cause of water pollution in aquaculture. High level of organic matter and poisonous chemicals like phosphorous, nitrogen and ammonia can have a bad effect in aquaculture system. Organic matter and dead fishes can be easily decomposed in water and this can cause low DO (dissolved oxygen) level of culturing water (Farrelly et al., 2015).

Poor water quality of aquaculture is a major problem for aquatic animal farming (Brönmark and Hansson, 2017; Hura et al., 2018). If more number of fishes are cultured in less area, it may have negative effects on water quality by increasing level of nitrogenous waste, hence there is more risk of disease outbreak, as polluted water is an appropriate environment for the growth of harmful bacteria, so it may increase death rate of fishes (Lieke et al., 2020).

Filtrations and polluted water drainage; these two techniques are used to overcome water pollution in fish farming (Crab et al., 2007). The general technique that is used to improve water quality is rapid water change, but it is tiring, time taking and the most costly method. Moreover, disease-causing bacteria can enter with re-added water in rearing water (Devaraja et al., 2013).

Some chemicals that are used for polluted water treatment are Geotox, Bio-tuff, and another chemical Aquazet. These chemicals can reduce water pollution of aquaculture, but this water can be toxic for human use (Faruk et al., 2008). Hence, in several researches, use of beneficial bacteria (probiotics) has been encouraged to improve water quality in culturing system (Hura et al., 2018). Probiotics are not only helpful in improving water quality, but it can also be used to stimulate the immune system of aquatic animals, it can also improve feed intake, survival rate and development rate of fishes (Hoseinifar et al., 2018).

Development rate and health status of fish depends on water quality and probiotics, or beneficial bacteria can reduce water pollution (Hura et al., 2018). According to some new researches, in probiotics *Bacillus ssp*. is considered to enhance the quality of the water in a culturing system (Devaraja et al., 2013; Soltani et al., 2019). *Bacillus* is more beneficial for aquaculture as compared to other probiotics, as not only it can reduce water pollution, but it can also form biomolecules which can fight with disease causing pathogens (Kuebutornye et al., 2019).

Unconsumed feed that accumulates at the bottom of pond and aquarium is also the main cause of water pollution (Amirkolaie, 2011). Regular aquatic animal feed contains a high level of nitrogen and phosphorous (Schwartz and Boyd, 1994). Their high level can destroy aquaculture by reducing water quality (Amirkolaie, 2011). Fecal material of aquatic animals can increase nitrogen content of culturing water (Devaraja et al., 2013). Ling et al. (2010) described that high level of excretory material in water can increase PH range and phytoplankton growth, it is also the reason of nutrient accumulation in water. Excretory waste can also increase phosphorous content of water, which ultimately causes water pollution (Primavera, 2006).

Dead and decaying fishes under water can also pollute culturing water, if they remain under water for a long time it may increase nutrient load in aquaculture and the water with overloaded nutrient can deplete oxygen level, hence, this water is not suitable for fish growth (Ananda Raja and Jithendran, 2015). In aquaculture, people use chemical substances and medicinal products such as (sodium chloride, potassium permanganate, calcium hypochlorite and lime) to yield good growth and the medicinal products are also used for disease cure (Ronquillo and Hernandez, 2017).

Probiotics can consume nitrate, nitronium ion and ammonium for their benefits, in return, they reduce nitrogen content of water that's how they improve water quality (Martínez-Córdova et al., 2015). In probiotics, only *Bacillus* spp. can change overloaded nutrients into carbon dioxide and this carbon dioxide is beneficial for pseudomonadota or gram-negative bacteria (Koops and Pommerening-Roser, 2001). While other probiotics can only change these overloaded nutrients into microbes (Mohapatra et al., 2013).

In aquatic ecosystem *Bacillus spp.* is helpful in reducing the level of nitrogenous waste and reusing organic matter by converting it into carbon dioxide (Soltani et al., 2019). Accumulation of organic substances in the aquatic ecosystem is mostly because of unconsumed feed or feed waste, *Bacillus* spp. Can also improve digestibility and feed intake in fishes (Hura et al., 2018). Sunitha and Padmavathi (2013) described that the addition of probiotics in pond can decrease orthophosphate content of culturing water.

Choi et al., (2002) described that Bacillus ssp. is more effective in reducing nitrogen level, overloaded nutrients and phosphorous level in the aquatic ecosystem. Bacteria use oxygen during decomposition in return, they release carbon dioxide, organic matter and water (Bokossa et al., 2014). Wang et al., (2005), described that this water and carbon dioxide is important for small photosynthetic plants and in return they release more oxygen. In aquatic ecosystem dissolve oxygen level upon the number of photosynthetic plants in culturing water. Probiotics or beneficial bacteria can regulate the dissolved oxygen level of culturing water by lowering the stress rate in aquatic animals (Zink et al., 2011). The benefits of *Bacillus* spp. for culturing water is shown in Fig. 5.

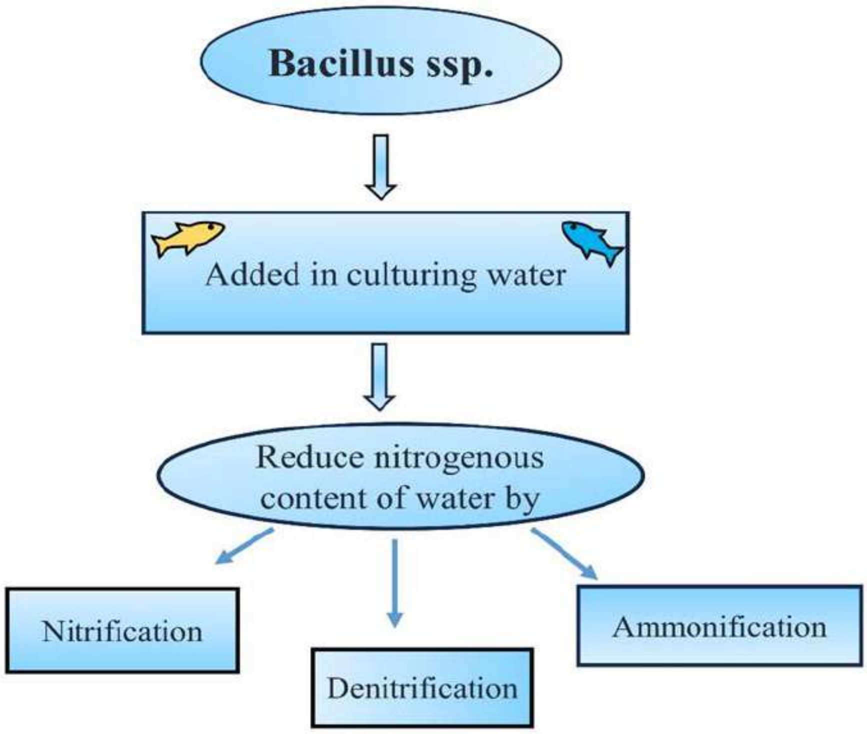

Fig. 5: Benefits of *Bacillus* spp. for culturing water

Different Ways to use Probiotics in Aquaculture

There are various ways to use probiotics in the aquaculture: it can be injected in aquatic animal body via injections, it can be directly added in culturing water, and it can also be mixed with a regular feed of fish (Jahangiri and Esteban, 2018). If probiotics are given by using appropriate technique, it can be more beneficial for aquatic ecosystem (Jahangiri and Esteban, 2018). According to previous research, if probiotics are directly added in culturing water it is more beneficial for all age groups of aquatic animals (Jahangiri and Esteban, 2018). Different ways to use probiotics in Aquaculture is shown in Fig. 6.

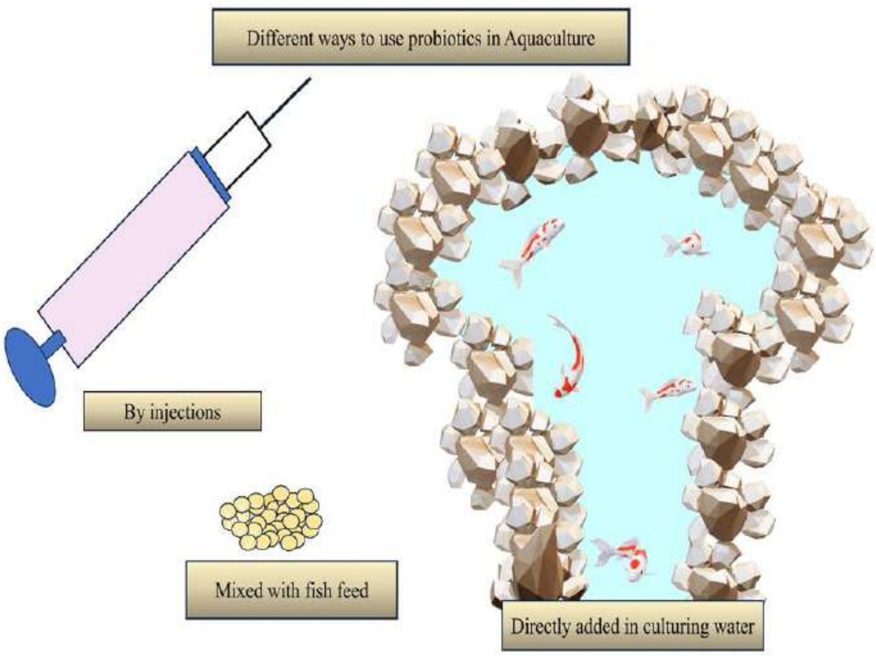

Fig. 6. Different ways to use probiotics in Aquaculture

If probiotics are given by using injections, it may increase stress rate of aquatic animal and moreover, it cannot be mixed with a regular feed of larvae, as digestive system of larvae is more sensitive as compared to adult (Jahangiri and Esteban, 2018).Some well-known advantages of probiotics are that it is good in maintaining nitrogen and phosphorous level, it is good in improving DO level;, it has lessened the chances of disease outbreak;, it is best in maintaining nitrite, ammonium and nutrient level (Boyd and Gross, 1998; Cha et al., 2013). Maintained water temperature and appropriate dissolved oxygen level are considered as the most important qualities of culturing water (Bhatnagar and Devi, 2013).

If DO level of water is less, it may increase risk of disease outbreak and it have a bad impact on growth of aquatic animal (Dabrowski et al., 2018). High level of ammonia, nitrogen, phosphorous and nutrients overload can decrease DO level of culturing water (dos Santos Simoes et al., 2008). In previous research by Hura et al., (2018) high dissolve oxygen level in water was observed when probiotic *Bacillus megaterium* was added in the aquarium. In another research by Hainfellner et al., (2018) DO level of water was increased when *Bacillus* spp. was added in aquarium.

Nitrogenous waste in culturing water can deteriorate water quality. This waste is poisonous for fish and aquatic animals that's the reason scientists are finding ways to reduce nitrogen content of water (Boopathy et al., 2015). High waste or nitrogen content of water can increase stress rate in aquatic animal, high nitrite and ammonia level can also increase disease risk in aquatic animal, that polluted water can also be harmful for physical condition of fish, shrimps and aquatic ecosystem (Lalloo et al., 2007).

Different bio-filtrations techniques are used to reduce nitrogen and nitrite content of water (Crab et al., 2007). According to Gao et al., (2018) addition of beneficial bacteria in the aquatic ecosystem is a cheap method to improve water quality. Among all probiotics, *Bacillus* spp. Is considered as most reliable and beneficial probiotic for aquaculture. *Bacillus* spp. can control nitrogen content of water through nitrification and denitrification processes. By these two processes, it can reduce the level of toxicity in culturing water (Kim et al., 2005).

Bacillus subtilis

Bacillus subtilis is widely used and the most important beneficial bacteria for ecosystem (Shao et al. 2020). *Bacillus subtilis* has antimicrobial properties and has the ability to reduce stress rate among aquatic animals and moreover it also has the ability to improve stability of the aquatic ecosystem (Pepi et al. 2016). This beneficial bacterium can also produce or release some important extracellular enzymes like protease (for protein breakdown), lipase (for lipid breakdown) and phospholipase (for phospholipid breakdown) (Lu et al. 2018). *Bacillus subtilis* also saves water from deterioration by decreasing development rate of disease-causing pathogens in culturing water (Lu et al. 2018).

Bacillus subtilis (Cha et al., 2013) and *Bacillus amyloliquefaciens* (Xie et al., 2013) these both probiotics can decrease ammonia content of water in the aquatic ecosystem. According to Liu et al. (2012) *Bacillus subtilis* can improve growth rate and immune system of *Epinephelus coioides*. According to Ding et al. (2012) *Bacillus subtilis* WH-5 can reduce nitrogen, sulphide, ammonium and nitrite content of water.

Bacillus subtilis strain (*B. subtilis* D9) was recently invented from seaside soil (Chen et al. 2016, 2017). Some important advantages of *Bacillus subtilis* is that it is effective to increase metabolism and it also decrease the risk of disease by reducing disease-causing agents (Chen et al. 2017). Chemicals and antibiotics are not good for the aquatic ecosystem, these chemicals are actually harmful for aquatic animals (Cabello, 2006). Microorganisms or beneficial bacteria are important for the aquatic ecosystem, as these bacteria can control disease spread and protect the aquatic animal from harmful disease (Bentzon-Tilia, 2016). Beneficial bacteria are eco-friendly. These can increase growth rate and reduce disease risk. Probiotics don't have any harmful effect on aquatic animals (Mohapatra et al., 2013)

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Chapter 20

Use of Prosopis on Feed Nutrition: Challenges and Opportunities

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ABSTRACT

The genus Prosopis include a variety of tree and shrub species commonly found in arid and semi-arid regions. These plants survive even in extreme conditions, (specially on dry climates) by storing carbohydrate reserves in different plant parts, making them valuable for multiples uses, like wood, food environmental services and feed. Incorporating Prosopis in animal feed has demonstrated improve in livestock performance, especially in both ruminants and non-ruminants (broilers, fish, chickens, and pigs), enhancing feed conversion ratio, reduce overall feed costs. This is because Prosopis can replace more expensive feed ingredients like corn or soybean meal. However, there is challenges to go through, due to the presence of anti-nutritional compounds which can be impact feed palatability and nutrient absorption, these negative effects can be vary depending on factors like animal species, Prosopis species, plant part added, and the inclusion rate in the feed. Therefore, proper evaluation and processing methods are essential to mitigate potential adverse effects and maximize the nutritional and the economic benefits of Prosopis-based feed resources.

KEYWORDS		
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INTRODUCTION

The genus Prosopis, includes around 44 tree and shrub species, with four native to Asia Africa and 40 native to North and south America, These species are predominantly found in extreme conditions specially in dry and semidry areas (Singh and Pareek, 2024) due their capability to store carbohydrate in lower regions such as stem bases, stolons, corms, and rhizomes (Vilela et al., 2016; White, 1973). Prosopis species are used for different purposes including medicine treating conditions such as asthma, rheumatism, venomous bites (Jakhar et al., 2024) combating plant pests and diseases in horticulture (Muro-Medina et al., 2022), plant–soil feedback (Ali et al., 2024) rehabilitating saline soils (Ewens et al., 2012), nitrogen-fixing in soil (Fterich et al., 2011), human food like flour (Hoffmann et al., 2024; Kord et al., 2024) sport beverage (Singh and Pareek, 2024b) and animal feed. Prosopis as gained attention in livestock due to rapid growth enabling efficient feed production, and the reducing total feed costs up to a 21% to 24% (Negrete et al., 2016; Peña-Avelino et al., 2016)

Pods with high sugar and protein content, offer valuable dietary supplement (Zhong et al., 2022a) demonstrate no adverse effects on feed intake or digestibility in pigs (Marii et al., 2022), broilers (Bone, et al., 2021; Sugiharto and Ranjitkar, 2019) fish (Souza et al., 2018; Vasile et al., 2019) and ruminants (Almeida et al., 2022), promoting weight and daily weight gain (Ram et al., 2022). However, certain Prosopis species contain alkaloids that may have cytotoxic effects, potentially leading to poisoning in cattle or negatively affecting feed palatability (Aguiar et al., 2015) and nutrient absorption, particularly in ruminants, (Cholich et al., 2020) leading to poisoning, as observed in cases in beef cattle (Micheloud et al., 2019) or ruminants. In this context this work seeks to analyze the current knowledge on the benefits, disadvantages, and costs of using Prosopis as a feed resource, providing a comprehensive review of its utilization.

Nutrient Value and Chemical Composition

Besides the wood or charcoal production, the plant is used for producing beverages and bread, *numerous studies have been conducted related composition and nutritive value of Prosopis. T*he high carbohydrates content has been used in diverse trials for bioethanol production considering bark as a novel source for the biofuel source (Sivarathnakumar et al., 2016). The nutrient profile of Prosopis varies depending on the specie, location, and part measured. The primary nutrient constituents include sugar, fibers, fat, protein, amino acids and fatty acids (Figure 1) (Ruiz-Nieto et al., 2020) Furthermore, micronutrients (minerals) and phytochemicals, have been extensively studied too (Zhong et al., 2022).

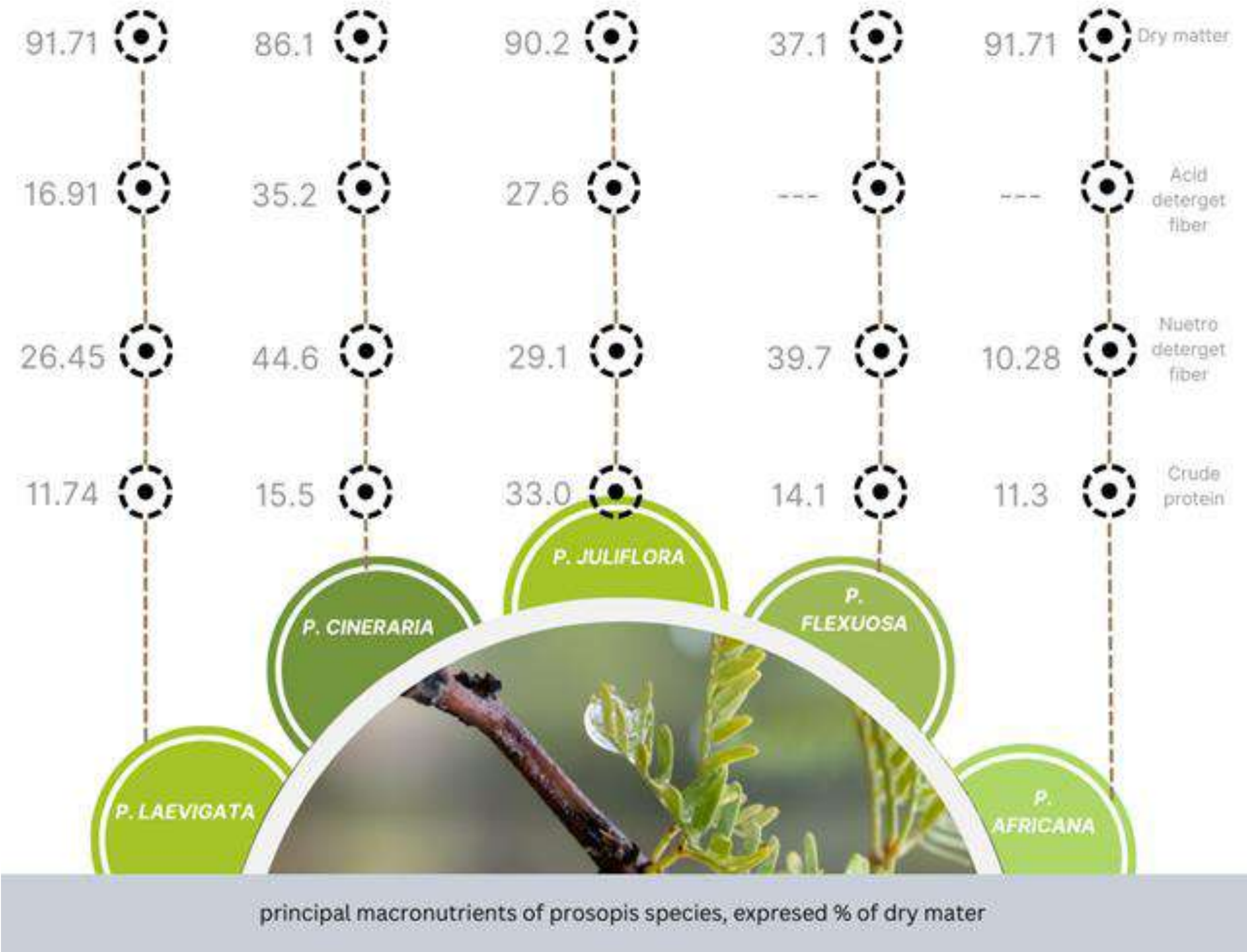

Fig. 1: Nutritional content of Prosopis species expressed in percentage of dry matter (Ruiz-Nieto et al., 2020).

Several studies have indicated that Prosopis pods contain a significant amount of crude protein, ranging from 70 to 120 g/kg (Almeida et al., 2022). Or 20 to 30% in dry weight (Ortega-Nieblas et al., 1996). Additionally, it has been highlighted that Prosopis pods have a significant amount of essential amino acids, (Lemos et al., 2023) that varies across different parts of the plant. (And and Alli, 1988), it was noted that isoleucine is the predominant amino acid in *P. juliflora* seeds, whereas de Lumen et al. (1986) found threonine to be the primary amino acid in Prosopis sp. seeds., indeed Odero-Waitituh et al. (2020) indicated that oilseeds, contained high amounts of crude protein and fat, with aspartic and glutamic acids being the most abundant amino acids present. Moreover, (Zhong et al., 2022) identified, hydroxyproline, glycine, serine, and valine as the mayor amino acids in Prosopis gum.

The Prosopis genus involve several chemical compounds (Figure 2), phenolics contributing to their antioxidant and anti-inflammatory capacities with various health benefits, such as anticancer, antidiabetic, antimicrobial, and antioxidant effects (Schmeda-Hirschmann et al., 2015; Sharifi-Rad et al., 2019; Pérez et al., 2024)

The plant has been used to combat vegetal pests and diseases (Muro-Medina et al., 2022b), and has been shown antimicrobial, and anthelmintic properties (Odero-Waitituh et al., 2020; Nava-Solis et al., 2022).

Incorporating *Prosopis juliflora* pods in place of concentrate mixtures in sheep nutrition maintains nutrient intake and utilization and does not disrupt rumen fermentation characteristics (Chaturvedi and Sahoo, 2013). However, it is important to consider the presence of antinutritional factors (ANF) that can be cause nervous disease or diminish the nutrient availability in cattle feed, highlighting the significance of proper evaluation of its use in animal feed (Cholich et al., 2020).

Anti-nutrition Factors

Despite the beneficial effects of several compounds, there are presence of anti-nutritional factors (ANFs) in Prosopis, the fruits, pods, and other plant parts contain: L-DOPA, condensed tannins, phenolic compounds, alkaloids, phytic acid, trypsin inhibitor activity, and glycosides (Zhong et al., 2022) (Fig. 3).

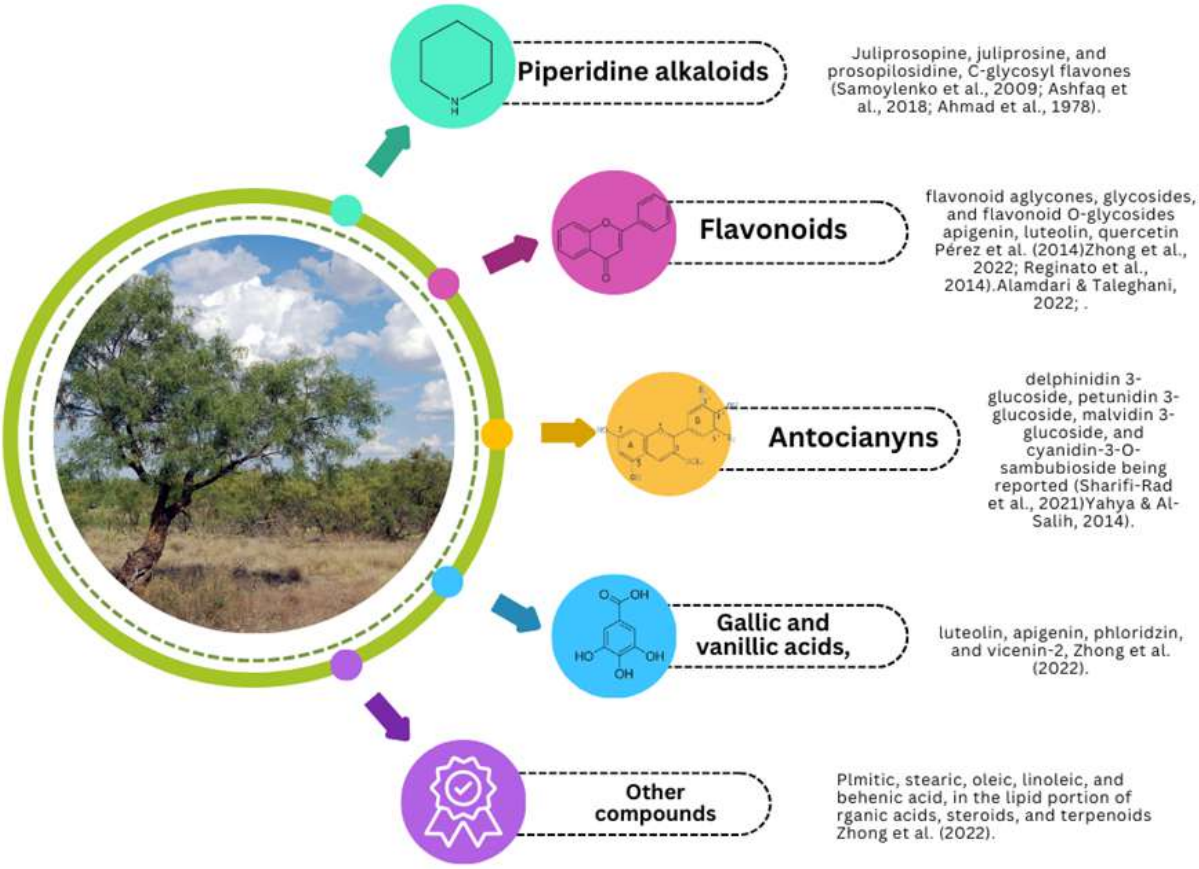

Fig. 2: Main chemical compounds in Prosopis genus

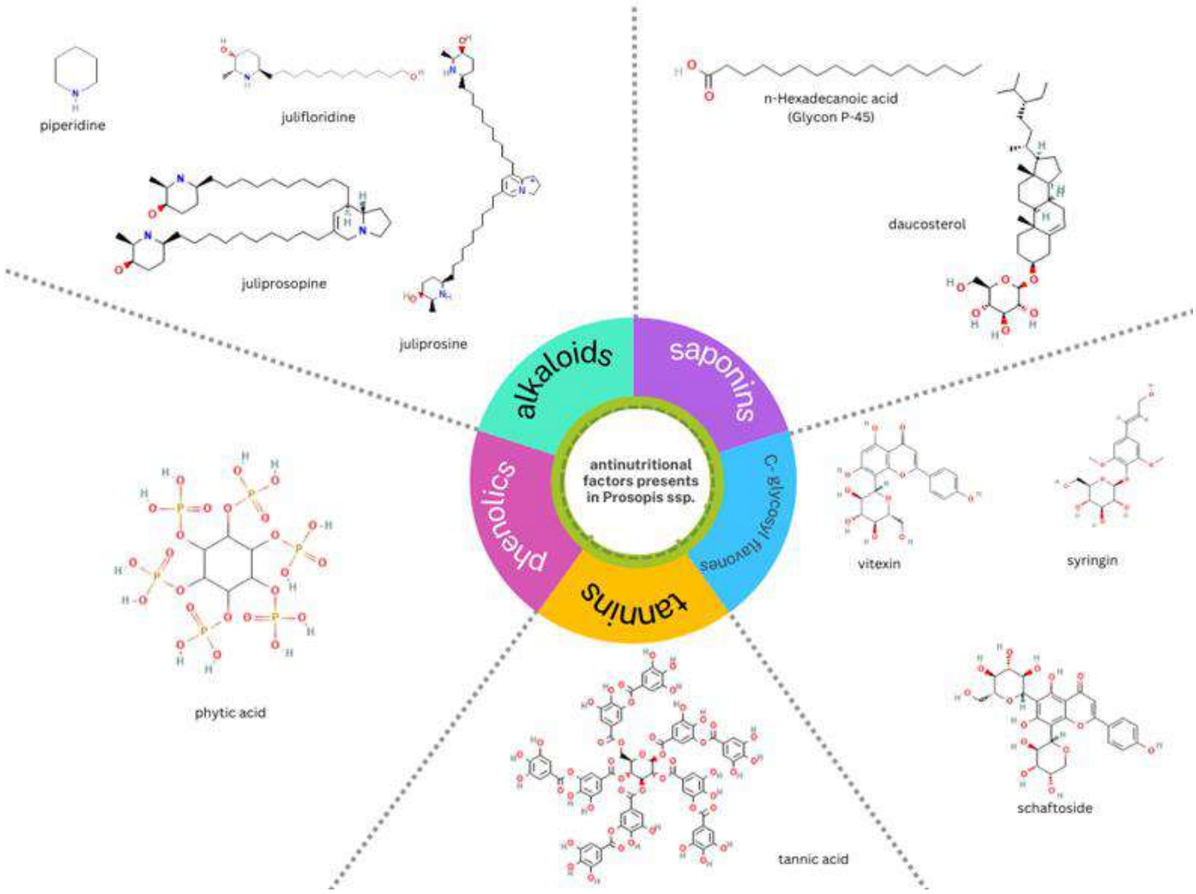

Fig. 3: Principal antinutrients factors (ANFs)found in Prosopis genus (Pub Chem 2024)

Saponins, a varied group of plant compounds, are distinguished by their structure, which includes a triterpene or steroid aglycone and one or more sugar chains. They have a distinct unpleasant taste, can foam in water, and may cause red blood cell hemolysis (Ravhuhali et al., 2021).

Tannins are a class of polyphenolic compounds also have been identified parts in Prosopis plants, such as pods, leaves and bark (Zhong et al., 2022) and is composed by two types: hydrolysable tannins (HT) are low molecular weight and condensed tannins (CT) with high molecular weight (Aboagye and Beauchemin, 2019). The CT are capable to precipitate several biomolecules, like carbohydrates, minerals, and proteins, leading to adverse effects when animals consumed without proper processing and can interfere with nutrient absorption and fiber digestion (Yusuf et al., 2013; Agaba et al., 2019) affecting ruminal fermentation and methanogenesis (Soltan et al., 2012)

Alkaloids comprises a group of naturally occurring compounds occur in various plants, including *Prosopis* species. Juliprosopine and juliflorinine have been isolated from leavesfrom *Prosopis Juliflora,* reveling the chemical diversity within this genus (Ahmad et al., 1989). These alkaloids, along with other phytochemicals are associated with medicinal properties in Prosopis plants (Sharifi-Rad et al., 2019; Zafari and Sharifi, 2020); however, they can also exhibit cytotoxic effects on glial cells and neurons (Dos Santos et al., 2013) or influence in vitro ruminal digestion, indicating a potential impact on animal feed efficiency.

Saponins belong to a class of bioactive compounds, which possess a wide variety of biological activities. They are steroid or triterpene glycosides, possessing at their structure a lipophilic acyclic or alicyclic aglycone and hydrophilic sugar residues; therefore, these molecules are amphipathic and highly surface-active (Moghimipour and Handali, 2015). Although these compounds do not directly influence ruminal fermentation, the decreased efflux of fermented amino acids into systemic circulation may alter the profile of amino acids available for absorption at the duodenal level (Benchaar et al., 2023). On the other hand, many aqueous ethanol extracts of *Prosopis juliflora* pods, containing saponins show effective antimicrobial activity (Jakatimath et al., 2021) and could possess usage in animal feed additives

Use in Farm Animals

Birds

The Prosopis plants has been extensively studied for its potential as a feed ingredient in broiler chicken diets, Alagbe et al., (2023) investigated the effects of supplementing broiler chicken diets with *Prosopis africana* essential oil on intestinal microbial populations and haemato-biochemical indices, they found Supplementing broiler chicken diets with essential oil up to a concentration of 800 mg/kg does not have any harmful effects on their blood profile (Bishop et al., 2021). Research by Girma et al., (2011); explored the utilization of ground *Prosopis juliflora* (GPJP) at 0 (T1), 10 (T2), 20 (T3) and 30% (T4) of inclusion levels, studying its effects on nutrient intake, muscle fatty acid composition, sensory quality, hematology, growth, and carcass characteristics of broilers, they found that 30% GPJP inclusion, diminish feed intake and growth, 10 and 20% helping to reduce the total fee cost. Bishop et al. (2021) focused on the fermentation of Prosopis seed coat with ruminal, (FPSCM) the results indicate that serum glucose 45.85-107.22 mg/dl varied significantly ($P<0.05$) among the dietary treatments, reveal that Prosopis can be incorporated in broiler or chickens diets up to 25% with no adverse effect on health. In the study realized by (Al-Marzooqi et al., 2015), they found that the inclusion of *Prosopis juliflora* pods as a partial replacement of maize, with or without the addition of exogenous enzymes. The research, changes in digesta masses of the tract, pancreas and caecum, causes gut health, with no adverse impact on carcass or meat quality. They show the pods caused a significant increase in the weights of total digestive tract, pancreas and caecum ($p<0.01$). whit no significant effect on carcass or meat quality characteristics, hematology, and sensory evaluation. Al-Harthi et al. (2018) investigate the nutrient profile, protein quality, and energy value of whole Prosopis pods meal for poultry, provide valuable and useful analysis for its protein content, for animal diets, however, they also suggest this protein quality is lower that soybean meal.

Pigs

On the other hand, pig feed research is very little, Bazurto and Sabando 2020, carried out a thesis work evaluated Prosopis chilensis flour in post-weaning pig diets, showing no significant effects on production parameters but higher cortisol levels and lower economic benefits. Marii et al. (2022b) compared effect of multi -enzyme complex and bacterial cultures on in-vitro digestibility, fermentation activity and growth performance of growing pigs fed *Prosopis juliflora* pods This model effectively predicted nitrate concentrations based on the treatments (enzyme-treated, untreated, naturally fermented and *Lactobacillus plantarum* fermented pods). Enzyme treatment showed 3.68% of increasing IVDMD compared to untreated pods. Lactobacillus plantarum and natural fermentation increased crude protein and decreased fiber content. Supplementation of pigs with up to 30% enzyme-treated pods in their diet did not alter body weight and feed conversion efficiency.

Fish

Bhatt et al. (2011) explored the use of raw and hydrothermally processed *Prosopis juliflora* seed meal as a dietary supplement for *Labeo rohita* fingerlings. Ten diets, equal in nitrogen and energy, used dehulled, soaked, and autoclaved seed meals to replace fish meal at 20%, 35%, and 50% levels. The study assessed weight gain, growth rate, feed conversion, and protein efficiency. Results showed superior fish performance with 20% and 35% seed meal replacements, as indicated by body growth, carcass composition, digestive enzyme activity, and digestibility, compared to 50% replacements containing higher non-protein components.

Sena et al. (2012) examined using *Prosopis juliflora* bean bran and cassava leaf bran to substitute soybean meal in Nile tilapia diets, finding that incorporating these brans up to 20% did not compromise growth or body composition.

Cattaneo et al. (2016) verified the nutritional and phytochemical characteristics of flour obtained from *Prosopis alba* cotyledons, supplemented with different percentages of P. juliflora pods, and that it was distributed in equal parts to oiled rice bran and barley. Prosopis pods are the least valued part that locally available for livestock feed, but the established this study that Prosopis pods contain valuable nutrients and bioactive compounds, which be implemented in feed formulations in reducing food waste and increase nutritional value. KG et al. (2021) evaluation of *Clarias gariepinus* fingerlings feed with 20% level of African mesquite seed meal found that the feed was well accepted, which resulted in optimal growth. Dosage of 45% SRM yielded the highest weight gain, specific growth rate and profitability indices respectively and it can be said that *Prosopis africana* seed meal can successfully replace soybean meal in fish diets at low inclusion levels economically.

Ruminants

Prosopis plants have been. utilized in various ways, including as animal feed (Ram et al., 2022) to their high carbohydrate and protein content. Several species of Prosopis, such, have been studied for their potential in animal nutrition during the dry season (Sirohi et al., 2017), particularly in semi-arid areas where other forage options may be limited (Ravhuhali et al., 2021), natural resistance to drought, and hard climate conditions turns the plant very suitable for small ruminants' consumption.

Peña-Avelino et al. (2017) evaluated the effects of *Prosopis laevigata* pods on lamb performance. Three diets were assessed in the study: PLP0 (0 g PLP/kg DM), PLP250 (250 g PLP/kg DM), and PLP500 (500 g PLP/kg DM) in lambs fed the PLP500 diet were significantly higher than those in lambs fed the PLP0 and PLP250 diets, the researchers declared that dietary inclusion level of PLP could be up to 500 g/kg in a lamb diet, without harmful consequence on their health. Meanwhile, (Negrete et al., 2016) developed the study to evaluate the performance, carcass characteristics, meat quality and fatty acid profile of subcutaneous fat of Rambouillet lambs fed PLP. PLPs replaced one third of conventional feed ingredients resulting in 21% reduction in total feed cost as revealed from the findings ($p < 0.05$) Thus they concluded that PLP be utilized in replacement of other feeds for growing lambs since it was safe and economically available.

Concurrently, Eissa et al. (2016) reached the conclusion that PLPs are an inexpensive and safe substitution of feed for growing lamb, whit no significant effect on methanogen activity (as methane production or methanogenic mRNA levels) was measured, nor were there effects on growth performance, nutrient utilization (apparent digestibility), rumen fermentation (volatile fatty acids, VFA), or microbial enzyme activity. Similarly, Mahgoub et al. (2005) use meskit pods up to 300 g/kg of DM and had no effects on body component proportions or carcass chemical composition, the inclusion of up to 200 g/kg of *P. juliflora* pods in the diets of Omani goats can increase feed intake, conversion efficiencies and weight gain with no adverse effect on carcass yield and quality. Similar results were demonstrated by Cook et al. (2008) who focused on the safety and potential adverse effects of goats consuming mesquite pods, providing valuable insights into the suitability of mesquite pods as a feed ingredient for goats. (Mosweu et al., 2013; Ravhuhali et al., 2021) emphasized the benefits of utilizing Prosopis plants in cow feed to enhance livestock production while managing the spread of these species in the environment. (Mosweu et al., 2013) explored the modification of soil properties by Prosopis plants in the Kalahari Desert, South-Western Botswana, enhancing soil organic carbon content and influence soil pH, potentially impacting the nutritional quality of forage for cows.

Sintayehu et al. (2019) investigated the influence of *Prosopis juliflora* invasion on bovine tuberculosis infection as a function of ecosystem services.

The impact of *Prosopis* on various aspects of ruminant health and productivity was research, mostly authors concurred that inclusion of Prosopis until 20-40% did not negatively impact their growth performance, reproduction, or cud chewing behavior. The feeding strategy was found to be more economical compared to commercial concentrate feeds. This cost-effectiveness is attributed to the lower expense of incorporating into the diets versus relying on commercially available feed. By using Prosopis plants farmers in arid regions can reduce feed costs without sacrificing the well-being of their livestock, the use of local feed resources.

Conclusion

Although used in the feeding of animals as an agronomic management strategy to improve animal productivity by increasing some growth parameters the feeding of this fruit is limited due to the presence of anti-nutritional factors (ANFs) such as alkaloids, tannins, and saponins. These compounds reduce feed palatability and lower nutrient absorption and affect animal health like cytotoxic effects due the alkaloids, as well interference with protein digestion eliciting a variety of processing methods due tannins. In aim to utilize the plants, is crucial to reduce these negative impacts and harness the potentials of Prosopis-based feeds, like the use of multienzyme or different temperature treatments to a whole plant. More research and development in the processing sector must be required to exploit the benefits of Prosopis in animal feed. Dealing with these challenges will render a sustainable and economically feasible solution increase livestock productivity and reduction of feeding costs especially in areas whereas the plants are abundant or considered invasive. The economic importance of Prosopis plants, come from the opportunities for socio-economic development in rural communities besides the feed resource, the plant may be used for ecosystem services or for grassland rehabilitation promoting soil carbon sequestration.

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Chapter 21

Potential Insights of Nutraceuticals in Optimized Farm

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ABSTRACT

Any substance having therapeutic or health benefits is considered a nutraceutical. It includes both disease prevention and treatment, and it can be eaten in full or in part as food. These products could include anything from meal planning, nutritional supplements, and isolated nutrients to herbal products, prepared foods including cereals, soups, and drinks, and genetically modified "designer" foods. Nutraceuticals are of different types which are beneficial for animals. The objective of this chapter is to give a general overview of nutraceuticals, their types, their mechanism of action, and their role in animal's metabolism and body weight maintenance. Nutraceuticals have antibacterial activity as well as medicinal benefits. We have also discussed the sources of nutraceuticals. Besides it's a lot of advantages, some limitations have also been discussed.

KEYWORDS		
Nutraceuticals, Functional food, Antibacterial activity, Infection	Received: 13-June-2024 Revised: 18-July-2024 Accepted: 21-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

In 1989, Dr. Stephen DeFelice, the Chairman of the Foundation Research in Medicine, merged the terms "pharmaceutical" and "nutrition" to create the term "Nutraceutical" (Brower, 1998). There is no legislative definition for the phrase "Nutraceutical," which is a marketing acronym used to describe nutritional supplements sold to treat or prevent disease (Zeisel et al., 1999). Therefore, a "Nutraceutical" is any material that has health or medicinal benefits, comprising illness prevention and care, and that can be consumed whole or in part as food. These goods could be anything from diet plans, nutrition supplements, and isolated nutrients to genetically altered "designer" foods, herbal products, and prepared food items including cereals, soups, and drinks. Above 470 nutritious foods and Nutraceutical items with established health benefits are already available on the market (Eskin and Tamir, 2006).

Nutraceuticals, sometimes referred to as "functional foods," have produced a great deal of controversy since they blur the lines that normally divide food from medicine. Because of this, they are frequently referred to as "functional foods" and have generated a lot of debate.

The term "functional food" refers to food that has been cooked or prepared using "scientific intelligence," regardless of the cooking method or goal between food and medicine. "Functional food" is defined as food that has been prepared or cooked with "scientific intelligence," whether the method or purpose of the cooking is known or not. Therefore, functional foods supply the body with the appropriate ratios of fats, proteins, and carbohydrates and vitamins to ensure a healthy and long life. A functional food is referred to as a "nutraceutical" when it helps prevent or treat a disease or disorders other than deficient illnesses like anemia (Valivarthi and Paidikondala, 2003). As a result, a functional meal may serve as a nutraceutical for different consumers. Orange juice is a pharmaceutical, while ascorbic acid, a component of orange juice, is a nutrient. Other Fortified dairy products are examples of Nutraceuticals (milk is a dietary intake as a whole itself, and its derivative casein is a pharmaceutical). In comparison to other medicinal agents, the usage of Nutraceutical has met with tremendous financial success in an attempt to achieve desired therapeutic outcomes with fewer adverse effects (Nelson, 1999; Whitman, 2001). The potential of nutraceuticals as a human food source is the foundation of one of the more expansive organizational models. Plant, animal, and microbiological (i.e., yeast and bacteria) groupings can be used to categories nutraceuticals. This organizational system's intriguing factor to take into account is that a substance's site of origin may not always be the food supply. Conjugated linoleic acid (CLA)), which is commonly found in dairy and meat products, is one simple example. Yet, microbes in the cow's rumen actually produce it. As such, for certain people working with this organizational structure, concerns about the food chain or symbiotic relationships may need to be taken into consideration. Numerous nutraceutical chemicals are present in both plants and animals, as well as occasionally in microorganisms, because of metabolic characteristics that are fairly conserved across species. Microbes, plants, and mammals are examples of organisms that include Phosphotidylcholine as well as Choline. Sphingolipids are likewise found in plants and animals, but they are not as abundant in them. Additionally, linoleic acid (18:3 ω -3 fatty acid) can be found in a range of foods, including meat, while being primarily synthesized in vegetation and other less nutritious parts of the food chain. The advent of contemporary fermentation techniques has made it possible to obtain nutraceutical elements from nonfood sources. For instance, microorganisms cultivated in fermentation systems have been shown to create amino acids and their derivatives. Nutraceutical chemicals can now be obtained through new channels thanks to the development of recombinant-genetic processes. Across the globe, regulatory concerns and the commercial sector are evaluating these methods and their goods. One instance is the synthesis of eicosapentaenoic acid (EPA) by microorganisms. Certain bacteria and algae create this fatty acid. Salmon get their EPA from algae, which the algae then absorbs and assimilates into the salmon. Through recombinant techniques, non-EPA generating bacteria can now create EPA by importing the necessary DNA (Barham et al., 2000). Fig. 1 shows classification of nutraceuticals.

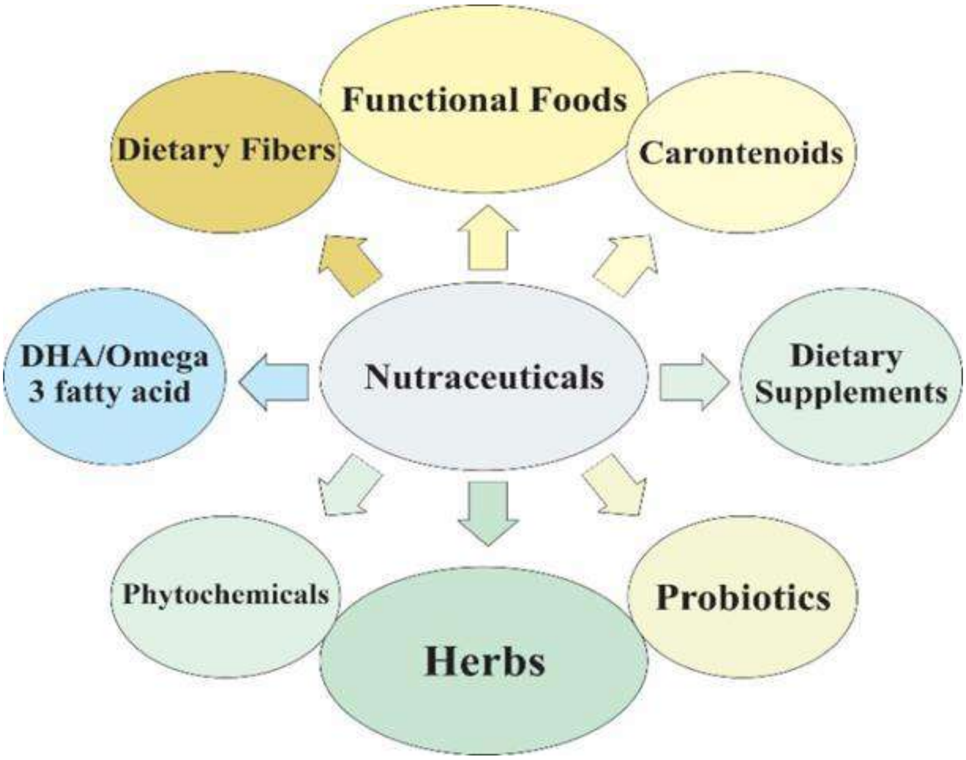

Fig. 1: Classification of Nutraceuticals.

Types

There are five basic types of nutraceuticals, discussed below:

Probiotics

The term of probiotic was created contemporaneously with the use of live cultures in feed for diseased animals as a replacement for the administration of nutritional antibiotics or chemotherapeutics that limit growth. Probiotics are currently used in dairy products, medications, meat products, fruit juices, and feed additives. Prebiotics are indigestible food components that benefit the host by promoting the targeted development or performance of several gut-beneficial microbial species (Gibson and Roberfroid, 1995).

Applications of Probiotics in Farm Production

Improved Growth Rate

Probiotics are bacteria that have been shown to have a favorable effect on the gut micro biome in animal nutrition. Feed consumption, total body weight, daily weight growth, and feed conversion rate in pigs, sheep, chickens, goats, cattle, and horses were all significantly enhanced when probiotic strains were given either alone or in combination (Chiofalo et.al., 2004; Torres-Rodriguez et al., 2007). Probiotics saved young sows from starving to death and decreased limb weakness in broilers (Plavnik and Scott, 1980). Probiotics are beneficial for a number of digestive processes, particularly microbial protein production and cellulolysis (Yoon and Stern 1995). Probiotics improved the absorption of some nutrients, stabilized ruminal pH and lactate, and promoted development in an identical fashion to that of avilamycin therapy (Mountzouris et al., 2017).

Egg Production

Probiotics enhanced egg quality and production while lowering egg contamination. (Kurtoglu and others, 2004). Probiotics also increased the thickness and weight of the eggshell, as well as serum calcium (Van Immerseel et al., 2006). Furthermore, probiotics dramatically lowered plasma cholesterol and triglycerides, supporting the critical roles that microorganisms in the gastrointestinal tract (GIT) play in the recycling of lipids (Panda et al., 2008). Probiotics had no impact on the breeder flock's either chick quality or productivity efficiency (Musa et al., 2009).

Milk Production

Probiotic supplements to animal diet have a positive impact on the amount of fat, protein, and milk produced later on (Sara et al., 2002; Kritas et al., 2009). Probiotic use dramatically improved increased Plasma cholesterol and whole lipid levels, as well as higher protein and fat content in milk, are indicative of abnormal blood and milk parameters in sows at the mid-suckling stage (Alexopoulus et al., 2004). In dairy cows, it has been demonstrated that Saccharomyces cerevisiae and Aspergillus oryzae increase milk output, milk protein percentages, and milk solids-not-fat (SNF) (Yu et al., 1997). This is a result of the rumen's concentration of bacteria that breaks down fiber, conversion to volatile fat acid (VFA), and cellulolytic bacteria (Martin and Nisbet, 1990).

Meta Production

Nowadays, there is a noticeable increase in the market demand for meat that is both safe and of high quality. Producers are keen to employ safe, natural fodder supplements that don't include chemicals because they enhance animal health, boost output, and enhance the quality of the product. Probiotics reduced cooking loss and meat hardness while also increasing carcass yield and water retaining capacity (Jukna and Simkus, 2005). Throughout the fattening phase, probiotics decreased the morbidity and mortality of growing rabbits (Matusevicius et al., 2006).

Bacteriocins

Bacteriocins are ribosomal synthesized short polypeptides or proteins with antibacterial capabilities that are closely linked to the strain that creates them. Bacteriocins function by attaching themselves to specific surface receptor-containing cells and destroying those (Sugrue et al., 2020). The ribosomes of bacteria produce bacteriocins, which are polypeptide antimicrobials that stop the growth of related or similar bacterial strains (Nishie et al., 2012). Numerous bacteriocins are identified and their diverse structures are explained, originating from an extensive array of bacteria. There is mounting data that suggests the structures, methods of action, biosynthesis, self-immunity processes, and gene control of bacteriocins vary. Bacteriocins are a chemical of interest to the food and pharmaceutical industries for their attempts to suppress the growth of harmful microbes and food spoilage. Furthermore, the clarification of their biosynthesis resulted in the application of bacitracin-regulated gene expression systems and antibiotic biosynthetic enzymes, a type of bacteriocins, as peptide synthesis tools.

Bacteriocins are crucial for preventing the overgrowth of potentially harmful bacteria in animal husbandry. Newly hatched broiler chickens are vulnerable to illness because they do not yet have a healthy immune system or mother bacterial flora (Karpinski and Szkaradkiewicz, 2013). after hatching, the application of E. fascism bacteriocins boosts the likelihood that chicks infected with *S. Pullorum*, a poultry disease, will survive, while *E. Coli* microcins help eradicate *S. typhimurium* in adult chickens. There are reports that adding colicin-producing bacteria to cow rumen reduces the number of intestinal infections in animals (Ovchinnikov et al., 2017). Animal farming typically uses probiotic mixes based on bacteriocin-producing crops or sorbic acid and bacteriocins. These blends are added to feed as supplements (Boone et al., 2018). Research has shown that the administration of pure bacteriocins or probiotics that produce bacteriocins can reduce the number of pathogens or alter the gut microbiota's makeup in pigs, fowl, and mice (Ge et al., 2019).

A Lactococcus lactic strain that produces nosing to stop the growth of streptococci and enterococci in the colon, ileum, duodenum, and caecum while promoting the growth of a bifid bacterium in rats' intestines (Baquero et al., 2019). Microcin C7, E1, colidin Ib, and Escherichia h22 are Microcin C7, E1, colidin Ib, and Escherichia h22 are derived from *E. coli* and can impede the development of bacteria, both harmful and benign, including Yersinia, Morganella, Salmonella, Shigella, Enterobacter, and Escherichia. Additionally, it has been shown that human-originated probiotic strains like Lactobacillus salivarius UCC118 generate bacteriocins Abp118, which has the ability to kill Listeria monocytogenes cells (Sun et al., 2018).

The potential applications of bacteriocins, also known as colicins and pyocins, which are produced by Gram-negative bacteria, are the main area of study interest. Despite the favorable evidence from in vivo experiments over the past few years about their use as antibiotics, important questions about their suitability as medicines remain unanswered. Initially, there is only early data on the toxicity or immunological reaction that bacteriocins may have on the patient (Chen et al., 2019). The material that is currently accessible, however, does not mention harmful or harmful impacts on the body. The death of hens treated with pyocins is the exception, yet it's unclear if endotoxins were removed from the mixture (Sharp et al., 2017).

One potential drawback of bacteriocin use could be the inherent immunity of the bacteria that produce them. Bacterial strains may become cross-immune if they share the same cytotoxic domains and target cell destruction mechanisms (Romero-Calle et al., 2019). However, the majority of bacterial strains either do not generate or do not express immune proteins (Baquero et al., 2019). Bacteriocins are so limited in the number of which bacteria can develop immunity. The use of a combination of bacteriocins is thought to avoid cellular immunity (Chikindas et al., 2018).

Organic Acid

Organic acids are weak acids with a low disintegration percentage. The pH at which 50% dissociation of an organic acid occurs, or pKa, is typically between 3 and 5 and is associated with antibacterial action. Numerous organic acids are utilized as feed additives (acidifiers) or as supplements to drinking water because of their diverse physical and chemical qualities. Many are also offered as partially esterified or as salts of calcium, potassium, or sodium. In the production of feed, salts have an advantage over acids because of their solid, less volatile form, which makes them odorless and easier to handle. Along with being less caustic, they may also dissolve more readily in water (Huyghebaert et al., 2011).

It has been demonstrated that applying organic acids protects the young chicks from competition by means of exclusion. Improved nutrition use, as well as efficient growth and feed conversion (Nezhady and colleagues 2011). (Luckstadt and Mellor, 2011). The production of chickens has not given as much thought to organic acids as they have in pig agriculture (Langhout, 2000). The modern grill industry needs high levels of productivity and effective conversion of feed, which can be partially attained by using particular feed additives. Organic acids can be used in place of antibiotics and have growth-promoting qualities. (Fascina et al., 2012). Broiler chickens' body weight and feed conversion ratio (FCR) rise when they received dietary supplements containing organic acids.

The performance of broiler chickens may be enhanced by organic acid mixes more effectively than by some antibiotic growth promoter. A study conducted by (Hassan, 2010) involved the addition of 0.06, 0.1, or 0.02% Eneramycin to basal meals that included two brands of organic acid combinations, Galliacid and Biacid, are available for purchase. The contents of Galliacid included hydrogenated vegetable oil, potassium sorbate, fumaric acid, calcium formate, and calcium propionate. An acidic matrix encapsulates and coats these organic acids, providing them with protection. Calcium lactate, calcium formate, calcium butyrate, citric acid, flavoring agents, and essential oils were all combined to create Biacid.

The findings indicated that the birds fed meals treated with biacid or enramycin grew weight 3 and 5.5% more, respectively, whereas the birds provided food supplemented with galliacid gained weight 16% more than the control group (Fascina et al., 2012).

Plant Extract

Plant extracts are mostly composed of microminerals, proteins, peptides, oligosaccharides, and fatty acids. There is a great variety of activities associated with plant extracts, and the classes of isoprene derivatives and flavonoids are usually composed of their active secondary plant metabolites (Tajodini et al., 2015).

Plant extract contains chemical compounds having antioxidant, anti-inflammatory, antimicrobial properties. Plant extracts and oils serve as feed additives primarily to improve the small intestine's digestion and to limit potential infections in the gastrointestinal microbial ecology. (Hashemi and Davoodi, 2011; Wenk et al., 2000). The activation of the endocrine system and the metabolism of intermediary nutrients have been shown to be strongly impacted by dietary plant extracts. It has also been found that broilers given a diet containing a variety of plant extracts had dramatically increased performance and survival rates (Tucker, 2002).

Two advantages of employing herbal extracts or their active ingredients in animal nutrition include the improvement of endogenous digestive enzyme synthesis and the stimulation of appetite and feed intake, according to Rahimi et al. (2011). According to Tollba et al. (2007), broilers that were fed different amounts of black pepper at two, four, and six weeks of age showed superior body weight gain. The majority of study results show that plant extracts improve the health and production of chickens. Conversely, a number of studies discovered that specific plant extract supplements had no effect on the well-being or rate of growth of hens. According to (Al-Kassie et al., 2011), broilers fed a diet containing black pepper show no difference. Furthermore, research by Aydin et al. (2008) and Hernandez et al. (2004) showed that adding essential oil extract from pepper, cinnamon, and oregano to meals had a little impact on grill performance. Nevertheless, feeding black cumin seed at concentrations of 1, 2, or 3% had no effect on the body weight gain, feed conversion rate, or feed consumption of laying hens.

Essential Oil

By distilling a variety of plant parts, such as buds, seeds, leaves, twigs, bark, wood, fruits, and roots, the aromatic, viscous liquids known as volatile oils, or essential oils, are produced (Miguel, 2010). For thousands of years, these extracts have been used all across the world. They are called organic solvent extracts (ethanol, methanol, toluene, or other organic solvents) or steam-volatile extracts. They are said to have wonderful flavors and scents and to be able to preserve food. Essential oil components can be derived from plant parts or synthesized artificially. Essential oils (EOs) often contain a wide range of compounds, including phenols, alcohols, acetones, terpenes, acids, aldehydes, and esters (Negi, 2012).

For the poultry industry, substituting safe, natural chemicals for antibiotic performance enhancers is a major goal. Given their versatility, essential oils can be employed in poultry production as growth boosters. Positive results have been observed when natural products, such as essential oils, are used to enhance performance. Typical performance measurements in chicken rearing include body weight, growth, intake of food, and the ratio of feed conversion (Al-Kassie, 2010; Calislar et al., 2009). Numerous writers attest to the beneficial effects of essential oils on the efficiency of chicken production (Demir et al., 2008). It seems that using essential oils in place of growth stimulators in broiler diets doesn't always increase production efficiency—in certain cases, it can even worsen it (Ocak et al., 2008). This is most likely the result of using too little oil or the incorrect oil concentration. It's possible that the stated findings change because of weak chicks, biosafety rule violations, or the influence of ambient elements like bedding, illumination, equipment, rodent presence, etc. Dietary errors that occurred throughout the trials, such as imbalanced feed or tainted feed or water, could potentially have contributed to this disparity (Mansoub, 2011). Drinking water is another product that incorporates essential oils.

(Alali et al., 2013). Investigated how grill chicken production characteristics, Salmonella enterica colonisation, water intake, and mortality were affected by adding a blend of oils (lemon, thyme, and eucalyptus) to drinking water. Weight increases and feed conversion were found to significantly enhance following the administration of 0.025 and 0.0125% oil mixture. Conversely, the 0.05% oil concentration lowered the amount of Salmonella in faecal smears when added to water. Furthermore, Khosravinia's (2015) Research has shown that incorporating flavorful oil into drinking water improves productivity while reducing exterior carcass damage. This is attributed to the oil's antimicrobial properties and its ability to reduce litter moisture.

Mode of Action

Polyphenols' Effects on Inflammation and Oxidative Stress in Research Involving Farm Animals

Numerous investigations have demonstrated that polyphenolic compounds can successfully reduce inflammatory processes that are generated in vitro, either on their own or in conjunction with other plant extracts (such as those from green tea, hops, cocoa, or grapes). These studies have used both animal models of inflammation (intestinal inflammation, systemic inflammation associated with obesity, metabolic syndrome, and atherosclerosis) and cell cultures (intestinal cells, immune cells, endothelium and smooth muscle cells, adipocytes, etc.). The complicated biological pathways via which polyphenols reduce inflammation are mostly associated with the inhibition of NF-jB, the main inflammatory regulator. Because antioxidants, polyphenols, they can prevent NF-jB activation by preventing IjB from being phosphorylated or degraded by proteases. This effect is attributed to polyphenols (Vendrame and Klimis-Zacas, 2015).

Polyphenols activate Nrf2, which in turn activates additional antioxidant enzymes, in addition to directly scavenging reactive oxygen species (ROS) (Na and Surh, 2008). Both direct scavenging of ROS and Nrf2 activation can mitigate oxidative stress by inducing proinflammatory pathways through the activation of NFjBthe protein 1 and protien kinases that are mitogen-activated (Chuang and McIntosh, 2011). Furthermore, polyphenols can activate transcription factors such as peroxisome proliferator-activated receptor C by blocking NFjB activation, which lowers inflammation (Chuang and McIntosh, 2011).

Fig. 2 presents a condensed summary of several important pathways via which polyphenols inhibit inflammation. One example of how polyphenols and many other phytochemicals often trigger hormetic pathways is the polyphenols' activation of Nrf2. The hormesis notion in relation to polyphenols implies that while slight cellular stress responses, such as Nrf2 activation, are triggered by subtoxic doses eaten by plant-eating animals, these also induce the activation of genes encoding enzymes that are antioxidant known as vitenes, heat-shock proteins, and biotransformation enzymes. Under stressful circumstances, these genes support cellular homeostasis and confer resistance against increasingly potent stimuli (Calabrese et al., 2012).

As a result, the phytochemicals that induce stress protect the cell against less specialized stresses such oxidative, metabolic, inflammatory, and thermal stress as well as from additional agents and higher concentrations of the stressor (Son et al., 2008), they collectively have an important effect on farm animals. Remarkably, common stresses including reactive oxygen species (ROS) and reactive nitrogen compounds, trigger autophagy through the cytoprotective Nrf2 pathway (Ishii et al., 2002). The amino acids, fatty acids, and nucleotides produced by organelles and cellular proteins can be recycled under extreme circumstances to produce new proteins and ATP. Through its ability to break down damaged mitochondria, which are a source of dangerous ROS and apoptotic proteins, and faulty proteins, which can cause apoptosis, the autophagic "selfcleaning" process helps the cell better withstand cellular stress (Lee et al., 2012). Due to hormetic phytochemicals like epigallocatechin gallate, (Kim et al., 2013) as well as calorie restriction, which activate autophagy (Lempiäinen et al., 2013).

Because autophagy reduces ER stress, inflammatory stress, and oxidative stress, it is a crucial biological activity that supports the health of cells and organisms. (Lee et al., 2012)

Antimicrobial Activity

Food antimicrobials are substances that are either added to or naturally present in food. Specifically, to ensure food safety and quality. Their objective, according to Davidson et al. (2013), is to stop the growth of hazardous or rotting bacteria. The family of chemical preservatives that comprises approved other kinds of agents, like antioxidant chemicals, are also present in food antimicrobials and serve to delay food decomposition (Davidson et al., 2013). Regulatory agencies have approved a range of artificial antimicrobials, comprising various organic acids and salts used as food preservatives, such as sorbic acid, potassium sorbates, sodium lactate, potassium lactate, ascorbic acid, citric acid, tartaric acid, triclosan, nisin, natamycin, and so forth (Kuorwel et al., 2011). However, using some of these offers risks to the consumer's health or nutrition. For instance, sulfites lead to the deterioration of thiamine, or vitamin B1, which is a necessary ingredient in diet

(Garcia-Fuentes et al., 2015). Foods can be physically treated in two ways: thermally and non-thermally, in addition to chemical antimicrobials. Thermal technologies are the most often used preservation methods in the food industry because of their high level of effectiveness. However, the intensities necessary to achieve high security levels could compromise the sensory appeal and nutritious content of a meal (Vasconcelos et al., 2015). Conversely, nonthermal food preservation techniques like pulsed electric fields (PEFs) and high hydrostatic pressure (HHP) are interesting because they maintain the organoleptic properties of the food. But occasionally, studies have shown that physical therapies are not able to ensure food safety because they can only partially break down the bacterial cell walls (Liu et al., 2017; Manas and Pagan, 2005; Wan et al., 2009). Additionally, there is a growing consumer backlash against the use of chemical additives and a desire for higher-quality food that has a longer shelf life without artificial preservatives. For all of these reasons, studies have concentrated on identifying natural substitutes for conventional remedies (Cherrat et al., 2013). Certain requirements must be met by a high-quality natural antibacterial, such as (a) affordability; (b) activity in its natural form at low concentrations; (c) preventing sensory changes in the product; (d) blocking a variety of pathogenic and spoilage bacteria; and (e) being harmless zaa (Davidson et al., 2013).

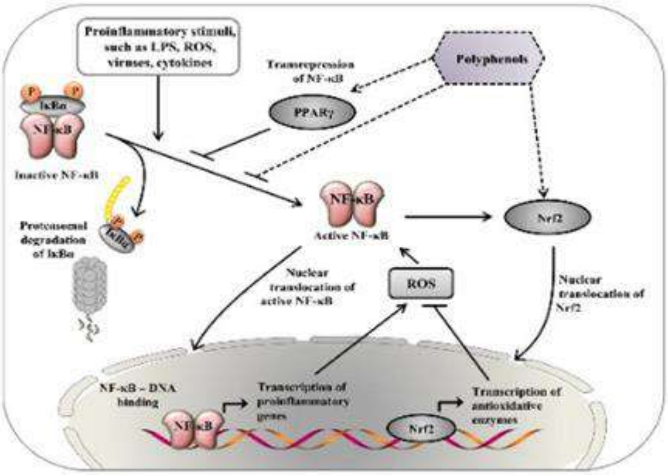

Fig. 2: Anti-inflammatory mode of action of Polyphenol (Nutraceutical)

Bioavailability

Bioactive chemicals are found in foods, pharmaceuticals, and dietary supplements. Terms like bioavailability, bio-accessibility, bioactivity, bioconversion, and bioequivalence are used to evaluate the usefulness of these compounds (Parada and Aguilera, 2007). When characterizing bioactive compounds, these concepts have occasionally been misapplied or stated inaccurately, which has caused misunderstandings. For instance, the bioavailability of a medication taken orally, which must pass through the gastrointestinal tract, is not distinguished from the bioavailability of a medication given parenterally, which is the injection of the bio-component directly into the systemic circulation (intravenously or intra-arterially). Because of this, in pharmacology, the term "absolute bioavailability of a medicine" refers to the proportion of a dose form that is delivered by a specific route and fully absorbed into the systemic circulation. Absolute bioavailability is defined as the amount of bioactive material that is fully absorbed into the systemic circulation after an intravenous administration; relative bioavailability is determined if the bioactive agent cannot be administered intravenously (Sinko, 2006). (Katouzian et al., 2017; Rafiee and Jafari, 2018). On the other hand, hydrophobic substances are predominantly soluble in intestinal fluid when lipolytic enzymes are present. The second stage of bioavailability is represented by a biocomponent's "absorption" at the level of GIT epithelial cells. The small intestine absorbs the majority of bioactive substances. Depending on its nature, the target bioactive molecule is transported across the intestinal epithelial membrane using a number of techniques, such as passive and active transport. One of the main obstacles to a molecule becoming accessible is its efflux, which is caused by transporters that reverse bio-components into the intestinal lumen and cause efflux (Jafari and McClements, 2017). Another method is that bio-components' "transformation" during digestion more precisely, their metabolism in the liver decreases their bioavailability (Rafiee et al., 2019).

Effects of Nutraceuticals

On Body Weight

Excessive energy intake and expenditure are the root causes of obesity and overweight (Stunkard., 1996; WHO., 2011). Reducing energy intake while maintaining energy expenditure can help produce a negative energy balance, which is necessary for weight loss (Wadden et al., 1988; Pasman et al., 1999). Given that thermogenic chemicals increase energy expenditure without carrying any energy, it is intriguing to know if utilizing them can prevent the usual decrease in energy expenditure that occurs while dieting. Researchers have recently focused a great deal of interest on nutraceuticals and functional foods because of their potential to treat obesity and related conditions by exerting a variety of beneficial benefits with little to no negative side effects (Lai et al., 2015; Kaur et al., 2015). Numerous studies on functional foods and nutraceuticals have shown that the gut-brain axis, energy homeostasis-thermogenesis, lipid metabolism (lipase inhibition), and adipocyte lifecycle (adipocytokines from aberrant adipocytes) can all be impacted by an epigenetic or genetic mechanism (Chiu et al., 2018; Yun, 2010). Zingiber officinale One of the spices that is used most frequently in the globe is roscoe or ginger. It was first described by William Roscoe in 1807. As a member of the Zingiberceae family, it includes a range of phytochemicals, including flavonoids and phenols (Palatty et al., 2013). Ginger may help with weight loss by promoting lipolysis, thermogenesis, and catecholamine release in white adipose tissue, according to several studies (Pulbutr et al., 2011; Ahn and Oh, 2012; Mansour et al., 2012; Pulbutr et al., 2011). Furthermore, in a study on cellular respiration, ginger extract accelerated the rate of palmitate-induced oxygen consumption in human and animal skeletal myotubes, indicating that fatty acid oxidation was taking place (Misawa et al., 2015).

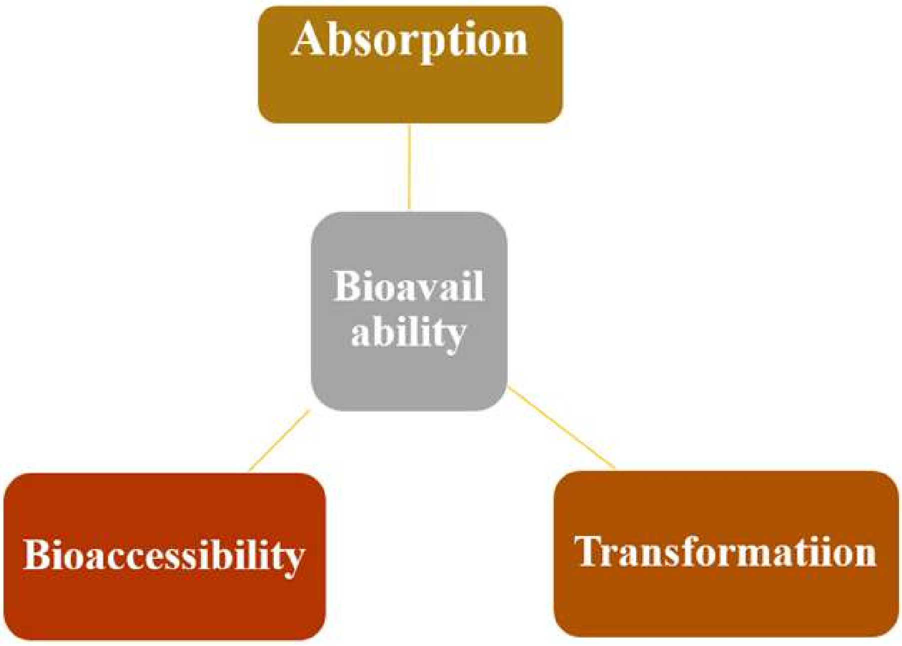

Fig. 1: Principal Procedure Associated with Bioavailability

Additionally, ginger has hypoglycemic effects in diabetic rats and enhances insulin sensitivity by inhibiting the activities of fatty acid synthase and acetyl-CoA carboxylase. Furthermore, it triggers the gamma-activated peroxisome proliferative receptor. Furthermore, in rats given a high-fat diet, it reduces the accumulation of liver fat (Okamoto et al., 2011; Rahimlou et al., 2016). Lastly, research has demonstrated that ginger lowers blood levels of cytokines that promote inflammation (Isa et al., 2008; Saravanan et al., 2014; Shalaby and Saifan, 2014).

Various studies have demonstrated the effectiveness of ginger as a dietary supplement in managing weight and preventing metabolic illnesses (Al-Amin et al., 2006; Chrubasik et al., 2005; Goyal and Kadnur, 2006; Matsuda et al., 2009; Nammi et al., 2009; Okamoto et al., 2011). According to studies, ingesting 75 mg/kg of 6-gingerol per day can aid in weight loss (Naidu et al., 2016; Saravanan et al., 2014).

Studies (Hurse et al., 2011; Hurse et al., 2009; Kovacs et al., 2004; MakiK et al., 2009; Phungo et al., 2010; Vieira et al., 2012; Westerterp et al., 2005; Cardoso et al., 2013) have shown that mixing green tea catechins with caffeine enhances long-term body weight loss and maintenance. Research on fat oxidation and energy expenditure—two crucial metabolic objectives for weight control—has dominated studies conducted shortly (Dulloo et al., 1999). Furthermore, the advantages of caffeine and catechins were demonstrated by meta-analyses of both short- and long-term studies (Hurse et al., 2011; Hurse et al., 2009; PhungO et al., 2010).

Additionally, research on people who are maintaining their weight has demonstrated that green tea catechins and caffeine work together to support weight maintenance following weight loss brought on by a low-calorie diet (Kovacs et al., 2004; Westerterp et al., 2005; Cardoso et al., 2013). Furthermore, a meta-analysis (Hurse et al., 2009) found that consuming a green tea catechins caffeine mixture was associated with a substantial decrease in body weight or body-weight maintenance of around 1.31 kg (95% CI: −2.05, −0.57 kg; I2 = 94%). Weight control is aided by nutraceuticals such as ginger and green tea.

Metabolism

Since enzymes are found in food products naturally, it has long been believed that they are harmless and won't harm consumers' health. However, the safety of commercially generated dietary enzymes, whether originated from tissues of plants and animals or through microbial fermentation, is evaluated. Exogenous enzymes have been shown to increase the physio-biochemical state, meat quality, growth performance, nutritional digestibility, and feed utilization of chickens (Attia et al., 2019; Kumanda et al., 2019). In the chicken industry, exogenous enzymes are well known for their nutritional value in increasing feed intake efficiency and stimulating growth (Alagawany et al., 2018b).

They assist in lowering anti-nutritional materials, including fiber and condensed tannins, increase body weight, meat quality, and the European Production Index (EPI) in addition to raising feed intake and enhancing feed conversion efficiency (Attia et al., 2019; Kumanda et al., 2019).

According to Slominski (2011), exogenous enzymes can be derived from mushrooms like *Aspergillus oryzae* and *Trichoderma longibrachiatum*, bacteria like *Lactobacillus acidophilus, Bacillus subtilis, and Streptococcus faecium*, or yeast-like Saccharomyces cerevisiae. According to Chanda et al. (2019), microbial enzymes are the best source, however, some can also be found in plants or animals. Animals have been administered digestive enzymes such as amylase, xylanase, and β-glucanase (Adeola and Cowieson, 2011). Numerous variables, including temperature, moisture content, animal type, age, and feed ingredients, affect the activity of the enzymes (Yang et al., 2008).

To enhance intestinal viscosity, nutritional metabolism, and digestibility, the enzyme is given to chicken feed. Furthermore, the enzyme can be used to prevent dangerous bacteria from proliferating and colonizing the stomach in place of antibiotics (Kum and Sekkin, 2012). Solis-Cruz et al. (2019) state that to optimize the exogenous enzyme's effects, the pH level must be lowered below 4. It is also recommended to utilize an enzyme mixture to prevent feed components from having anti-nutritive effects (Adeola and Cowieson, 2011). Protease has been shown in research by Abd El-Hack et al. (2016) to improve feed utilization, performance, nutritional digestibility, and energy availability in poultry feed. Adding phytase to the feed of white pekin ducks has improved their growth performance and zinc consumption (Attia et al., 2019).

Animal Performance

Nutraceuticals are products that lower the risk of disease while improving physiological processes in the body and mind (Helal et al., 2019). Animals with digestive health issues may benefit from probiotics, prebiotics, or synbiotics—a combination of probiotics and prebiotics—among various nutraceuticals. Other important organs appear to benefit from these chemicals as well. They are approved as secure alternatives to organic feed additives (Slizewska et al., 2020). Nutraceuticals have synergistic benefits and prevent antibiotic drug resistance due to their pharmacological and biological properties (Maass et al., 2005). Nutraceuticals are becoming more and more well-liked since they may offer therapeutic and nutritional benefits over drugs without side effects, according to recent research by Sachdeva et al. (2020).

Because they can change the gut microbiota, nutraceuticals—which include antibiotic alternatives include organic acids, prebiotics, probiotics, and exogenous enzymes (Dhama et al., 2008; Dhama et al., 2014a, 2014b; Yadav et al., 2016; Yadav and Jha, 2019). According to Cencic and Chingwaru (2010), these nutraceuticals can increase gut microbiota, raise immunity, encourage chicken growth, and shield the host from infectious diseases. Sugiharto (2016). When taken in the appropriate dosage in conjunction with a diet, nutraceuticals, and functional foods—which are composed of fortified nutrients in addition to the ordinary vitamins and minerals in the diet—offer a number of health benefits (Hasler, 2002). According to studies by Attiq et al. (2018), Dhama et al. (2014), 2014a, 2014b, Gupta (2016), and others, nutraceuticals have a wide range of physiological effects on animals, including anti-inflammatory, antimicrobial, sedative, adaptogenic, immunomodulatory, antioxidant, and free radical scavenging. Medicinal herbs are becoming more and more well-liked since they may raise the general quality of chicken products (Dhama et al., 2014a, 2014b; Dhama et al., 2015; Vinus et al., 2018; Alagawany et al., 2019a, 2019b). For a long time, the active ingredients in herbs and plant oils have been added to chicken feed to keep the birds healthy and boost output. Antibacterial, antioxidant, and anti-inflammatory substances also have positive effects on physiological processes (Vinus et al., 2018; Alagawany et al., 2019a, 2019b; Khafaga et al., 2019; Reda et al., 2020;). According to certain research (Simsek et al., 2015; Ding et al., 2017), chickens produced more eggs and had a higher feed conversion rate when essential oils like cinnamon or rosemary were added to their diet.

Limitations

For nutraceuticals to be beneficial for a given ailment, they must be taken and digested at rates that allow the blood to reach optimal concentrations. Nutrients include iron (Jefferies et al., 1984), glucose (Gjedde, 1981), amino acids (Oldendorf and Szabo, 1976), and vitamins (Spector and Johanson, 1989; Spector and Johanson, 2007) contain specific transport systems. The way these nutraceuticals interact with efflux transporters and stereochemistry will determine how well they are absorbed and transported (Pandareesh et al., 2015). For example, animals receiving naringin, a citrus fruit flavonoid, peripherally did not exhibit any brain naringin. However, naringin's amount in the brain increased when it was combined with an inhibitor of p-glycoprotein, a part of the ABC drug efflux transporter at the BBB (Tsai et al., 2002). It is connected to DNA damage brought on by oxidative stress and triggers several cancers (Perocco et al., 2006). Similarly, consuming too much of other nutraceuticals, such as vitamins and minerals, cannot be beneficial to your health. The substantial correlation between dietary and lifestyle choices and the application of nutraceuticals in the management of neurodegenerative diseases has not yet been covered by the majority of research.

There are particular limitations with nutraceuticals as well. They act more like food than like medicine, so their activity is a little slow. Furthermore, the composition, concentration, and source of the elements in nutraceuticals vary by region; as a result, the health advantages associated with different nutraceuticals can differ greatly. Thirdly, individuals may have a preference for fresh food items over processed ones based on their ethnicity; hence, the appearance and palatability of nutraceuticals may limit their intake. Furthermore, there is a lot of disagreement concerning the validity of nutraceuticals. Although certain researchers back up the health advantages of nutraceuticals—which were discussed in the preceding paragraph, others contend that because they originate from traditional medicine, they work more slowly and one should instead rely on medicines for optimal health. Nutraceuticals are currently valued more as status symbols than as dietary supplements because many of them are too expensive for the average man to buy. Among these are Spirulina sp., herbal beverages, green tea, and green coffee beans (Costa, 2017).

Conclusion

It is concluded that Nutraceuticals have antibacterial activity as well as medicinal benefits for animals as well as for humans. A Class of substances known as Nutraceuticals, when added to livestock, has been shown certain positive effects on animals' health. Because this industry is developing quickly without governmental control, there is still a great deal of uncertainty surrounding nutraceuticals. We refer to analyze nutraceuticals in this review as probiotics, prebiotics, Bacteriocins, organic acid, plant extracts, and essential oils. These substances function through a variety of mechanisms, i.e., stabilization of commensal microbial communities, enhancement of gastrointestinal immunity, collecting and adhering toxic or hazardous pathogens, and enhancing the ability to absorb antioxidant and immediate antibacterial action. Because of their host protective properties, i.e., their anti-inflammatory,anti-oxidant antibacterial effects, and their ability to enhance productivity, nutraceuticals provide an excellent substitute as nutritional supplements. The sources of nutraceuticals have also been discussed. It has been mentioned that, in addition to its many benefits, there are several drawbacks.

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Chapter 22

Nutritional Innovations and Nutraceuticals: Safeguarding Fisheries through Disease Prevention

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ABSTRACT

Fisheries sector has undergone significant demand-driven expansion in recent decades as a result of the development and acceptance of novel technologies and production practices like intensified culture systems. This expansion, however, has coincided with an increase in multiple environmental-related stresses, creating significant hurdles to the fisheries sector and impending global growth. These stressful circumstances damage the health of reared species, predisposing them to diseases that cause financial losses. As a result, enhancing the stress resistance of reared animals is critical for assuring aquaculture's long-term success. To address these concerns about disease prevention in fisheries, a variety of investigations have been conducted all over the world, with a considerable focus on the management of cultured environments and reared species. Among different preventing measures, nutritional interventions in terms of functional feed and nutraceuticals appear to be a flexible and sustainable approach to developing immune competence and stress resistance in rearing species as the need for certain nutrients may rise under stressful settings. Optimal amounts of various essential and non-essential dietary nutrients influence immunological performance and stress or disease resistance. This chapter discusses the safeguarding of fisheries through disease prevention by using multiple nutritional and nutraceutical innovations in aquafeed like as an amino acids, essential fatty acids, enzymes, vitamin and mineral premix, probiotics, prebiotics, synbiotics, antimicrobial peptides, and antivirulence therapies, for improving the overall performance of reared species.

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INTRODUCTION

Fisheries perform a critical role in food security and livelihood as a means of income and social development (FAO, 2016). The fish, comprising shellfish and finfish, contribute17% to the animal protein sources and are important for rising population's nutrition (FAO, 2018). The Fish gives good-quality essential amino acids like eicosapentaenoic (EPA) and docosahexaenoic (DHA) fatty acids; minerals i.e.,iron, zinc; and vitamins that are present in highly bioavailable forms (Golden et al., 2016). This larger demand is due to greater utilization of fisheries products and reducing production from wild fisheries which has led to a high dependency on aquaculture practices. Aquaculture is a promising way to meet the demanding gap for aquatic food because wild fisheries are undergoing reduction. Total world's fish output is anticipated to increase, reaching more than 200 million tons in 2030, due to rising demands and technological advancements (FAO, 2020).

The expansion of conventional aquaculture is restricted due to land, water, and protein-rich feed constraints, making it a less effective and sustainable practice. Yet, there is a shift towards alternate methods such as closed or intensive aquaculture systems, which address these challenges while providing more eco-friendly and economically viable solutions over conventional systems (El-Saadony et al., 2021). Despite the socioeconomic advantages of intensive aquaculture practices, it remains linked with several issues like high production expenses, water pollution, overcrowding stress, and pathogenic propagation. These challenges cause significant harm to the performance of aquatic species (i.e., growth and reproduction performance) and also increasing their susceptibility to diseases outbreak that ultimately leads to higher death rate (Stentiford et al., 2020). These multiple pressures cause some components of the immune system of rearing species to be dysfunctional, rendering aquatic species more prone to infections and leading in economic losses to the farmer.

Different approaches and strategies are employed to control diseases because prevention is better than cure. A current approach to disease mitigation in aquaculture comprises three levels: comprehensive protocol, good husbandry strategies, and effective antimicrobial application. But the application of conventional antibiotics is under strict control and regulatory challenges due to drug resistance and residue-related problems in fisheries products (Muteeb et al., 2023). These antibiotic products are under scrutiny, and some are banned for utilization in several countries due to their challenges. So, there is a demand for alternate strategies to provide an additional defense against diseases-causing organisms (Rohani et al., 2022). Alternative substitutes to traditional antibiotics cover a wide category of strategies and products that supports immunological system of aquatic animals (Bondad-Reantaso et al., 2023). Vaccination is a highly effective and protective method against pathogens (e.g., bacteria, viruses, fungi) instead of an antibiotic method. But its application is limited due to its higher prices and laborious practices. Maintaining an effective defense system against diseases-causing organisms is vital for the success and sustainability of aquacultures, by utilizing alternative approaches like stock selection to get desired traits; and adopting nutritional innovations in terms of functional feed concepts and nutraceuticals in fisheries, offers pragmatic and promising solutions to prevailing diseases challenges.

The idea of functional feed is an emerging novelapproach forthe formulation of nutritionally balanced aquafeeds for sustainable aquafarming (Encarnação, 2016). The functional feeds not only fulfill basic dietary needs through a wide range of dietary supplementsbut can also support the health and disease resistance of the rearing aquatic species by boostingtheir growth andfeed efficacy. This can reduce production expenses and simultaneously improve consumers' perception (AlAli et al., 2021). The nutritional additives boost health by either stimulating the immunological system or helping immunity functions by aidingbeneficial gut microbiota (Hasan et al., 2018). Several types of supplements like vitamins and minerals, proteins, probiotics, lipids, prebiotics, synbiotics, as well as certain immune-stimulants are used for improving fish health (Reverter et al., 2021). Many of the prebiotics also act as immune-stimulants because they influence immunological indices in multiple ways. Other additional immune-stimulants instead of prebiotics, which representa guaranteed way in the aquaculture includes lactoferrin, beta-glucan, and various substances extracted frommedicinal plants and seaweeds (Wang et al., 2017).

The conventional antimicrobial products follow specific pathways to control the viability of disease-causing organisms, but they cause negative effects like pathogenic resistance. So in this way, there is a need to discover novel nutraceuticals like antimicrobial peptides and antivirulence compounds, which are efficient alternative productstocurrent traditional antimicrobials, with a lower risk of developing antimicrobial resistance (Valero et al., 2020). These novel antimicrobial therapies target specific virulent mechanisms that pathogenic microbes utilize to cause diseases (Johnson and Abramovitch 2017). The antimicrobial peptides are compounds that are formed naturally by the host body and perform critical roles in the immunological system over traditional products (Wang et al., 2017).

Factors Causing Diseases Outbreak in Fisheries

Globally, fish diseases are among the major challenging factors that restrict aquaculture production and sustainability with subsequent influences on food security, and human health (Ali et al., 2020). Multiple factors are linked to the development and propagation of aquatic diseases in intensive culture practices (Stentiford et al., 2020). These factors are high stocking density, poor husbandry practices, poor water quality, and improper nutrition which sometimes lead to high mortality rates and lower productivity (Huicab-Pech et al., 2016). Typically, there are two factors that which predispose fish to diseases:

Intrinsic Factors

Intrinsic factors originate from metabolism, feeding, and other activities within the aquatic environment. These are essentially environmental stressors i.e., factors that cause stress to fish in their cultural conditions. Diseases usually manifest due to the stress produced by changes within the environment, and provide suitable environmental conditions for the growth and proliferation of pathogenic microorganisms like bacteria, viruses, fungi, etc. The stressful conditions weaken fish immunity and increase disease susceptibility (Abdel-Tawwab et al., 2019). These environmental stress factors include poor water quality, overcrowding, improper fish nutrition, and aquatic vegetation. Water quality parameters are a major limiting factor in the rearing of aquatic species and directly affect feeding efficiency, growth, health, and survival rate (Wanja et al., 2020).

Extrinsic Factors

These are factors that arise from outside the aquatic environment. They include high culture intensity and the aquatic contaminants that gain access to the aquatic environment through water pollution (Bashir et al., 2020). Water pollution occurs when a water body is negatively impacted due to the addition of large quantities of substances to the water. The water pollution sources are classified as point sources and non-point sources. Point sources of pollution occur when the polluting substance is released directly into the water e.g., a pipe discharging toxic chemicals directly into a river. Non-point sources of pollution arise when there is runoff of pollutants into a waterway e.g., when fertilizers from a field are carried into a stream of water by surface runoff (Xu et al., 2022).

Current Approaches to Disease Prevention

The immunological system of fish is same as other vertebrates' systems because of two basic systems: the adaptive and innate immune systems. The innate immune system comprises of physical barriers (e.g., temperature, epithelial layers,

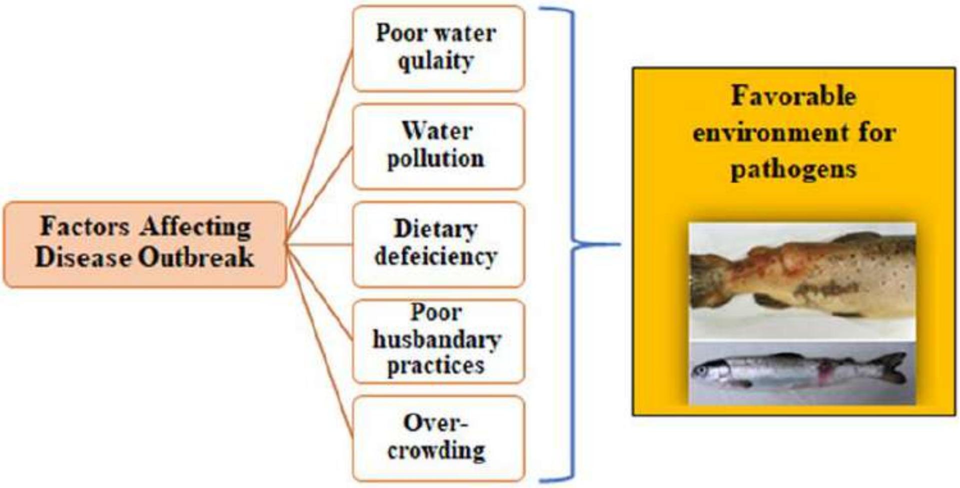

Fig. 1: Factors affecting disease outbreak in Fisheries

mucosal, or pH ingredients), non-specific effect or elements, and immune cells capable of identifying, catching, and removing pathogenic microbes (Wright et al., 2023). These two systems work as the 1st and 2nd line of defense in the immunological system. If any pathogenic microbes cross these defenses, then the adaptive system is stimulated, and stores memory of these threats linked with pathogens. If aquaculture is to flourish and continue offering food to the population, then there is a requirement for comprehensive approaches and efficient treatments to tackle the disease issues posed by evolving resistive disease-causing organisms (Easwaran et al., 2022).

Currently, the main approach to disease control that is used in aquaculture comprises three levels: comprehensive protocol, good husbandry approaches, and antimicrobial application. Comprehensive protocols standardize the practices used by staff members to prevent contamination and foster their alertness for disease incidents (Schwarz et al., 2019). When a comprehensive protocol is applied properly, aquaculture actions will lower the risk of contamination and disease outbreaks (biosecurity) and increase the speed and preparedness of response to a wide variety of animal health threats (disease response) (Leandro, 2021). Good husbandry practices refer to animal care within the aquaculture system to strengthen animal health (Wright et al., 2023). However, if any pathogen overcomes these protocols and enters in aquaculture system, then appropriate antimicrobial products can be utilized to control diseases when fish's immune system is not capable of removing these pathogens. With uncertainty surrounding the continued efficacy of traditional antimicrobial products, alternative approaches are required for providing an extra defensive system against pathogenic microbes (Wright et al., 2023).

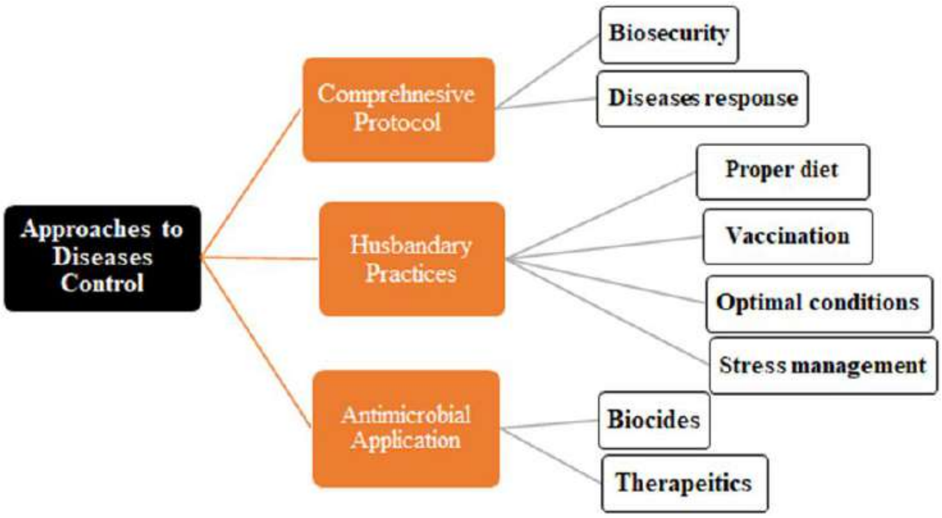

Fig. 2: Current approaches to disease control

Nutritional Innovations: Safeguarding Fisheries

Research on the fish immunological system has made significant improvements over the last years, and these inventions are now reshaping how the aquaculture sector acts to disease control by utilizing multiple alternative strategies (Wright et al., 2023). These alternate strategies include nutritional innovations in terms of functional feed and nutraceuticals.

Nutritional Innovations to Prevent Diseases

Diseases management in fisheries has attracted wide attention from researchers in recent years (Assefa and Abunna 2018). In this regard, one of the most potential aspects of investigation has been the development of multiple methods for controlling diseases in fisheries which includes maintaining the quality of water, guaranteeing environment-friendly feed, and adjusting optimum stocking density. Diseases management approaches in fisheries can be widely classified into two classes: managing cultural environment that involves overall environmental condition management such as maintaining water quality parameters; and management of the reared species such as control of disease outbreaks through direct dietary interventions like the development of functional feed (Ciji and Akhtar 2021).

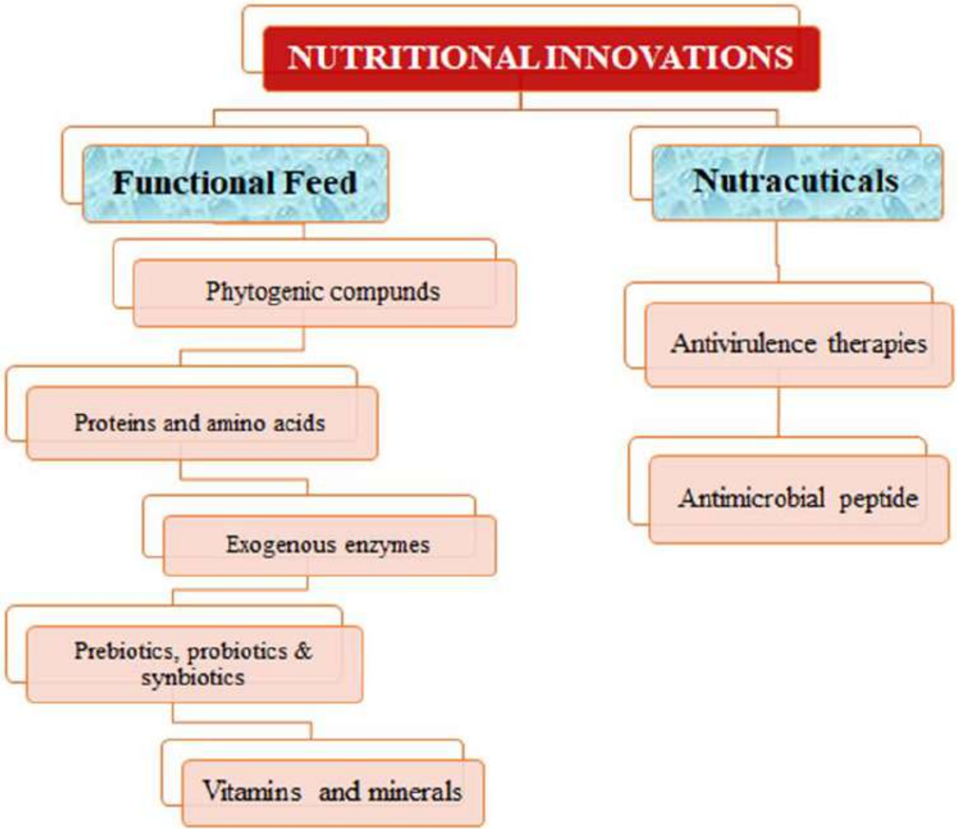

Fig. 3: Nutritional innovations for safeguarding fisheries through diseases prevention

Functional Feed

Several terrestrial animals as well as plants by products have been utilized with varying levels of success as substitute's to fish oil (FO) or fishmeal (FM) in optimized feed formulation (Gasco et al., 2018). But the addition of these alternate ingredients in large amounts in diets often shows some adverse impacts on rearing animals, as well as the aquatic environment. In this way, the functional feed idea has been established to tackle feed formulation's challenges. Functional feeds are shifting the primary focus from weight gain of rearing species to offering solutions to current problems in animal production cycles (i.e., health management, disease control) (Dawood et al., 2018). Thus, the addition of functional feed additives (FuFAs) in formulated feed is very important in these regards. Efficient utilization of agro-industrial by-products and plant-source feeds will not be feasible without the addition of FuFAs. The addition of certain FuFAs improves the immunological system, health status of rearing animals, and also strengthens them against the attack of multiple pathogenic organisms (Rohani et al., 2022). Thus, for successful aqua-farming practices and safe aqua-food production, different FuFAs are used which are given below:

Phytogenic Compounds

Phytogenic or phytobiotic products are derived from plants, supplemented in the aqua feed to enhance the palatability of feeds, growth performance and health of the aquatic animals (Karaskova et al., 2015).These plant compounds have multiple characteristics such as antimicrobial, anti-carcinogenic, antioxidant, analgesic, insecticidal, anti-parasitic, growth enhancement, stimulant of bile secretion, and digestive enzyme activity (Bharathi et al., 2019). These compounds are heterogeneous feed additives arising from different parts of the plants like roots, leaves, fruits, tubers, and spices. These components are utilized in diverse forms like extract, oil, or powder (Alemayehu et al., 2018). Various products utilized in aquaculture like *Moringa oleifera*, *Allium sativum*, *Rosmarinus officinalis*, *Withania somnifer*, and *Ipomoea batatas (*Alemayehu et al., 2018).

Protein and Amino Acids

Proteins are synthesized by linkages of different individual amino acids. There are more than 200 amino acids present in the natural world, but only about 20 amino acids are common. Among these, 10 amino acids are essential (indispensable) which cannot be produced by fish. The 10 essential amino acids that must be provided by the feed are arginine, threonine, tryptophan, methionine, leucine, histidine, isoleucine, valine, lysine, and phenylalanine. Among these, methionine and lysine are often limiting amino acids (Ayub et al., 2021). The fish feeds formulated with plant-based proteins, bacterial, and yeast-based proteins typically contain methionine in small amounts. Therefore, these amino acids must be added to aqua feeds when these protein sources are utilized to substitute fishmeal. Yet, it is necessary to know and provide the dietary protein as well as amino acid needs of each aquatic species for promoting their optimum growth and health (Li et al., 2021).

The high protein content in the feeds has been shown to control diseases by alleviating multiple stresses like salt stress in *Litopenaeus vannamei*, thermal stress in *Labeo rohita*,intensity stress in Nile tilapia and stress of pH in *Eriocheir sinensis*by enriching the amino acid pool (Lieke et al., 2020). The higher demands for certain amino acids observed in different species of the fish under stressing circumstances can be correlated with the synthesis of immunological proteins like antibodies and other specific molecules, besides meeting the energy demand. Because of anti-stress effects of several amino acids like aromatic amino acids (tryptophan, tyrosine, phenylalanine), acidic amino acids (glutamine, aspartate), basic amino acids (arginine, histidine, lysine), sulphur containing amino acids (taurine, methionine), branched-chain amino acids (isoleucine, valine, leucine), they are utilized in the formulated feed (Herrera et al., 2017).

Lipids

Lipids are high-energy substances that can be used to replace protein in formulated aqua feeds partially. Lipids have about double the energy mass than carbohydrates and proteins. Dietary lipids offera suitable quantity of fatty acids as a fuel to fulfill the increasing demands of energy throughout the stressful conditions. Docosahexaenoic (DHA) and eicosapentaenoic (EPA) omega-3 fatty acids perform roles in growth response, mortality control, and stress tolerance by altering basal cortisol levels (Lund and Steenfeldt 2011). The long-chain polyunsaturated fatty acids (PUFAs) like EPA and DHA, serve as precursors of eicosanoids (leukotrienes, prostaglandins, thromboxanes) are released during stress and inflammatory conditions. The phospholipids play an important role in enhancing stress tolerance capability of several rearing aquatic animals. The soy lecithin, a rich source of phosphatidyl choline improving tolerance of stresses including thermal tolerance limits in rearing species (Ciji et al., 2021). The phosphatidylinositol, rich in arachidonic acid, boosts tolerance of stresses by changing lipid composition of membranes (Liu et al., 2022).

Exogenous Enzymes

Enzymes are proteins that accelerate the metabolism or chemical reactions in living bodies. Nowadays, several exogenous enzymes are utilized in aqua feeds to tackle the adverse impacts of anti-nutritional factors, for enhancing the digestibility of dietary additives, and for boosting the growth of rearing animals (Ebru and Cengiz 2016). The commonly used enzymes in aqua feeds are pepsin, protease, phytase, carbohydrase, papain lipase, and alpha-amylase (Liang et al., 2022). Eighty percent of the phosphorus in the seeds of plants is found only in phytate form. The phytate phosphorus digestibility and bioavailability are very poor for rearing aquatic species. Hence, phytase in aqua feed enhances the phytate phosphorus digestion and decreases phosphorus excretion and it also enhances the protein and phosphorus utilization. The digestible efficacy of the non-starch polysaccharides (NSPs)is improved by the addition of non-starch polysaccharides degrading enzymes in the aqua feeds (Bharathi et al., 2019).Pepsin, papain, and amylase improve the growth and feed efficacy in aquatic species (Alemayehu et al., 2018). The microbial phytase incorporation in the feed enhances the availability of phosphorus and energy. Alpha-amylase enhances the starch digestibility and improves the growth performance (Bharathi et al., 2019).

Vitamins

Vitamins are an organic essential substance in the feed which support the normal growth of fish. These substances cannot be synthesized in the fish body, and they must be supplemented in the feed (Khalili Tilami and Sampels 2018). Vitamins are categorized into two categories: the fat-soluble vitamins and water-soluble vitamins (Gasco et al., 2018). The fat-soluble vitamins are vitamins A (retinol and beta carotene), D (cholecalciferol), E (tocopherols), and K (phylloquinone). Among these vitamins, vitamin E attracts great attention for its significant roles as an antioxidant substance. Vitamin E is a potential vitamin that is addressed for disease control in aqua-farming, and employs a protective shield through its antioxidant characteristics, lowering glucose and cortisol levels, and boosting immunity responses (Liu et al., 2022). On the other hand, water-soluble vitamins include vitamin B (riboflavin, pantothenic acid, folic acid, niacin, and biotin), choline, inositol, and vitamin C (ascorbic acid). Among these water-soluble vitamins, vitamin B attracts great attention for fisheries sustainable production. Among the B-group vitamins, thiamine (vitamin B1); riboflavin (vitamin B2); niacin (Vitamin B3); pantothenic acid (vitamin B5); pyridoxine (vitamin B6); and folic acids play multiple roles like provide protection against the oxidative damage and improve immune systems (Ciji and Akhtar 2021).

Minerals

Minerals are inorganic essential substances for the normal physiology of the body. They can be categorized into two categories: micro-minerals and macro minerals, depending on the amount needed in the diet and the quantity that already exists in the body. Fish can absorb several minerals directly from the water through their skin and gills, permitting them to cover the mineral deficiencies to some extent in their diets (Gasco et al., 2018). Important minerals in aquaculture are several including zinc, selenium, copper, manganese, etc. Among these, selenium(inorganic/organic/nano-selenium) is the most widely utilized trace mineral, which helps in lowering the influence of stress associated with poor husbandry conditions like high temperature, hypoxia, low salt-stress, ammonia and nitrite stress, and over-crowding stress (Iqbal et al., 2020). Copper (Cu), zinc (Zn), and manganese (Mn) are the other trace minerals that are helpful in the mitigation of stressful conditions by acting as cofactors of multiple enzymes like superoxide dismutase (SOD) (Lall and Kaushik, 2021). The dietary calcium and sodium supplementation in feed perform multiple roles like protecting aquatic species against toxicity of metals by down-regulating the rate of sodium and calcium uptake across the gills, thereby reducing the entry and accumulation of lethal metals. Dietary magnesium also boosts the antioxidant activity in aquatic species and can lessen the adverse effects of stressors.

Nucleotides

Nucleotides are the basic components of nucleic acids and can modulate the proliferation of immune system cells, resulting in enhanced immune functions (Hossain et al., 2016). The dietary inclusion of individual and mixed nucleotides can modify immune performances and improve stress acceptance in several aquatic species (Hossain et al., 2020). The dietary supplementation of nucleotides/nucleosides i.e., guanosine monophosphate (GMP), inosine, adenosine monophosphate (AMP), and hypoxanthine can increase peroxidase and lysozyme activity; boosts innate immunity functions; increases the WBC and lymphocyte counts; prevent and repair DNA impairment; improve total plasma immune globulin levels; improve iron bioavailability and absorption (Kenari et al., 2013). But the optimum feeding time and dietary content of nucleotides must be recognized for different aquatic animals before administering them as stress-reducing molecules to tackle the adverse impacts of the effects of nucleotides.

Prebiotics

Prebiotics are defined as non-digestible valuable nutritional supplements for enhancing the microbial activities to improve immunological responses and disease resistance ability of rearing species (Kaushik et al., 2022). They are also considered as immune-saccharides, which perform significant improvements in the innate immunity functions of aquatic species. There are multiple prebiotics utilized in culture systems like as fructo-oligosaccharide (FOS), yeast cell wall (YCW), xylo-oligosaccharides (XOS), mannan-oligosaccharide (MOS), isomalto-oligosaccharides (IMO), galacto-oligosaccharide (GOS), soybean oligosaccharides (SOS), and several others (Carbone and Faggio 2016). The plant-based sources have a great quantity of fructan (garlic, kiwi, onion, artichoke, and soybeans), and inulin (jimca and chicory root), which are also valuable natural prebiotic sources (Hughes et al., 2022). The prebiotics positively enhance the feeding efficacy as well as growth response of aquatic species, by stimulating digestive activity, boosting immune responses, modification of gut morphology, and limiting pathogenic attack (Butt et al., 2021).

Probiotics

The probiotics are defined as live microbes which can be added as a feed additive for favorable health performances in aquatic species (Markowiakand Slizewska 2018). The probiotics act in several ways for increasing aquaculture productivity, by improving feed consumption, enhancing growth performances, boosting immunity functions, and decreasing disease outbreaks (Rohani et al., 2022). Mostly utilized bacterial probiotic supplements include *Lactobacillus sp., Bacillus sp., Pseudomonas sp.,Bifidobacterium sp., Arthrobacters sp.,Streptococcus sp., Microbacterium sp., Micrococcus sp.,* and *Enterococcus sp.,* etc.; yeast probiotic supplements include *Debrayomyces hansenii*, *Saccharomyces cerevisiae*, and cell wall of yeast, etc.; micro-algal probiotics include *Spirulina platensis, Tetrasehnis suecica*etc.;and bacteriophage probiotic supplementis *Bacteriophages sp*. (Van Doan, 2023).Probiotics can be added to aqua feeds for triggering the growth performances of rearing species and provide protection from several pathogenic invasions, and several are increasingly considered as potential alternatives for antimicrobial agents (Chauhan and Singh, 2019).

Synbiotics

Synbiotics is a combined application of different feed supplements such as prebiotic sand probiotics. They are used broadly and are considered to be growth and immune-stimulating factors in multiple culture systems (Hoseinifar et al., 2017). The inclusion of synbiotics in the diets permits the survival of valuable bacteria in the gut and boosts the total enzymatic activity of the intestine; and improving feed digestibility thus leads to an enhanced growth of aquatic organisms (Rohani et al., 2022). The application of synbiotics plays impressive roles in the processing of complex particles into simple particles, thereby guaranteeing the availability of essential nutrients needed for the growth (Huynh et al., 2018). Furthermore, the inclusion of symbiotic supplements has resulted in improved activity of lysozymes, antioxidant activity, and immunity responses in aquatic species.

Nutraceuticals to Prevent Diseases

Traditional antimicrobial compounds target certain pathways for controlling the growth or proliferation of pathogenic organisms. But with the development of antimicrobial resistance (AMR), there is a need to discover other products that provide protection to the aquatic species against pathogenic microbes by using different molecular mechanisms than traditional products' mechanisms (Wright et al., 2023). The innovative antimicrobials include a wide range of compounds and strategies that provide strength to multiple parts of the immunological systems (Bondad-Reantaso et al., 2023).

Antimicrobial Peptides

The antimicrobial peptides (AMPs) are developed by multiple kinds of cells or tissues of all invertebrates and vertebrates. Due to their rapid antimicrobial activities, these peptides have great potential as a new category against bacterial resistance and also have attracted great focus as promising candidates for the future generations of products (Rima et al., 2021). The AMPs have various benefits over traditional antibiotic products. These peptides can eliminate bacteria rapidly, also act on bacteria despite their bacterial resistance, and consequently remain unaffected by their AMR mechanisms (Raheem and Straus 2019). In comparison to conventional antibiotic products, these peptides are biodegradable and cannot stay in the host body or surrounding environment after their application (Liu et al., 2022). Some peptides also act as immune-stimulants because of their capability for triggering multiple aspects of the innate immunological system. The activities of these peptides include the regulation of pathogen-recognition and inflammatory signaling mechanisms; regeneration of tissues; and development or maturation of immune cells. Due to these immune-stimulatory and ant- microbial properties, these peptides are considered as potential products for aquaculture practices (Valero et al., 2020).

Anti-virulence Therapies

These include a broad range of products, which target the virulent methods that make pathogenic microbes capable of causing diseases instead of affecting the pathogen itself (Johnson and Abramovitch 2017). When using traditional anti biotic compounds, there is no difference between pathogenic microbes and beneficial or non-pathogenic microbes. These therapies also interfere with ecological sensing as well as bacterial signaling, lowering the capability of the pathogenic microbes to respond to signals associated with the environment, and impacting the gene regulatory factors that cause virulence (Defoirdt, 2014). Before the use of anti-virulence therapies, large-scale experiments will be required to prove their efficacy and assess their potential impacts in aquaculture. Furthermore, continuous investigation of the virulence mechanisms of aquatic pathogenic microbes is needed for recognizing the suitable kind of antivirulence products that will destroy the pathogenic microbes and control the propagation of diseases (Wright et al., 2023).

Conclusion

Several stresses in fisheries are inevitable and they always lower the sustainable production. These issues in fisheries have resulted in extensive research focused on mitigating the effects of disease on cultured animals. Among multiple diseases preventing measures in fisheries, nutritional interventions have appeared as sustainable and realistic approach in terms of functional feed additives and nutraceuticals. In the concept of functional feeds, a broad range of feed supplements can be utilized to extend beyond meeting the primary nutritional demands of the target cultured species to enhance growth and feed consumption, but also to support the health and stress resistance of the farmed species. The nature and properties of these additives are quite broad, and their use in aqua diets focuses on a specific purpose. Some supplements like exogenous enzymes, are used to improve the animals' performance by giving improved digestion of the feed ingredients or counteracting the adverse effects of anti-nutrients. Additionally, other additives, such as photogenic, probiotics, prebiotics, and synbiotics target the improvement of gut health and disease resistance. Additionally, nutraceuticals like antimicrobial peptides and anti-virulence therapies are also used to control pathogens efficiently despite of their microbial resistance.

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Chapter 23

Nutritional Strategic Control of Mastitis

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ABSTRACT

The most prevalent management disorder in dairy cattle is mastitis that lowers milk production as well as quality, which results in significant financial losses. Determining exposure duration, characterising pathogen-specific characteristics, defining clinical and subclinical states of disease, and identifying pathways of infection are all essential. Many scientists struggled to determine efficient ways for controlling mastitis carried by the *Staphylococcus aureus*, *Streptococcus agalactiae*, and other microorganisms. The scientific literature shows that there is a relationship among mastitis and nutrition. The major impact of nutrition on udder health is via suppression of the immune system. Cows in negative energy balance are at a higher risk of clinical mastitis. Dairy cattle' health is negatively impacted by oxidative stress throughout the pre- and post-partum periods, which might result in immune suppression. Maintaining appropriate nutrition is therefore an essential management approach to avoid mastitis in the herd. While making a mastitis control strategy, it is important to take consideration the vitamins and minerals including calcium, zinc, selenium, and copper, vitamin A, vitamin E and vitamin C play role in maintaining immunity and udder health. Nutritional deficiency leads to metabolic diseases which in turn suppresses immune mechanisms.

KEYWORDS		
Nutritional Strategic Control, Mastitis, Subclinical states of disease	Received: 23-Jun-2024 Revised: 12-Jul-2024 Accepted: 09-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Mastitis is defined as inflammation of the mammary glands, a costly and complex disease involving the environment, pathogens, and host with variable causes, severity, and consequences, frequently associated with intra-mammary bacterial infection (Thomsen et al., 2012). Mastitis is one of the economically devastating diseases affecting dairy animals. Mastitis can be further classified as subclinical (i.e., recognised via ancillary tests such as the somatic cell count, California mastitis test or Surf field mastitis test etc.) or clinical (i.e., visually evident changes to milk, the gland, or udder). The incidence of mastitis in heifers is higher than in older animals (McDougall et al., 2007). It exerts a negative impact on production potential of dairy animals. It deteriorates milk quality and decreases milk yield. There will be significant reduction in economic benefits to farmer. The fields of animal breeding, animal nutrition and husbandry practices that had undergone a paramount advancement play a significant role in increasing production potential of dairy animals over the last decades (Shook, 2006). Pathogens that causes mastitis are often classified into two categories, environmental or infectious pathogens, still it has been uncertain (Zadoks et al., 2014). Other factors that contribute to the development of mastitis are related to the cow origins, such as age, lactation stage, and an increase in the number of somatic cell count (SCC) (Steeneveld et al., 2008). Mastitis has zoonotic and economic significance. It can have harmful impacts on milk yield and health of consumers (Al-Majali et al., 2008). Sub-clinical mastitis is major cause of decrease in milk yield and had large impact on productive performance of lactating animals. Sub-clinical mastitis can lead to lose function of one or more quarters by inflammation of tissues (Younan et al., 2001). When udder of animal is affected by mastitis, it not only poses threat to overall health of animal, but also induces biochemical changes in the milk. These changes are not only responsible for poor keeping quality of milk but also deteriorate the nutritional composition of the product making it less beneficial for humans. It also poses threat to human health if consumed unchecked (Bagri et al., 2018). Presence of this disease is disturbing because it jacks up expenditure and causes losses. Among direct losses are expenses on diagnosis and treatment, expenditure on labour force, rejection of milk by the processing industry, and mortality are counted. In the indirect losses reduction of milk yield, reduction of milk shelf life and quality and cost on replacement and culling of infected animals are included (Petrovski et al., 2006). In addition to production and economic losses it has detrimental effect on the overall health of animal. This effect can be so catastrophic that it can even lead to loss of pregnancy of animal in the early gestation. In this way it can sabotage the breeding plan and increase in feeding cost and delay in getting the next generation of animals which play a vital role in the economics of a dairy enterprise (Dahl et al., 2017). This disease is cause of huge financial calamities for the livestock farmer because it incorporates direct expenses of testing, veterinary expenditures, medicine, loss of milk and work force, reduced production and culling of affected animals. The expenses of preventive measures are also considered as the losses because of mastitis. Due to miscalculation or lack of record keeping by farmers, dairy ranchers normally think little of the expenses of mastitis. Moreover, the losses of future production of milk are hard to measure (Heikkilä et al., 2018). Among the factors which cause involuntary culling of animals in dairy enterprises, mammary diseases were second most leading causes along with reproduction problems and low milk protein level (Chiumia et al., 2013)

Causal Agents for Intra-mammary Infection

Streptococcus uberis

Streptococcus uberis is a pathogen considered as mastitis causing bacteria of environment can cause clinical and sub-clinical mastitis. This is mostly present in bedding material and also linked with improper cleaning and washing of udder before and after milking (Rebhun et al., 2008).

Streptococcus dysgalactiae

This pathogen is gram positive, beta-haemolytic, coccal bacterium considered as environmental and contagious both (Rebhun et al., 2008).

Streptococcus agalactiae

When milking in unhygienic conditions *Streptococcus agalactiae* is a pathogen that is transferred from animal to animal. This can also be transfer from dam to the calf by sucking milk. This is the major source of sub-clinical mastitis (Keefe, 1997). This species can cause skin infection, uterine infection and also respiratory infections (Younan et al., 2000).

Staphylococcus aureus

Staphylococcus aureus is a most common and contagious pathogen that can cause of udder infection which leads to clinical and sub-clinical mastitis (Persson et al., 2011). This is not only prevalent on udder, it may also found in colonized in other parts of body such as skin, tonsils, vagina and other body regions (Rebhun et al., 2008). This bacterium can be transmitted via milker or milking equipment (Zadoks et al., 2014). The calf is also a source of transmission by suckling on infected quarter then suckling an un-infected quarter (Mitsuda et al., 1996).

Coagulase-negative staphylococci (CNS)

CNS is the heterogeneous group of *staphylococci* (Becker et al., 2014). Previously it was considered as minor isolate of udder infection but now group of *CNS* cause mastitis with mild clinical mastitis and sub-clinical mastitis (Pyörälä and Taponen, 2009). *S. haemolyticus, S. chromogenes, S. simulans, S. epidermidis, and S. xylosus* are the species of *CNS* isolated from milk. The species of CNS influence the herd considerable different, which that herd-level factors impact *Coagulase-negative staphylococci* (Piessens et al., 2011).

Coliforms

Enterobacter spp., Klebsiella pneumoniae and *Escherica coli* are the environmental pathogens often refers to the coliform mastitis. These are the gram negative bacteria. Improper management can lead up to increase the risk of coliform mastitis (Rebhun et al., 2008). The most of bacteria isolated in different studies were gram positive in camels, but coliforms were also isolated in different studies in sub-clinical cases of mastitis (Ahmad et al., 2012; Husein et al., 2013; Regassa et al., 2013).

Mastitis can be caused by a variety of viral and non-infectious reasons, and there is mounting evidence that dietary variables are linked to mastitis in cows (Heinrichs et al., 2009). Even dairy producers' efforts to avoid intra-mammary infections in herds, it is not always obvious that there is a substantial association among nutrition and susceptibility to mastitis. When dairy cows consume insufficient amounts of minerals and vitamins, their immunity suffers. Animals become more vulnerable to infections like mastitis because their immune system is compromised and is unable to neutralize pathogens that infiltrate the udder. Dietary amounts of vitamins A and E, as well as minerals like Cu, Zn and Se, may affect susceptibility to intramammary infections (NRC, 2001)

Mastitis Control Programme

Mastitis is the result of multiple factors interacting with the environment, pathogen(s), and host. Most of the cases of mastitis occur in lactating cows, often soon after calving, with the abnormal milk. If clinical mastitis is predicted to develop, treating the condition before signs and symptoms appear can reduces the number of cases of clinical mastitis, shortens the convalescent period, and returns SCC to normal. The severity of the condition is determined by the cell count at the time of diagnosis. The efficacy of therapy during non-lactating period is better than during lactation. The usual method of treatment involves the use of antibiotics, whereas homoeopathic and herbal remedies also hold a certain significance. Early mastitis treatment improves the likelihood that bacteria can be eliminated (Sharif et al., 2009).

Immune Response of Mammary Glands

There are two types of defense mechanisms: innate immunity and acquired immunity. During the early phases of infection, innate immunity, also known as non-specific immunity, is the primary defense mechanism. This initial defense is promptly triggered at infection site by a variety of stimuli; however, it has no memory and does not improve with repeated exposure to the same injury. This nonspecific defence begins at the teat end, a physical barrier, and progresses with immune cells like as natural killer (NK) cells, neutrophils, macrophages, and other soluble substances like cytokines. On the contrary, acquired immunity, also known as specific immunity, provides the foundation for vaccination. It identifies certain pathogen determinants that trigger a selective response which leads to its eradication. Lymphocyte's antibodies, and macrophages recognise pathogens and activate a response. This sort of immunity retains memory and is increased by subsequent exposure to the same pathogen. Physical barriers to bacterial entry in the udder, such as teat skin, teat sphincter muscle, and keratin plug, function as part of the innate immune system (Figure 1). However, absence of their normal function leads to intra-mammary infection. Abrasions and breaches in the teat skin promote pathogenic colonization, increasing the possibility of bacterial penetration, especially during milking processes when the duct is stretched. Another protective component of the teat is the keratin plug, which is produced by the cells that coat it. In addition to having antibacterial properties, this substance also traps and inhibits bacteria from ascending into the mammary gland, lowering the risk of intra-mammary infections and, therefore, the somatic cell count (SCC) (Bruno, 2010).

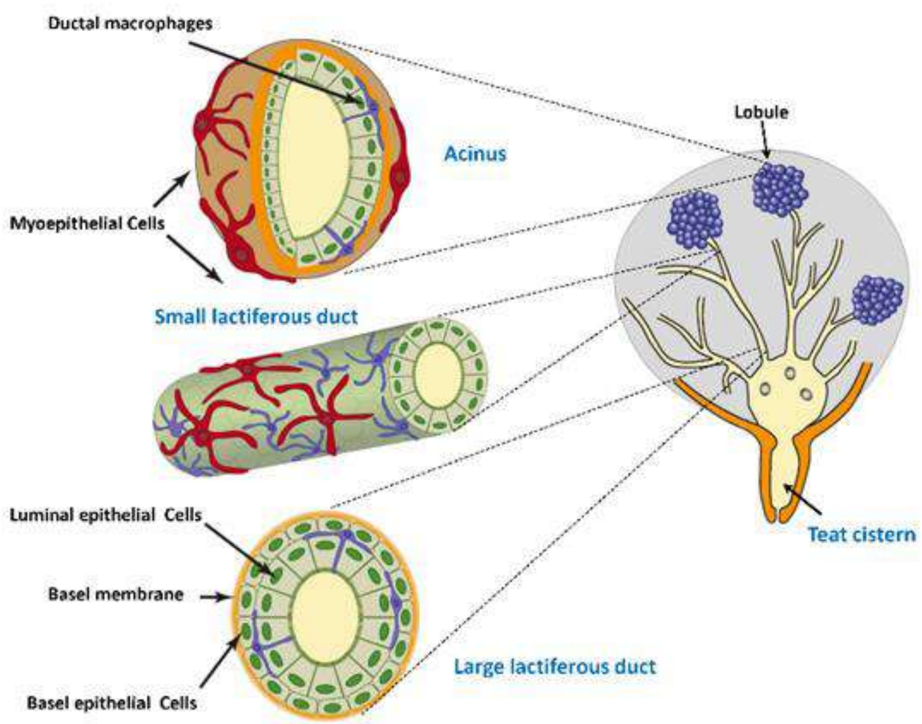

Fig. 1: Physical barrier of mammary glands

The development of mastitis in dairy cows is caused by a multitude of predisposing conditions. The predisposing factors may be environmental, pathological, genetic, or physiological (Sordillo, 2005). The mammary glands are getting exposed to potential pathogens frequently. The adequate immunity of animal prevents the mammary gland from getting infected and keeps them away from mastitis. The nutrition has numerous roles to uplift the immune response of dairy animals. Nutrition affects immune system through two major mechanisms:

- Certain nutrients are crucial for specific functions of immune cells and diet that lacks those nutrients can impair immune mechanisms. Vitamin A and Zinc have impact on epithelial health. The phagocytic cells are influenced by micronutrients like Copper, Zinc, Selenium, Vitamin E and Vitamin A.
- Proper nutrition decreases the prevalence of metabolic diseases that can inhibit or suppress immunity. Proper nutrition thereby enhances the immune function and lowers mastitis risk.

Vitamin E and Selenium

Vitamin E is a fat-soluble antioxidant, a group of eight fat soluble compounds that fights against free radical-induced lipid peroxidation. It has been found to have an essential role in the reproductive, muscular, circulatory, neurological, and immunological systems of both animals and humans. Vitamin E serves several interrelated functions because it is the main antioxidant in cell membranes that is soluble in lipids. It serves as an internal defence mechanism against reactive oxygen species' harmful effects. The immune response is strengthened by vitamin E and selenium against a variety of harmful pathogens. Enhancement of both antibody titre and phagocytosis of pathogens is observed with increasing dietary Vitamin E supplementation in calves, lambs and dairy cows (Spears and Weiss, 2008; Tresamol and Nissar, 2020). Vitamin E directly affects neutrophil activity among dairy cows throughout the periparturient stage by increasing neutrophil activity and blood neutrophils' ability to destroy (Hogan et al., 1992). Additionally, during the transition period, vitamin E supplementation prevented a decrease in the production of neutrophil superoxide anion, MHC-II expression and interleukin-1 (IL-1) by blood monocytes following parturition. Additionally, it prevented a decrease in neutrophil chemotactic reactivity that started two weeks prior to parturition and lasted for four weeks after (Politis et al., 1996). The minimum Vitamin E requirement for dairy cows is estimated to be between 10 and 60 IU per kilogramme of dry matter. Vitamin E requirements for pregnant heifers and dry pregnant cows range from 80-120 IU per kg, whereas lactation cows require 16-27 IU per kg (NRC, 2001)

Selenium is a crucial component of the enzyme’s glutathione peroxidase and thioredoxin reductase, both of which are situated in the cell's cytoplasm in order to prevent oxidative stress. Furthermore, selenium appears to protect phagocytic cells during the respiratory burst from oxidative damage. Phagocytic cells' capacity to fight microbes and carry out metabolic processes may be hampered by the release of free radicals from phagolysosomes or by their incapacity to be detoxified (Larsen, 1993). Vitamin E and selenium supplementation strengthens dairy cows' immune systems and lowers their risk of mastitis. It has been claimed that the Se content in colostrum is four times more than in milk (Underwood and Suttle, 1999).

Vitamin A and β-Carotene

A vital micronutrient, vitamin A is essential for healthy vision, growth and development, epithelial protection, and mucus integrity in the body. Vitamin A could amplify the anti-inflammatory response of organisms and called Vitamin A the ‘anti-inflammation vitamin’. Vitamin A performs a critical role in development of immune system. Additionally, vitamin A regulates humoral immune responses as well as cellular immunological responses. Vitamin A deficiency causes the keratinization of epithelial tissues, which impairs their ability to defend the alimentary, genital, reproductive, respiratory, and urinary tracts and increases their vulnerability to infection (Tresamol and Nissar, 2020).

As a precursor to vitamin A, beta-carotene reduces the production of superoxide inside phagocytes and acts as an antioxidant. It also directly improves immunity, which has benefits for the reproductive system and the mammary glands. It is crucial for protecting the integrity of the mucosal surface and the health of the epithelial tissue, both of which may help stop infections that cause mastitis from entering the mammary gland (Bruno, 2010). One kilogram of feed must contain 3,900 IU for lactating cows. The amount of IUI needed per kg of feed for lactating and gestating ewes is 2,667 and 3,305 IU, respectively. For late gestation, small ruminants require 45.5 retinol equivalent (RE) per kg body weight of vitamin A, and for lactation, 53.5 RE per kg body weight of vitamin A (NRC, 2001).

Vitamin C

Vitamin C is a water-soluble antioxidant found in the gastrointestinal tract, tissues and cells. It has a role in the production of adrenal steroids and catecholamines, carnitine (hydroxylation of trimethyl lysine), and bioactive amines in the brain and nervous system. Toxins, natural chemicals, and other xenobiotics are inevitably detoxified by liver microsomes. It is necessary for the proper function and stability of leukocytes and erythrocytes. It has both antihistamines and anti-inflammatory effects. It is an anti-endotoxin. Vitamin C acts as oxidative stress biomarkers. Subcutaneous vitamin C administration in cows may be beneficial for treating mastitis, however because of lipid peroxidation, the therapeutic impact is diminished. Together with cupric ions, vitamin C prevents and treats dairy cow mastitis by teat dip or intramammary infusion (Kleczkowski et al., 2005; Ranjan et al., 2005).

Zinc

For mammals, zinc (Zn) is a necessary nutrient because it plays a major role in enzyme systems, protein synthesis, the metabolism of carbohydrates, and several other biochemical processes. Zn is crucial for skin health and integrity since it aids in cellular repair and replacement, as well as speeding up wound healing. Zinc has an impact on the immune system in a number of ways, ranging from the skin barrier to lymphocyte gene regulation. A zinc deficit also hinders the development of acquired immunity by limiting T lymphocyte activation, Th1 cytokine generation, and B lymphocyte assistance, among other T cell activities. Zinc also functions as an antioxidant and can stabilize membranes. Zn's participation in keratin synthesis limits the number of somatic cells (Bruno, 2010). Due to a drop in DMI, Zn transfers to colostrum, elevated stress during parturition, and a return to normal levels within three to five days postpartum, as Zn levels in dairy cows fall during parturition. Additionally, the blood concentration of zinc falls during mastitis caused by *Escherichia coli*, suggesting an antibiotic mechanism that lessens the mineral's availability for bacterial proliferation (Erskine and Bartlett, 1993). The recommended supplementation for nursing cows is 40-60 mg/kg (NRC, 2001).

Copper

Copper is a component of the enzyme ceruloplasmin, synthesized in liver, this facilitates the transfer and absorption of iron. In addition, copper is a crucial component of the enzyme superoxide dismutase, which shields cells from the damaging effects of oxygen compounds generated through phagocytosis. Copper plays an important role in immune mechanisms. Cu may play a role in reducing the incidence of periparturient inter-mammary infection, particularly in association with coliform IMI. Cu supplementation can decrease the severity of *Escherichia coli* induced mastitis and also reduce the risk of intramammary infections caused by major mastitis pathogens (Bruno, 2010).

Calcium

For muscles to contract properly, calcium is necessary. Severe hypocalcaemia causes dropped muscular contraction, which culminates in the clinical manifestation of milk fever. Any reduction in blood calcium levels decreases muscle contraction. The amount of calcium in the blood directly correlates with the strength and rate of contraction of the digestive tract's smooth muscle. For the teat end to close, smooth muscle in the teat sphincter has to contract. Low blood calcium levels may decrease the contraction of the teat sphincter, which might leave the teat canal open and allow external infections to enter the mammary gland. Cows with milk fever are more likely to get mastitis. Calcium is required for proper functioning of immune cells. The immune cells got supressed if hypocalcaemia persists. In hypocalcaemic animals the plasma cortisol level will be higher that leads to suppression of immune system. The quantity of calcium/kg of milk produced varies slightly depending on the breed and the amount of protein in the milk. 1.22 to 1.45 gm of absorbed calcium are needed per kg of milk produced. A cow needs around 2.1 gm of absorbed calcium/kg of colostrum produced (Tresamol and Nissar, 2020).

Conclusion

One of the most common ailments affecting dairy cattle is mastitis, which has a detrimental financial effect on the industry. The management of dairy cows today is centred on maximising milk production, which has led to an increase in the incidence of health disorders because free radicals are produced and eliminated without control. Free radicals activate tissues metabolically, causing oxidative stress and, ultimately, health problems in dairy cows. The periparturient period, which has a significant impact on dairy cow health, is defined by oxidative stress and immunological suppression. One of the most important components in preventing mastitis is maintaining the animals' nutritional level in order to prevent health problems. Nutrition enhances the animal’s resistance to mastitis, though it has no influence on exposure of teat ends to pathogens. Nutrition can affect mammary gland immunity, and consequently mastitis. Allowing for optimal immunity is crucial when supplementation is necessary, especially during the periparturient phase. Nutritional and administrative issues can be resolved to reduce the prevalence of mastitis. One of the most important aspects of treating mastitis in animals is strengthening their immune systems to increase their ability to fight against bacterial invaders.

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Chapter 24

Nutraceuticals in Child Brain Development

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ABSTRACT

This research explores the role of nutraceuticals in child brain development. Nutraceuticals are bioactive substances having therapeutic qualities that are produced from dietary sources. They have drawn attention to their ability to boost cognitive function during crucial stages of brain development. This research investigates the processes by which nutraceuticals affect neurodevelopment, including neurogenesis, synaptogenesis, and neurotransmitter modulation, through an extensive examination of the body of existing literature. Our investigation includes examining the effects of important nutraceuticals, such as vitamins, antioxidants, and omega-3 fatty acids, on children's brain health and cognitive outcomes. The report also discusses the benefits and difficulties of incorporating nutraceutical therapies into public health campaigns and pediatric healthcare practices. Through the combination of existing literature and the identification of knowledge gaps, this study advances our understanding of the potential advantages of nutraceuticals in improving the development of the child's brain. Also, it guides future approaches for this field of study, which aim to improve methods for supporting children's cognitive health. To optimize the cognitive capacity and well-being of future generations, this study offers insights that can guide clinical practice, policy-making, and parental decisions through a detailed analysis of the effects of nutraceuticals on infant brain development.

KEYWORDS		
nutraceuticals, Advancements, Neurodevelopment, Cognitive function, Clinical practice, Pediatric healthcare practices	Received: 07-Jun-2024 Revised: 21-Jul-2024 Accepted: 08-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

The term 'nutraceuticals' combines elements of both 'nutrition' and 'pharmaceuticals'. Nutraceuticals are the foods or components of foods that are essential to establishing and sustaining normal physiological function, which keeps people healthy. Nutraceuticals have tremendous significance in infant brain development. The early years set the stage for later cognitive skills, emotional control, and general mental health development. Thus, it is crucial to maximize nutrient intake at this crucial time to ensure ideal brain growth and long-term cognitive performance (Egbuna and Dable-Tupas, 2020).

Overview of Nutraceuticals

The term "nutraceutical" initially appeared in a survey conducted in the United Kingdom, Germany, and France. In these countries, consumers prioritized nutrition over exercise and genetics to obtain optimal health (Pandey et al., 2010). The Foundation for Innovation in Medicine (FIM), Cranford, NJ, chairperson, and founder Stephen De Felice, created the phrase "nutraceutical" in 1989 by combining the words "nutrition" and "pharmaceutical" (Maddi et al., 2007; Williamson et al., 2020). A nutraceutical is "a food (or a part of food) that provides medical or health benefits, including the prevention and/or treatment of a disease," according to De Felice. Health Canada, on the other hand, defines a nutraceutical as "a product prepared using foods but sold as pills, or powder (potions), or in other medicinal forms, typically not linked with foods" (Heland et al., 2022).

The world market for nutraceuticals is expanding primarily due to two factors: the present population and health trends. Among the food items used as nutraceuticals include dietary fiber, prebiotics, omega-3 fatty acids, antioxidants, and many types of herbal or natural foods (Chopra et al., 2022). Nutraceuticals encompass most therapeutic categories, such as depression, diabetes, cancer prevention, osteoporosis, cholesterol and blood pressure management, analgesics, cold and cough, sleep issues, and anti-arthritic. The attraction of nutraceuticals is their ability to alter gene expression, modify biochemical pathways, and improve physiological functions related to health and well-being. They provide an alternative to traditional medicine by endorsing the notion of "food as medicine" and acknowledging the inextricable connection between dietary practices and health consequences (Biesalski, 2022).

Nutritional supplements including polyphenols, choline, and omega-3 fatty acids stimulate the growth of new neurons and the development of synaptic connections between neurons, which is known as neurogenesis (Georgiou et al., 2011). These substances improve the fluidity of the membrane surrounding neurons, promote the release of neurotransmitters, and alter signaling pathways related to synaptic plasticity. Nutraceuticals support the development of cognitive abilities, including learning, memory, and attention, by promoting neuronal proliferation and differentia tion in important brain regions like the hippocampus and prefrontal cortex (Rathnakumar et al., 2019; Khalid et al., 2022).

Nutraceuticals, like iron, zinc, and vitamin B12, are vital for myelination, which is the process of axons losing their myelin sheaths to allow for effective signal transmission (Makkar et al., 2020). Sufficient concentrations of these micronutrients are essential for nerve conduction, preservation of white matter integrity, and cognitive functions that depend on rapid and coordinated neural transmission. By improving micronutrient levels throughout important brain development phases, nutritional interventions can help avoid myelination defects and reduce the risk of neurodevelopmental problems linked to poor axonal connection (Williams et al., 2015).

Importance of Childhood Brain Development

It is impossible to overestimate the significance of early brain development since it sets the stage for all later learning, behavior, and environmental adaptation. Studies show that past life events and environmental factors significantly mold brain circuitry, creating neural pathways that support emotional and cognitive functioning throughout an individual's life (Chanda et al., 2019). A person's susceptibility to neurodevelopmental disorders includes autism spectrum disorders (ASD), attention deficit hyperactivity disorder (ADHD), and learning disabilities can also result from disturbances or departures from normal neurodevelopmental trajectories during childhood (Casey et al., 2010).

Early childhood is a crucial time for brain development since fast neuronal growth, pruning of synapses, and functional specialization mark it. Environmental factors, including diet, have a significant impact on the development of the brain's anatomical and functional integrity throughout this period. Sufficient nourishment is necessary to maintain neurogenesis, myelination, neurotransmitter synthesis, and synaptic plasticity, all of which are basic mechanisms underlying emotional control and cognitive function (Farmer-Dougan and Alferink, 2013).

Optimal brain development lays the foundation for several cognitive areas, such as attention, memory, language, executive function, and social skills during childhood. During this delicate time, deficiencies or imbalances in important nutrients can have long-term effects, putting kids at risk for behavioral issues, learning impairments, developmental delays, and mental health issues in the future. Additionally, new research indicates that dietary interventions made during crucial periods of brain development may have long-term effects by affecting resilience and cognitive reserve against age-related cognitive decline (Cusick and Georgieff, 2016).

Nutrients Essential for Child Brain Development

Nutraceuticals such as omega-3 fatty acids, choline, iron, zinc, and vitamin B12 play essential roles in brain health and cognitive outcomes in children.

1. **Omega-3 Fatty Acids:** The growth and function of the brain depend on omega-3 fatty acids, especially EPA (Eicosa Pentaenoic Acid) and DHA (Docosa Hexaenoic Acid). Walnuts, flaxseeds, and fatty seafood like salmon are excellent sources of them. It's common practice to provide omega-3 supplements to kids who don't get enough from their diet. From a pharmacological standpoint, these omega-3 fatty acids enhance mental well-being and lower the likelihood of brain-related illnesses such as mild cognitive impairment, autism spectrum disorders, Alzheimer's disease, epilepsy, schizophrenia, stroke, and Parkinson's disease (Khalid et al., 2022).

2. **Vitamin D:** For cognitive function and brain growth, vitamin D is essential. It safeguards brain tissue and aids in the regulation of neurotransmitters. Sunlight exposure, dairy products with added nutrients, and fatty fish are all excellent dietary sources. Supplements, however, can be required, particularly in places with little sunlight or in the winter (Luchtman and Song, 2013).

3. **Choline:** For the brain to develop properly, choline is also necessary, especially for the processes of learning and memory. Foods, including eggs, liver, and peanuts, contain it. Proper brain growth during pregnancy and early childhood requires sufficient consumption of choline (Derbyshire and Obeid, 2020). Both the peripheral nervous system (PNS) and the central nervous system (CNS) use acetylcholine as a neurotransmitter. Cholinergic projections from the basal forebrain to the cerebral cortex and hippocampus in the central nervous system (CNS) facilitate the cognitive processes of those target regions (Korsmo et al., 2019).

4. **Iron:** For the brain to operate properly, iron is required for myelination, neurotransmitter synthesis, and cognitive growth. Foods high in iron include beans, chicken, fish, red meat, and fortified cereals. Children who are at risk of iron deficiency, such as those with specific medical disorders or poor nutritional intake, may require iron supplementation (Thomas et al., 2009).

5. Zinc: Zinc plays a role in memory formation, synaptic plasticity, and neurotransmitter activity. Meat, seafood, beans, nuts, and seeds are wonderful sources. The two most common clinical signs of zinc deficiency are dermatitis and growth retardation. Researchers should revise current recommended intakes to meet the zinc requirements of extremely preterm neonates, as more a nd more data suggest that moderate zinc deficiency may have significant subclinical effects, increasing the risk of several complications common to preterm neonates (e.g., necrotizing enterocolitis, chronic lung disease, and retinopathy) (Terrin et al., 2015).

6. B Vitamins: B vitamins like folate, B6, and B12 are essential for healthy brain growth and operation. They have a role in myelination, DNA methylation, and neurotransmitter production. Whole grains, leafy greens, meat, fish, eggs, and dairy products are foods high in B vitamins. Supplementation could be required in some circumstances, particularly for kids with specific medical issues or dietary needs (Ajibade, 2018).

Role of Nutraceuticals in Cognitive Function

Executive Cognitive Function

Cognition is a high-order brain function that indicates changes in aging affect the quality of life as labeled in Fig. 1 (Tucker-Drob, 2019). Cognition encompasses mental processes like problem-solving, planning, attention, language, and memory, with a diversity of cognitive domains, including attention, language, memory, and executive function.

Memory and Learning

Memory retrieval is a crucial cognitive domain, influenced by genetic and epigenetic factors that regulate cellular, neurochemical, and behavioral parameters in the multidimensional brain aging process (Smith et al., 2020).

The aygdala is responsible for processing emotions and forming emotional memories, the thalamus helps with memory consolidation, and the hippocampus plays a crucial role in the formation of new memories. Together, these subcortical structures help store and retrieve memories in the brain. No doubt, the activity of subcortical structures would be the source of cognitive issues and emotional states.

Attention and Focus

Caffeine, a stimulating compound that is contained in coffee and tea, improves concentration, attention, and focus by electronically blocking adenosine, a neurotransmitter that leads to relaxation and sleepiness.

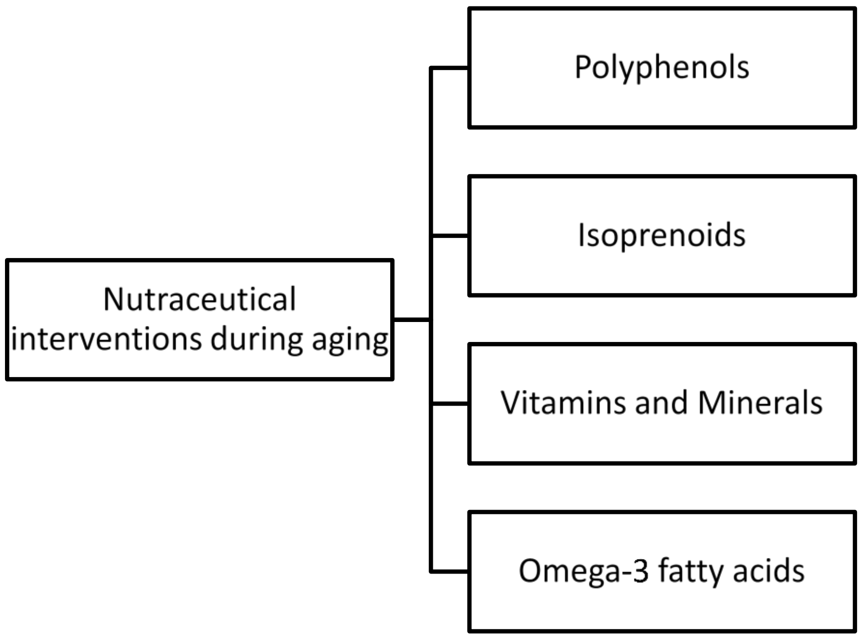

Fig. 1: Nutraceutical treatment for the cognitive decline in aging and impairments.

Ginkgo biloba and *Bacopa monnieri* are herbal remedies that can enhance attention and focus by increasing cerebral blood flow, enhancing neurotransmitter balance, and protecting against oxidative stress, which can support cognitive function as discussed in Table 1.

Table 1: Nutraceuticals that have a cognitive enhancing effect

Nutraceutical	Effects claimed
Gingko biloba	Restore function in those with cognitive impairments
Bacopa monnieri	Restore function in those with cognitive impairments
Caffeine	Acute improvement in cognition and prevention of cognitive decline

Executive Function

Executive function is a set of cognitive processes that are associated with goal-oriented behavior, including planning, decision-making, and impulse control. Nutraceuticals that positively affect brain health and neurotransmitter function can inflict, to a lesser extent, executive function.

The antioxidants such as vitamins C and E and polyphenols in fruits and vegetables remedy oxidative stress within the brain and inflammation, thus keeping cognitive function, which includes executive function, intact even in aging individuals.

Nutraceutical Interventions in Childhood Neurodevelopmental Disorders

Neurodevelopment is a complex process influenced by genetics and the environment, beginning post-conception and lasting into adulthood, potentially resulting in severe neurobehavioral morbidities (Nishimura et al., 2021).

Researchers increasingly recognize that nutraceuticals benefit childhood neurodevelopmental disorders by regulating brain physiology and aiding in the prevention of neurodegeneration and cognitive decline (Santini et al., 2017).
Childhood neurodevelopmental disorders like autism spectrum disorder (ASD), ADHD, and developmental disability are also being studied to be administered in conjunction with therapies to mitigate their symptoms.

Autism Spectrum Disorders
Disease Pathology

Autism Spectrum Disorder (ASD) is a neurological syndrome that causes troubles in social communication. And stereotyped behaviors, often manifesting after a period of typical early development. It is a leading cause of intellectual disability (Courchesne et al., 2011).

ADHD

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental condition that frequently begins in infancy and can last until adulthood.
Symptoms:
1. Lack of attention
2. Restlessness
3. Impulsivity

Intellectual Disability

Mental retardation, otherwise known as intellectual disability (ID) encompasses severe developmental impairments in cognitive skills, speech and language, and motor operations as labeled in Fig. 2 (Pratt et al., 2007).
Symptoms:
1. Subpar intellectual capabilities
2. Delayed language development
3. Behavioral and emotional issues
4. Impaired gross motor skills

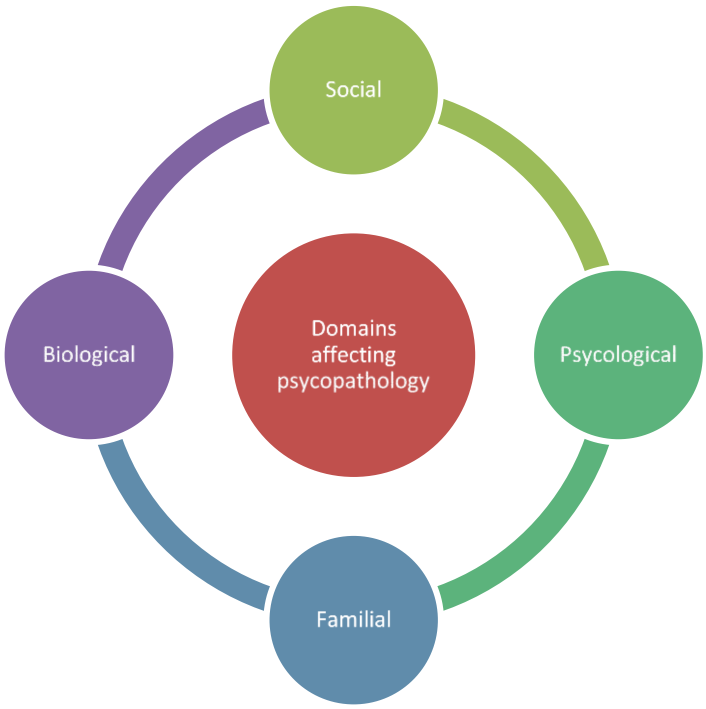

Fig. 2: Factors mediating the expression of psychopathology in children with ID

Use of Nutraceuticals

Nutraceuticals are being studied for aiding individuals with ASD because of reported nutrient deficiencies and biochemical issues like oxidative stress and mitochondrial dysfunction (Owen-Smith et al., 2015).

Nutraceuticals can complement current treatments to promote gut health, detoxify the body, boost antioxidants, and reduce stress and environmental risks (Levy and Hyman, 2008). One approach for treating complex brain problems is to focus on enhancing or supporting the body's natural ability to repair, regulate, and detoxify.

Challenges and Considerations

Dosage Guidelines

Age, weight, and certain medical problems are usually taken into account when determining the dosage of nutraceuticals for kids.

Consistently adhere to the dose recommendations listed on product labels or as directed by a medical practitioner.

Depending on the kind of nutraceutical and how it will be used, dosages might differ significantly (Santana-Gálvez et al., 2019).

Safety Considerations

Children are typically safe when given adequate dosages of nutraceuticals. However, toxicity and negative consequences might result in high dosages. It is important to adhere to prescribed dosages.

Before providing any nutraceuticals to children, check with a healthcare professional because some may interfere with prescription drugs.

To reduce the chance of alteration or contamination, make sure the nutraceuticals come from reliable producers (Mali et al., 2022).

Compliance and Accessibility

Nutraceuticals frequently need to be taken daily, and things like complicated dosage schedules, big tablet sizes, or unpleasant tastes might make it difficult to follow them. Nutraceuticals should be made in user-friendly forms, such as those that are simple to swallow or have a nice taste, to improve adherence (Visen et al., 2022).

Accessibility is concerned with the cost and accessibility of nutraceuticals. Access may be restricted by high costs. Accessibility can also be influenced by cultural acceptability and knowledge of their advantages. Enhancing compliance and accessibility can optimize the beneficial effects of nutraceuticals on public health as discussed in Table 2 (Chopra et al., 2022).

Dietary and Supplementary Nutraceuticals

Table 2: Dietary VS Supplementary Nutraceuticals

Characteristics	Dietary	Supplementary
Bioavailability	More Bioavailability	Less bioavailability with some exceptions.
Nutrients diversity	Provide a wide range of nutrients	Lack of synergetic food effects
Fiber contents	Rich in Fiber	Most do not contain Fibers
Phytochemicals/Anti-oxidants	Whole food contains a variety of phytochemicals and antioxidants	Contain isolated antioxidants may not beneficial as whole-food
Gut absorption	Promote healthy gut microbes, help in absorption	May not easily absorb
Overconsumption	Low over-consumption risk	High overconsumption risk leads to toxicity

Future Direction and Research Needs

Nutraceuticals can provide more rapid growth and development times, and they may additionally be provided as native chemicals in herbal form or as basic food elements. The subsequent research should focus on longitudinal studies to determine the long-term impact of nutraceuticals on child brain development. Their health effects can be easily evaluated since epidemiological research may identify safety profiles, reducing the length and expense of clinical trials. Disease prevention measures are costly and heavily regulated. Nutraceuticals can be helpful in avoiding disease while saving money, time, uncomfortable medication, and medical treatments. Preclinical investigations with active molecules could offer clarity regarding excellence, effectiveness, and their mechanisms of action. The clinical examination of these organic compounds can provide additional evidence of nutraceutical safety and effectiveness. Clinical evaluation will also result in a paradigm shift in nutraceutical categorization to include medications instead of supplements (Chopra et al., 2022). Given the present regulatory structures governing nutraceuticals and the increasing interest of the public in this market, there is a need to locate and comprehensively analyze existing literature on the pros and cons of nutraceuticals.

Future research should identify possibilities and limitations in the therapeutic characteristics of nutraceuticals, identify significant target markets, and recommend strategies for boosting health utilizing nutraceutical products. A meta-analysis of current clinical research or pilot research might be a valuable tool for evaluating the efficacy of more than one nutraceutical compound. Together, these investigations can offer the framework for delivering clinical advice and strong guidance regarding efficient nutraceutical marketing. A system of regulation should facilitate the recognition and categorization of these commodities, as well as provide clarity for potential users regarding excellence, effectiveness, way of action, and security. Long-term research studies are necessary to clinically confirm nutraceuticals for a variety of medical problems. Another factor to consider is how nutraceuticals interact with diet and medicines (Pandey et al., 2010).

Conclusion

Nutraceuticals are foods or parts of foods that have beneficial health effects, regardless of whether they include nutrients. For many years, such nutraceuticals have been continually acquiring significance as complementary or supplementary treatments alongside pharmaceuticals for either the avoidance or therapy of an array of disorders. The purity (fewer side consequences), affordability, and dietary benefits of nutraceuticals make them an appealing, dependable, and appropriate choice for disease prevention or treatment. The increased use of nutraceuticals nowadays also urges us to consider the need for a regulatory authority to oversee their efficacy and prevent abuse. In today's world, new technologies should be used to demonstrate clinical efficacy as well as a comprehensive mode of action, thereby supporting the evidence-based use of nutraceuticals as substitutes and supplementary medications to supply mankind with the greatest health benefits.

Public health organizations recognize nutraceuticals as a powerful tool for sustaining health and combating nutritionally induced acute and chronic disorders, encouraging good health, durability, and a high standard of living. Clinical and regulatory regulations will provide vital tools heading ahead to capture the positive effects and precautions of nutraceuticals, generate understanding about nutraceuticals, and offer them a more suitable position within the healthcare sector. Nutraceutical businesses must prioritize the quality of their accessible goods. This can be accomplished by recognizing and organizing active ingredients in organic goods while offering thorough product information on labeling. Furthermore, it is probable that nutraceuticals will be utilized as an adjunct to pharmacotherapy rather than as a primary therapy.

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Chapter 25

Use of the Various Feed Remedies for the Treatment and Control of *Salmonella* in Poultry

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ABSTRACT

Salmonella presents a significant menace to both poultry well-being and human health, necessitating efficacious control measures within poultry farming systems. One emerging strategy involves the application of feed solutions aimed at curtailing Salmonella contamination. Initially, probiotics have surfaced as auspicious feed supplements due to their capacity to bolster intestinal health and competitively exclude pathogens such as Salmonella. Subsequently, prebiotics, indigestible feed constituents, stimulate the proliferation and functionality of beneficial gut bacteria, thereby indirectly impeding Salmonella colonization. Prebiotics like oligosaccharides and fructooligosaccharides act as nourishment for beneficial bacteria, fostering their growth and enhancing gut vitality. Organic acids, encompassing formic acid, propionic acid, and acetic acid, demonstrate potent antimicrobial characteristics against Salmonella. Through acidifying the gastrointestinal environment, organic acids create an inhospitable milieu for Salmonella propagation while concurrently enhancing nutrient breakdown and intestinal resilience. Essential oils derived from botanical sources have garnered attention for their antimicrobial and immune-modulating attributes. Varieties like oregano, thyme, and cinnamon harbor bioactive compounds that impede Salmonella proliferation and augment the host's immune response. Enzymes such as phytase and carbohydrates have been harnessed to refine nutrient utilization and intestinal well-being in poultry health. In this review article, use various free -antibiotic strategies to control of salmonella in poultry along with advantages, boost the immune system of host for preventing the salmonella infection by bacteriophages, and reduce the side effect of drugs.

KEYWORDS		
Salmonella Infection, Feed Remedies, Prebiotics, Probiotics, Acidifier	Received: 21-Jun-2024 Revised: 11-Jul-2024 Accepted: 11-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Infectious diseases are thought to be a primary cause of morbidity and mortality. A wide range of pathogens, including both unicellular and multicellular organisms, brings on these diseases (Antabe and Ziegler, 2020). Bacteria continue to be the most common noxious pathogens, causing a wide range of illnesses in both human and non-human hosts. Warm-blooded animals are typically the target of disease caused by Salmonella, a facultative anaerobic bacillus that is gram-negative and does not form spores (Antabe et al., 2020). Poultry is a common source of Salmonella. Every year, it affects approximately 94 million food-borne cases in public. More than 2500 salmonella serotypes have been identified, and 60% of these are linked to the subspecies Salmonella enterica, which is primarily associated with infections in humans (O'Bryan, et al., 2022). Raw poultry meat has a high prevalence of bacteria, including Campylobacter and Listeria spp., which may be harmful to humans (Kostoglou et al., 2023). Pathogens like Campylobacter, Cryptosporidium, Cyclospora, Listeria, Salmonella, Shiga toxin-producing E. coli, Shigella, Vibrio, and Yersinia have been linked to 24,029 infections, 5,512 hospitalizations, and 98 deaths. Food borne Diseases Active Surveillance Network (Food Net), a program of the Centers for Disease Control and Prevention (CDC), identified (Benduhn et al., 2017). Salmonella bacteria are now primarily responsible for foodborne illnesses, which poses a serious risk to public health. A significant percentage of foodborne illnesses in various geographical areas are attributed to the dangerous salmonellosis brought on by infectious Salmonella. In the US, there were over 35,000 cases of human salmonellosis reported in 2004 and during the same time period, the European Union received reports of over 192,000 cases (Callejón et al., 2015).

The prevalence of Salmonella in poultry production systems can be influenced by multiple factors, including farm management practices, biosecurity measures, and the use of antimicrobial agents in feed (Jibril et al., 2020). Traditionally, antibiotics have been extensively employed to control Salmonella in poultry. However, concerns regarding antimicrobial resistance and the potential impact on human health have led to regulatory restrictions and a global push towards reducing antibiotic usage in animal agriculture. Feed remedies encompass a wide array of products and interventions aimed at controlling Salmonella colonization, proliferation, and transmission in poultry flocks (Manyi-Loh et al., 2018). It will examine the efficacy, mechanisms of action, and practical considerations associated with different feed additives, including probiotics, prebiotics, essential oils, organic acids, enzymes, immunomodulators, and emerging technologies. Each of these approaches offers unique mechanisms of action and potential benefits in terms of reducing Salmonella load and enhancing gut health in poultry (Abd El-Hack et al., 2022). By synthesizing and critically analyzing existing knowledge on feed remedies for Salmonella control in poultry, this review aims to inform poultry producers, veterinarians, and policymakers about the diverse options available for mitigating the risks associated with Salmonella contamination in poultry production systems (Raufu et al., 2019).

This comprehensive review seeks to explore and evaluate the efficacy, mechanisms of action, and practical considerations associated with various feed remedies for the treatment and control of Salmonella in poultry production. Drawing upon the latest scientific literature, we aim to provide a thorough understanding of the current landscape of feed-based interventions, their applications, limitations, and prospects in poultry health management.

Feed-based Remedies

The presence of Salmonella spp. in many type of ingredients such as grains, oilseed meals, fishmeal has been documented many years ago (Maciorowski et al., 2006), especially in food sources rich in protein (Wierup and Haggblom, 2010). Feed can serve as both a direct and/or an indirect route of transmission. This depends partially upon whether individual feed ingredients were originally contaminated prior to or during feed mixing or the mixed feed becomes contaminated during feeding (Tomičić et al., 2018). In compounded feed and even in heat-treated and pelleted feed Salmonella may be found due to environmental contamination of feed mills and the high likelihood for cross contamination in the feed mill and during transport and storage at the farm (Berge and Wierup, 2012; Ross et al., 2011). In the production environment, Salmonella tends to form biofilms on both inert and organic surfaces. Recent studies have shown that Salmonella are capable of forming biofilm on different contact surfaces like glass, polymer, steel (Čabarkapa et al., 2015). In this state, bacteria are better protected against environmental stresses. Once a biofilm is formed, it becomes a source of feed contamination in processing lines, representing a serious concern for the feed industry (Hovda et al., 2007). *Salmonella* antibiotics resistance, possible methods for prevention and control of such problems using promising antibiotics alternatives including probiotics, prebiotics, symbiotics, organic acids, essential oils, cinnamaldehyde, chitosan, nanoparticles, and vaccines (El-Saadony et al., 2022).

Probiotics

Some Live microorganisms are probiotics that treat the health benefit of host. And in which include the many benefits of probiotics and enhanced as well as attention the immune system of host (Dennis et al., 2009). Salmonella is a deadly and antibiotic resistance disease that this disease threat world wide of security risk. In gastrointestinal tracts of chicken, probiotics help the host and fight the against of pathogens. Bacillus species, this probiotic is the most effectively used for salmonella in chicken. Probiotics are used for various types of strains of bacteria, and it is implant in the gut of chicken with cross feeding technique. And reduce the blood cholesterol levels. Recently salmonellosis cases enhance due to the multiple antibiotic resistance (Rashid *et al., 2023*). Salmonella disease in poultry, probiotics are determining an alternative of antibiotics in the prevention and treatment of disease (Kowalska *et al.,* 2020).

Prebiotics

Prebiotics encompass various carbohydrates and related compounds, including galactooligosaccharides (GOS), mannan-oligosaccharides (MOS), and fructooligosaccharides (FOS). Upon ingestion, these substances are metabolized either by the host or by gut-related microbiota, predominantly lactic acid bacteria and bifid bacteria. Thus, prebiotics are commonly administered to modulate the intestinal microbiota by promoting the proliferation of beneficial resident bacteria (Ricke et al., 2020; Ricke et al., 2015; Khan et al., 2020). These compounds are metabolized or utilized by the host and can also function as substrates for specific indigenous bacteria such as lactic acid bacteria and bifidobacteria (Kaplan et al., 2000). Prebiotics represent non-digestible dietary components that stimulate the growth and function of beneficial microflora within the digestive tract. Typically, prebiotics consist of carbohydrates, predominantly oligosaccharides, although they may also include non-carbohydrates. These substances are selectively fermented in the colon by beneficial bacteria such as Bifidobacterium and Lactobacillus. The probiotic bacteria exert a competitive influence in the gut and produce bacteriocins, which possess antimicrobial properties against other bacteria (Patterson and Burkholder, 2003).

Acidifiers

Short-chain fatty acids have been extensively employed as feed supplements to manage Salmonella contamination in poultry (Van Immerseel et al., 2005). Acidifiers are substances that lower the pH of a solution, making it more acidic. Acidic compounds utilized as feed additives consist of short-chain and medium-chain fatty acids. Initially, it was believed that incorporating these acids into feed would sanitize the feed itself and hinder Salmonella absorption by the chickens. Subsequently, it was realized that the addition of acids to feed also impacts the crop and the gastrointestinal tract of the animal. Several investigations have been conducted using various organic acids added to the feed or drinking water, in infection models employing different Salmonella serotypes either directly inoculated into the crop or introduced into the feed (Van Immerseel et al., 2006). Additionally, acidifiers are used in water treatment processes to control pH levels and in industrial applications such as cleaning agents and chemical synthesis. Limited knowledge exists regarding the influence of organic acids on Salmonella, yet it should be noted that both E. coli and Salmonella are enteric bacteria with apparently similar physiology. Medium-chain fatty acids (C6 to C12; caproic acid, caprylic acid, capric acid, and lauric acid) appear to be notably more effective against Salmonella than short-chain fatty acids (formic acid, acetic acid, propionic acid, and butyric acid). However, it's important to distinguish between bactericidal and bacteriostatic effects. Concentrations as low as 25 mm of C6 to C10 acids were bacteriostatic to Salmonella Enteritidis, whereas the same strain tolerated 100 mm of short-chain fatty acids (Van Immerseel et al., 2003, 2004; Sprong et al., 2001).

Enzymes

The utilization of feed enzymes is increasingly being advocated as a strategy to reduce the intestinal presence of Salmonella spp. in poultry. Overall, the idea is that by optimizing the digestion process in poultry through the addition of feed enzymes, the growth and survival of Salmonella bacteria in their intestines can be reduced, thereby lowering the risk of Salmonella contamination in poultry products intended for human consumption (Micciche et al., 2018). Exogenous enzymes like xylanase are commonly added to wheat-based diets for poultry to break down the anti-nutritional arabinoxylans present in wheat, potentially enhancing nutrient digestibility and poultry growth performance (García et al., 2008).

Essential Oils

Essential oils is a non-antibiotic aromatic compound that work as a growth and health promoters, enhanced the lipid metabolism, that trigger the digestion of nutrients, and produce antioxidant and microbial properties , and inflammatory potentials (Parizadian Kavan et al., 2023). Many essential oil components have been identified, such as carvacrol, thymol, eugenol, these are effective antimicrobial agents. These are all hydrophobic essential oil component that activate the leakage of the lipophilic interior of cell membrane of cell contents that causes bacterial cell death (Burt *et al.,* 2004). For the good food industry, the addition of aromatic compound of plant essential oils (PEOs) can be used against pathogenic bacteria of salmonella (Dorman and Deans, 2000).

Advantage of Feed Remedies

The advantages of using the fed remedies in poultry for prevent salmonella growth and effect on poultry production. There are many control strategies but overall them is to enhance the production and prevention from lose in any way like salmonella or other bacteria.

Reduced Stress

Delivering medication through feed can induce less stress in birds when compared to alternative methods like injections, thereby reducing the likelihood of handling stress and potential injury (Ricke et al., 2018).

Convenience

Including feed remedies for treating salmonella in the poultry diet can offer convenience to farmers by eliminating the necessity for individual bird treatment, ultimately saving time and labor (Caly et al., 2015).

Precautions while using Feed Remedies

The variable efficacy of feed treatments in poultry due to factors such as Salmonella strain differences, dosage levels, and the general health condition of the birds highlights the need for tailored treatment approaches. By considering these variables, poultry producers can optimize treatment protocols, improve bird health and productivity, and mitigate the risks associated with Salmonella infections (Landers *et al.,* 2012).

Minimizing Resistance

Employing feed additives thoughtfully can significantly reduce the emergence of antibiotic resistance by targeting Salmonella within the gut environment. Additives such as probiotics, prebiotics, organic acids, enzymes, and essential oils create unfavorable conditions for Salmonella, thus lowering its prevalence without antibiotics. These strategies enhance gut health, promote better nutrient absorption, and support sustainable farming practices, ultimately reducing reliance on antibiotics and minimizing the risk of antibiotic-resistant strains (Ricke et al., 2018).

Residue Concerns

Concerns about residues from specific feed additives in poultry products can cause significant consumer unease and market rejection. Consumers are increasingly wary of potential health risks associated with chemical residues in their food. This can lead to reduced demand and loss of brand reputation for producers. Ensuring that feed additives are thoroughly tested, meet regulatory standards, and are transparently communicated to the public is essential. Additionally, adopting natural and residue-free additives can further enhance consumer confidence and market acceptance see Figure 1 (Caly et al., 2015).

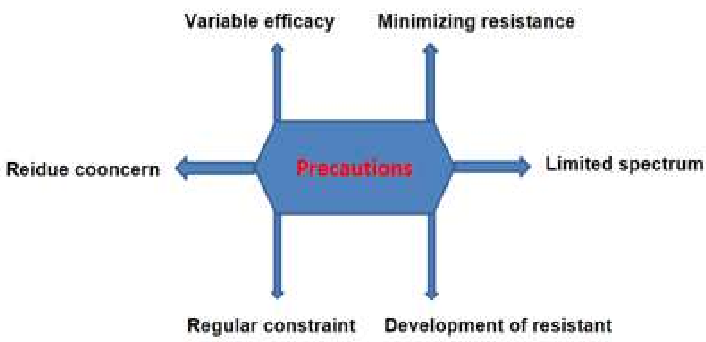

Fig. 1: Precautions for Effective use of feed additives

Limited Spectrum

Certain feed treatments are designed to target specific strains or serotypes of Salmonella, which can leave poultry susceptible to infection by other, untreated strains. This selective efficacy can lead to incomplete protection, necessitating a comprehensive approach that includes broad-spectrum treatments, regular monitoring, and adaptive management practices to address the diverse and evolving nature of Salmonella strains in poultry environments (Nhung et al., 2017).

Regulatory Constraints

Specific feed supplements employed to manage salmonella might encounter regulatory limitations or necessitate withdrawal periods before poultry products can be brought to market, influencing production schedules and profitability outcomes (Nhung et al., 2017).

Development of Resistance

Continued utilization of certain antibiotic feed additives could contribute to the emergence of antibiotic-resistant strains of salmonella, presenting a threat to both animal and human well-being (Ricke et al., 2018). The safety of consumers is jeopardized due to the potential existence of remnants from specific feed supplements in poultry items, resulting in consumer doubt and the potential refusal of products in the market. The utilization of feed antibiotics heightens the probability of resistance emergence, especially in detrimental strains like salmonella, presenting considerable hazards to both animal and human well-being (Mak et al., 2022).

Antibiotic Resistant of Salmonella in Poultry

Salmonella strains sourced from eggs consistently exhibit a notable degree of antimicrobial resistance. Despite the application of various antibiotics throughout poultry production, the highest resistance among Salmonella strains is consistently seen towards nalidixic acid and ampicillin (Castro-Vargas et al., 2020). Meta-analysis involving 91.1% (41 out of 45) of the articles surveyed indicates a global trend in this resistance pattern. Notably, Salmonella isolates from broiler chickens, commonly subjected to antibiotics typical in poultry farming, show alarmingly high resistance rates, particularly towards nalidixic acid (80.3%) and ampicillin (64.8%). Moderate resistance levels are also observed towards other antibiotics like streptomycin (33%), amoxicillin/clavulanic acid (29.4%), and trimethoprim/sulfamethoxazole (39.3%). Interestingly, despite widespread use in day-old chickens, resistance to gentamycin remains relatively low at 6% (Singer et al., 2006).

Bacteriophage

Commonly referred to as viruses of bacteria and archaea, bacteriophages are the most common organisms on Earth (Sulakvelidze et al., 2001) Usually, Salmonella phage Felix O1 is used in the treatment of salmonella (Merril et al., 2003) There are two main uses for Salmonella phage treatment in the poultry industry. First, phage treatment reduces the harm that bacterial pathogens do to animals' health and productivity. Secondly, it is thought that phage-based biocontrol is an effective method of reducing the frequency of foodborne illnesses in people. The main factors that affect how effective phages are as a treatment are choosing the right phages, phage titer, application method, and application duration (Wernicki et al., 2017).

Control Strategies for *Salmonella* in Broilers

Various approaches are necessary to prevent the spread of Salmonella to humans throughout the entire broiler meat production process, including storage and meat handling, from farm to table. This entails implementing control measures not only before harvesting (on broiler breeding and farm sites) (Obe et al., 2023) but also during harvesting (such as catching and transportation) and after harvesting (at slaughterhouses, retail venues, and in kitchens or restaurants). Diverse resources are accessible to assist in managing Salmonella at each stage of this process. Preventive measures and hygienic practices are crucial for controlling Salmonella, alongside physical and chemical decontamination treatments of feed, drinking water, and bird environments (Mkangara et al., 2023).This overview provides insight into feed additives used to manage Salmonella in poultry, outlining the benefits and drawbacks of these products. These additives fall into several categories, including antibiotics, prebiotics, probiotics, enzymes, and short-chain fatty acids (Van Immerseel, et al., 2009; 2002).

Conclusion

In conclusion, feed remedies offer a multifaceted approach to the treatment and control of Salmonella in poultry production systems. Probiotics, prebiotics, organic acids, essential oils, and enzymes collectively contribute to maintaining gut health, enhancing immune function, and inhibiting Salmonella colonization. Integrating these feed remedies into poultry diets holds promise for reducing Salmonella prevalence, enhancing food safety, and safeguarding public health. However, further researches are warranted to optimize their efficacy, dosage, and application methods for practical implementation in poultry production systems. Future of Salmonella control in poultry lies in innovative feed remedies, precision technologies, and holistic management approaches. By leveraging advancements in microbiome modulation, precision nutrition, novel antimicrobials, and integrated management systems, we can work towards minimizing Salmonella outbreaks and ensuring the safety of poultry products. Collaboration between stakeholders and adherence to evolving regulatory standards will be key in driving these strategies forward.

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Chapter 26

Optimizing Reproductive Health in Dairy Cattle: Strategies for Preventing and Managing Reproductive Disorders

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ABSTRACT

Reproductive management is crucial for addressing ailments and maintaining the health, performance, and economics of dairy cows. Dairy cows undergo various life stages, including prepartum, peripartum, and postpartum, each of which significantly impacts their performance. Globally, reproductive disorders such as ovarian cysts, pregnancy loss, anestrus, uterine issues, early embryonic mortality, and complications during the peripartum and postpartum periods can lead to substantial economic losses, compromise animal welfare, and reduce fertility. Preventive measures, such as ensuring proper nutrition, maintaining hygiene, implementing appropriate handling practices, and providing timely veterinary interventions, are fundamental in reducing the occurrence and severity of reproductive diseases. Early detection, accurate diagnosis, and targeted treatments are also essential for effective management. Strategies like nutritional adjustments, hormonal therapies, and surgical interventions can be employed to address specific reproductive issues and optimize herd performance. Proactive management of reproductive health is essential for achieving optimal herd fertility, maximizing productivity, and ensuring the success of dairy farming enterprises. With dedicated efforts and a commitment to excellence in herd management, the dairy industry can overcome the challenges posed by reproductive diseases and thrive in the competitive global market.

KEYWORDS		
Dairy cows, Herd performance, Reproductive management, Reproductive disorders, Preventive measures	Received: 08-May-2024 Revised: 03-Jul-2024 Accepted: 13-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Maximizing reproductive performance is paramount for the prosperity of dairy operations. Inefficient reproduction can lead to significant economic setbacks for both smallholder dairy farms and the dairy industry. These setbacks include extended calving intervals, premature culling of potentially productive cows, diminished milk production over their lifetime, and escalated expenses related to veterinary services (Cardoso Consentini et al., 2021). Several reproductive issues significantly influence the reproductive efficiency of dairy cows, including retained fetal membranes (RFM), repeated breeding (RB), abortion, anestrus, dystocia, uterine discharge, uterine and vaginal prolapse, mastitis, and stillbirth. These challenges have been identified as the most prevalent economic concerns in the dairy industry (Celander, 2017).

These various disorders share a common trait: they can all lead to compromised reproductive function (Fricke et al., 2007). They can be categorized based on their occurrence relative to gestation: those occurring before gestation (such as anestrus and repeated breeding), during gestation (including abortion, vaginal prolapse, and dystocia), and after gestation (like retained fetal membranes, hypocalcemia, and uterine and vaginal prolapse). The dysfunction of the reproductive system ultimately fails cows to consistently produce a calf annually (Lobago et al., 2006; Shiferaw et al., 2005).

Predisposing Factors

Numerous etiological agents, including viruses, bacteria, and fungi, contribute to complications in dairy cattle. Among them, Brucella and Leptospira bacteria are particularly significant in the onset of reproductive disorders in dairy cattle (Mariya et al., 2006). Additionally, inadequate nutrition, unhygienic conditions, and improper handling during various disorders can exacerbate future problems. Dairy cattle are particularly vulnerable during episodes of dystocia, retained fetal membranes, and other postpartum issues (Menamvar et al., 2022), as indicated in Fig. 1.

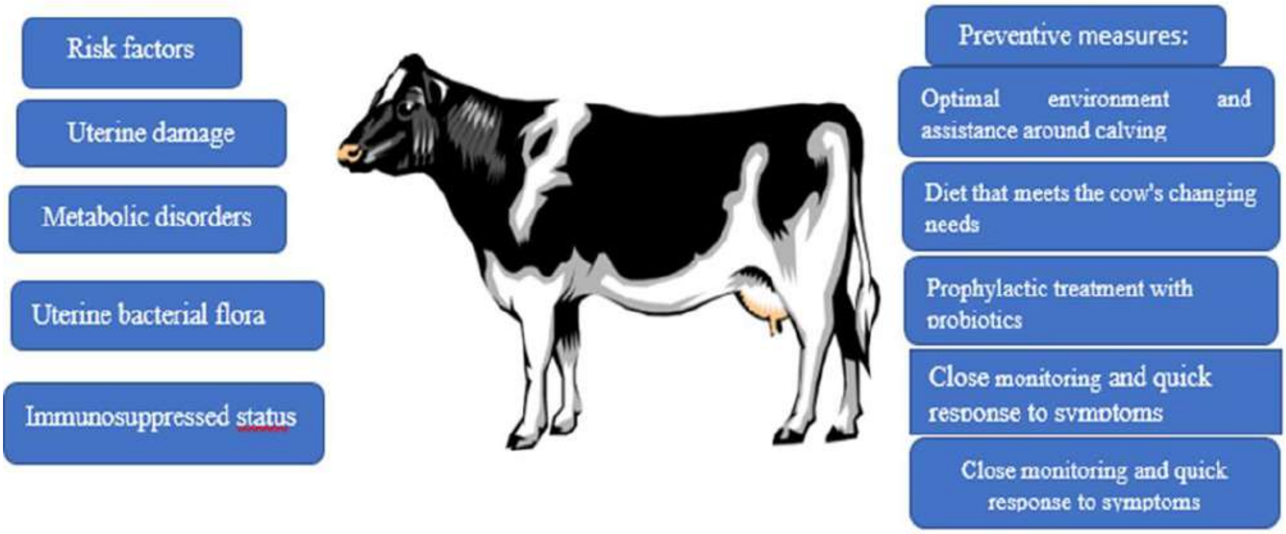

Fig. 1: The most important risk factors for cattle uterine disease and which measures can help prevent them

Reproductive Diseases in Dairy Cattle

Reproductive diseases in dairy cattle encompass a spectrum of prepartum, postpartum, and peripartum challenges that can significantly affect herd health and productivity. Prepartum disorders such as dystocia, hypocalcemia, and ketosis can compromise the health of both the dam and the calf. Postpartum complications like retained placenta, metritis, and endometritis can hinder uterine health and fertility, leading to extended calving intervals and reduced conception rates. Peripartum disorders, including mastitis and milk fever, further compound reproductive challenges during the transition period. Effective management strategies, including proper nutrition, hygiene, and timely veterinary intervention, are essential for minimizing the impact of these reproductive diseases on dairy herd performance (Sheldon et al. 2006 and LeBlanc 2008).

Prepartum Diseases

Prepartum diseases in dairy cattle are health disorders that occur during the late stages of pregnancy, typically within the last three weeks before calving. These diseases pose significant challenges as they can affect the health and productivity of the cows during a critical period. Common prepartum diseases include cystic ovarian diseases, pregnancy losses or abortion, early embryonic mortality, and anestrus. These conditions often arise due to metabolic and nutritional imbalances as the cows transition from gestation to lactation.

Cystic Ovarian Diseases

Cystic ovarian disease (COD) affects 5% to 30% of dairy animals, because of poor management. It is commonly related to heredity, age, high milk production, body condition, lactation stage, seasons, retained placenta, stress, metabolic problems, and hormone imbalances (Channo et al, 2022). Ovarian follicular cysts can be seen as a unique manifestation of anovulation. In this scenario, follicles grow to sizes equal to or exceeding the typical ovulatory threshold (usually 15–18 mm) and may undergo partial luteinization. In essence, follicles become functionally cystic when they fail to ovulate, which can occur even at smaller sizes (Lapp et al., 2020). These follicles may produce physiological levels of oestradiol but fail to trigger a preovulatory luteinizing hormone (LH) surge, despite normal pituitary LH concentrations. The exact pathogenesis of cystic ovaries remains incompletely understood, but there is evidence suggesting that once an LH surge occurs, the hypothalamus may not generate another ovulatory LH surge if it isn't exposed to progesterone in the interim. Support for this hypothesis comes from experiments where preovulatory follicles were aspirated post-LH surge but pre-ovulation. In some instances, a functional corpus luteum formed, leading to normal cycles in cows. In contrast, in cases where a corpus luteum failed to form, subsequent dominant follicles grew into cysts until the placement of a progesterone-releasing intravaginal device, which restored normal ovulatory function. Surgical removal of the corpus hemorrhagic yielded similar results (Bosch et al, 2021).

The treatment of ovarian follicular cysts revolves around reinstating or inducing an ovulatory surge of LH. Since cystic cows possess sufficient stores of pituitary LH and are responsive to GnRH, the exogenous administration of GnRH typically prompts ovulation or luteinization of a functional follicle rather than the cystic one. Progesterone treatment, such as through the administration of a Controlled Internal Drug Release (CIDR) for three or more days, may restore the hypothalamic capacity to induce an ovulatory surge of LH via appropriate GnRH release. Therefore, GnRH, LH analogs (e.g., human chorionic gonadotropin), or progesterone represent suitable treatments for cows afflicted with ovarian follicular cysts. Given that current protocols for synchronizing ovulation incorporate GnRH, they are often effective in treating cystic follicles (Alviggi et al., 2018).

Several alternative medicine treatments and management strategies show promise in addressing cystic ovarian diseases in dairy cattle, like the use of Vitex agnus-castus extract, acupuncture, and herbal medicine. Specific complementary treatments for cystic ovarian diseases in dairy cattle include the use of Vitex agnus-castus extract, commonly known as chaste berry, for its efficacy in regulating hormonal imbalances and reducing cyst size in dairy cows. Chasteberry contains bioactive compounds that act on the hypothalamic-pituitary axis, promoting the secretion of luteinizing hormone and follicle-stimulating hormone, thereby regulating ovarian function (Safdarian et al., 2023).

Acupuncture is a useful technique for its potential to regulate hormonal imbalances and improve reproductive function. Studies have demonstrated the efficacy of acupuncture in reducing cyst size, promoting estrous cyclicity, and enhancing fertility in dairy cows (Feng et al., 2023; Zhang et al., 2023). Herbal medicine is another avenue worth exploring, with formulations containing Cimicifuga racemosa, also known as black cohosh, showing notable anti-cystic properties. Research highlights the benefits of black cohosh in reducing ovarian cysts and improving reproductive outcomes in dairy cattle. Moreover, homeopathy offers a non-invasive approach to managing cystic ovarian diseases, with remedies such as Folliculinum and Ovarinum showing the potential to restore hormonal balance and ovarian function (Wu et al., 2021).

Pregnancy Losses or Abortion

Pregnancy loss or abortion is the abnormal ending of gestation. Abortion is also known as a miscarriage. Infectious diseases and poor management mainly contribute to bovine abortion. Most pathogens are infectious microbes, such as Brucella abortus, Leptospira spp., Bovine herpesvirus 1 (BoHV-1), bovine viral diarrhea virus (BVDV), Mycoplasma bovigenitalium, and protozoa (Anderson, 2007). Additionally, poor management also aggravates the miscarriage. Some cows initially identified as pregnant at 28 or 35 days after insemination may no longer exhibit signs of pregnancy at 60 days or later. These losses are significant as they delay the establishment of a successful pregnancy. Moreover, cows mistakenly assumed to still be pregnant may not receive intensive observation or management for re-insemination (Müller et al., 2015).

The incidence of pregnancy loss between 28 and 60 days after insemination can reach 9% in cows with no other postpartum disease. This rate rises to 14% with a single diagnosis of disease and further increases to up to 16% with the diagnosis of two or more postpartum diseases before insemination. Diseases linked to pregnancy loss in dairy cows encompass obstetric complications, endometritis, postpartum fever, mastitis, and lameness (Santos et al., 2010). Endometritis shows a significant correlation with pregnancy loss; cows previously diagnosed with endometritis, even if resolved, face a heightened risk of pregnancy loss compared to those without a history of endometritis. Moreover, cows with unresolved endometritis at the time of insemination experience a three-fold increase in the risk of pregnancy loss, with rates exceeding 40% (Lima et al., 2013).

Various interventions have shown promise in enhancing embryo survival rates in dairy cows. One such intervention involves treatment with recombinant bovine somatotropin, which may accelerate embryo development. This acceleration potentially contributes to improved embryo survival rates. Nutritional interventions offer another avenue for improving reproductive outcomes in dairy cows. For instance, feeding high-starch diets during the postpartum period increases the proportion of cows that resume cyclicity by the end of the voluntary waiting period. This alone has a positive impact on pregnancy per insemination and reduces the risk of pregnancy loss. Additionally, certain fatty acids have been identified to positively affect embryo quality. Cows fed diets supplemented with fats after 30 days postpartum exhibited a decreased risk of pregnancy loss between 30 and 60 days after insemination (Cremonesi et al., 2020).

The efficacy of herbal preparations like the use of red raspberry leaf, nettle, and dong quai in reducing abortion rates and promoting reproductive health in dairy herds (Jiang et al., 2016). Furthermore, nutritional interventions, such as supplementation with omega-3 fatty acids and antioxidants, have shown promise in supporting reproductive function and reducing abortion risk. Integrating these alternative medicine treatments and management strategies can mitigate abortion risks and optimize herd fertility. Prevention of reproductive disorders in dairy cattle is achievable through several measures. Ensuring adequate nutrition with a balanced diet, shielding animals from adverse climatic conditions, and implementing measures to prevent venereal diseases, particularly brucellosis, are essential strategies for safeguarding reproductive health (Yu et al., 2023).

Anestrus

Anestrus represents a functional disruption of the reproductive cycle, marked by the absence of overt signs of estrus, either due to a lack of estrus expression or the failure to detect it. This condition is observed in post-pubertal heifers, during pregnancy, lactation, and the early postpartum period in adult animals (Kumar et al., 2014). Anestrus is a multifactorial issue associated with various causes, often indicating factors such as inadequate nutrition, environmental stress, uterine pathology, and improper management practices (Yavas and Walton, 2000). Vitamins C, D, E, and B are among the most crucial vitamins for dairy cattle, either present in common feedstuffs or synthesized by the body. Under natural conditions, these vitamins are typically maintained at adequate levels. However, deficiencies in these vitamins can lead to various reproductive complications, including delayed estrus and disruptions in the estrus cycle (Schwab et al., 2007).

Uterine pathology encompasses a range of diseases that impact the reproductive cycle. Pyometra is an acute condition characterized by the presence of pus in the uterus. It can occur due to the persistent presence of the corpus luteum on the ovary, leading to an interruption of the estrus cycle in a cow. Alternatively, it can result from the transmission of infection from an infected bull, carried by bacterial or parasitic pathogens, to a cow during insemination (Földi et al., 2006; Sheldon et al., 2006). Mummification is a relatively rare gestational occurrence in most domestic species, characterized by the intrauterine death of the fetus, typically occurring during the fourth, fifth, or sixth month of gestation (Jana and Ghosh, 2014). Herbal supplements rich in phytoestrogens, such as red clover (Trifolium pratense) or alfalfa (Medicago sativa), have shown promising results in promoting ovarian activity and estrous behavior. Recent studies by Sharma et al (2023) highlight the efficacy of herbal extracts in restoring estrus cycles and improving conception rates in dairy cattle. Homeopathic remedies like Pulsatilla, Sepia, and Folliculinum are sometimes used to support reproductive health in cattle.

Early Embryonic Mortality

The death of the developing conceptus or embryo, whether before or after implantation, can occur due to various factors. Researchers have found that the fertility of dairy cows and heifers ranges from 85% to 90%, with a conception rate at a single service averaging around 70% (Andersen-Ranberg et al., 2005). However, it is noteworthy that approximately 30-40% of cows do not maintain the embryo. According to some authors, in certain cases (ranging from 5% to 40%), embryo mortality occurs during the first days after conception, both before and after implantation, and during early stages of development such as zygote formation, blastocyst stage, and early gastrulation (Bolgov et al., 2020).

An energetic imbalance in the diet during the period of increasing milk yield is considered the most common cause of reproductive function reduction in high-yielding cows (Beever et al., 2006). The concentration of early embryonic mortality (EEM) in cows is influenced by numerous intrinsic factors. Among these factors, the feeding regimen stands out as paramount. Both excessively low and excessively high energy levels in feed exert detrimental effects on embryogenesis (Puklova et al., 2011). Some scholars argue that the heightened embryo mortality observed in cows fed low-energy fodder and experiencing energy and protein deficiencies is linked to disruptions in both endocrine function and uterine activity. Furthermore, this phenomenon is associated with declines in body weight and inadequate physical condition (Guelou et al., 2010; Saidani et al., 2012), as well as disturbances in metabolic processes (Rodriguez-Martinez et al., 2008).

Reducing the incidence of early embryonic mortality (EEM) in dairy cows is achievable through the implementation of comprehensive preventive measures and the optimization of various intrinsic and physiological factors. It is essential to provide cows with a high-energy diet carefully balanced with essential nutrients, thereby eliminating negative energy imbalances, particularly during the early stages of embryo development (Bolgov et al., 2020). Additionally, optimizing the timing of insemination post-calving is crucial, alongside the meticulous management of stressors, health status, metabolism, body mass fluctuations, and body condition. Furthermore, integrating the index of early embryonic mortality into the comprehensive index of breeding value for both dairy cows and bulls is advisable. Emphasis should be placed on the selection of dams of bulls and elite sires, as well as on effectively managing the incidence factors of EEM within herds and populations. This holistic approach ensures a proactive strategy towards reducing early embryonic mortality and enhancing reproductive success in dairy farming (Alfieri et al., 2019).

Peripartum Diseases

The peripartum diseases pose significant challenges to dairy cattle health and productivity, particularly during the transition period around calving. The periparturient period of dairy cows refers to the time frame near parturition. Although there are many interpretations for this time, it generally covers the period from approximately 3 weeks before calving to 3 weeks after calving. It is a pivotal time in the production cycle of the cow, during which cattle are at high risk for the occurrence of abnormal events (Vergara et al., 2014). More specifically, the immediate few weeks following parturition can be particularly problematic, and cattle readily develop diseases related to metabolic disturbances, gastrointestinal upsets, mammary gland infections, and reproductive tract disorders (Ghodasara et al., 2012).

Stillbirths

Calving complications and stillborn calves represent two significant challenges at the dairy farm level. Cows and heifers experiencing difficult calving are prone to subsequent issues such as compromised health, reduced fertility, and decreased milk production during the following lactation. Additionally, both the calf and its dam are at risk of mortality in cases of challenging births. Dystocia, or calving difficulty, stands as a primary contributor to stillbirths. Notably, even normal-sized calves born without complications can succumb to stillbirth or perish shortly after delivery in certain instances. Numerous factors contribute to the occurrence of stillbirth in cattle. These factors include the parity number of the dam, the sex of the calf, the presence of twins, the age at first calving, the length of gestation, the sire of the calf, and the degree of inbreeding (Benjamínsson., 2007). Additionally, stillbirths may result from poor fetal viability, placental dysfunction, or prolonged duration of calving. Understanding and addressing these various factors are crucial steps in mitigating the incidence of stillbirths in cattle. The probability of stillbirth was observed to be approximately three times higher in primiparous cows compared to multiparous ones, a figure slightly elevated compared to previous reports in dairy cattle, which ranged from 1.5 to 2.6 times. This challenge can be addressed by examining various factors. However, implementing appropriate nutritional strategies, considering climatic fluctuations, managing disease presence, ensuring proper breeding practices, and providing diligent care to cattle during the early stages of breeding can significantly mitigate this issue (Berry et al., 2007).

Dystocia

Dystocia, a common reproductive issue in cattle, occurs when the first or second stage of labor is prolonged, necessitating assistance for delivery. The term "dystocia" originates from the Greek words "dys" meaning difficult and "tokos" meaning birth. Also known as calving difficulty, dystocia is characterized by prolonged and challenging parturition, often requiring assistance. The incidence of dystocia in cattle has been extensively studied due to its significant effects on productivity (Youngquist and Threlfall, 2006; Weldeyohanes and Fesseha, 2020), with variations observed across species and breeds. Dystocia exerts direct negative impacts on both calves and dams. Calves may experience prolonged hypoxia, significant acidosis, reduced vigor, and increased rates of stillbirths, among other complications. Similarly, dams are susceptible to trauma, paresis, metritis, endometritis, and other postpartum complications as a result of dystocia. Understanding and effectively managing dystocia are crucial for optimizing both calf and dam health and welfare during the calving process (Abera, 2017).

Dystocia primarily arises from fetal abnormalities in presentation (the part of the fetus entering the vaginal canal first), position (the orientation of the fetal spine concerning the dam's pelvis), or posture (the positioning of fetal extremities relative to its body). However, it can also stem from factors such as fetal oversize or maternal issues like pelvic abnormalities or uterine inertia. The reported incidence of dystocia ranges from 4% to 10% of all births. It is imperative to approach dystocia systematically to ensure the prompt delivery of a live calf with minimal complications (Moges, 2016).

The typical clinical indicators of dystocia include the onset of labor without the delivery of the fetus and/or fetal membranes, followed by a regression of parturition signs. Affected animals may display mild discomfort, adopting a rocking horse stance and exhibiting mild colic pain (Fossum et al., 2007; Haben Fesseha, 2020). Partial anorexia, dullness, and depression may also be apparent. In cases of dystocia, one or both lips of the vulva may be retracted due to the torsion of the birth canal. Additionally, when the cervix is fully dilated, it cannot be palpated as a separate structure and is seamlessly continuous with the vagina. Conversely, an incompletely dilated cervix will retain some distinguishable structure and may appear cone-shaped upon manual examination (Weldeyohanes and Fesseha, 2020).

Postpartum diseases

Cattle exhibit a higher susceptibility to uterine disease compared to other mammals, such as other ruminants, primarily due to the dynamic alternation between bacterial contamination and clearance within the uterus (Sheldon et al., 2004). In the initial two weeks following calving, the majority of cows undergo bacterial contamination of their uterus. Issues arise when this bacterial load persists. The compromised physical barriers of the female genital tract during and after parturition create the potential for ascending infections, leading to uterine disease. Bacteria can infiltrate the uterine lumen from environmental sources, as well as from the skin and feces of the animal, particularly if hygienic conditions are subpar in the calving stable. When combined with endometrial tissue damage and the immunosuppressed state of the recently calved cow (which can worsen with increased stress levels due to inadequate handling), this scenario can easily result in inflammation of various genital tract organs, especially the uterus, leading to delayed involution (Sheldon et al., 2004).

Retained Fetal Membrane

Retained fetal membranes (RFM) occur when a cow doesn't expel her placenta within 12 hours after giving birth. It is one of the most common issues dairy cows face after giving birth. The fetal membrane, which plays a crucial role in transferring nutrients and oxygen from the mother to the fetus during pregnancy (Hanafi., 2011), usually detaches and is expelled within 8 hours postpartum. If this process takes up to 12 hours, it is considered delayed removal. However, if the placenta is retained for more than 24 hours, it is termed "Retention of Placenta" (ROP). This condition can cause significant problems, as it provides a breeding ground for microorganisms in the uterus, leading to inflammation, fever, weight loss, decreased milk production, and prolonged calving intervals (Patel and Parmar, 2016). This detachment typically begins during the final month of pregnancy as the blood flow to the placenta decreases (Jaster, 2009).

Retention of the placenta for more than 12 hours after giving birth is linked to increased postpartum diseases, decreased milk production, poor reproductive performance, and higher culling rates in dairy cattle (Sheldon et al., 2008). The incidence of retained placenta ranges from 4.0% to 16.1% but can be significantly higher in problematic herds. Factors contributing to this issue include specific infections such as Brucella, Leptospira, Campylobacter, listeriosis, and infectious bovine rhinotracheitis (IBR), as well as nonspecific infections caused by various bacteria and viruses that can occur during pregnancy or at calving. Additionally, twin births, nutritional deficiencies, and lack of essential nutrients like selenium, vitamin E, and vitamin A are associated with a higher risk of retained placenta (Abdisa, 2018; Ahmad et al., 2022).

The most effective approach to prevent retained fetal membranes (RFM) involves ensuring cows have continuous access to feed during the prepartum period, avoiding social stress like regrouping, and ensuring adequate dietary selenium and vitamin E. Nutritional strategies aimed at preventing milk fever may also help reduce RFM incidence. Routine administration of either PGF2a or oxytocin at calving is not effective in preventing RFM (Melendez et al., 2006). Feeding monensin has been shown to decrease RFM incidence in multiparous cows, although results from another trial were inconclusive. Supplementation with beta-carotene may also reduce RFM incidence in multiparous cows (Oliveira et al., 2015). Homeopathic remedies such as Arnica montana and Sabina are sometimes used in cases of retained placenta in cattle (Weisbart and R.H., 2012). Herbs like Chamomile (*Matricaria chamomilla*) and Echinacea (Echinacea purpurea) have anti-inflammatory and immune-boosting properties, which may support the natural expulsion of retained fetal membranes (Papatsiros et al., 2013).

Puerperal Metritis

Acute puerperal metritis typically manifests within the first 10 days following parturition and is characterized by specific clinical features, including an enlarged, flaccid uterus, a malodorous discharge that is often watery and reddish-brown in color, and frequently accompanied by fever (Sheldon et al., 2006). Additionally, affected cows may exhibit other signs of systemic illness, such as depression or a decrease in milk production. The onset of fever in acute puerperal metritis may follow the development of other clinical signs by 1 or 2 days, although it may sometimes go undetected (Benzaquen et al., 2007). Risk factors for metritis include retained fetal membranes (RFM), obstetric complications, and twin births. Additionally, it is more prevalent in cows that are either over conditioned or underconditioned. There is evidence suggesting that feeding urea to dry cows may contribute to the development of postpartum uterine infection (Lima et al., 2014).

Metritis is more commonly observed in dairy cows compared to beef animals, with a higher frequency noted in primiparous cows. The lactation incidence rate of metritis typically ranges from 15% to 20%, although it may be considerably higher in certain herds. Affected cows often experience a reduction in milk yield. Metritis also contributes to delayed conception and an increased risk of culling (Wittrock et al., 2011; Giuliodori et al., 2013). The costs associated with acute metritis include treatment expenses, increased culling rates, and impaired fertility. Cows affected by metritis are also at an elevated risk of developing other postpartum complications, such as displaced abomasum, as well as endometritis (Dubuc et al., 2011).

Cows experiencing reduced food intake during the late dry period are at an elevated risk of developing puerperal metritis (Huzzey et al., 2007). These cows often exhibit elevated concentrations of β-hydroxybutyrate or non-esterified fatty acids in peripheral blood. Additionally, they demonstrate impaired immune function, partly attributed to the low intracellular glycogen content of neutrophils. Circulating cortisol and estradiol concentrations are also typically increased immediately postpartum in affected cows. Milk yield is notably decreased, especially in first-lactation animals affected by puerperal metritis. Common bacteria associated with puerperal metritis include Escherichia coli, as well as the gram-negative anaerobes Prevotella melaninogenica and Fusobacterium necrophorum (Santos et al., 2011; Machado et al., 2012; Santos and Bicalho, 2012). Specific strains of E. coli expressing particular virulence factors are implicated, with E. coli being the initial invaders, thereby increasing the risk for subsequent uterine invasion by other pathogens (Santos et al., 2008; Sheldon et al., 2010).

Effective preventive measures for metritis would be highly beneficial to dairy producers. While reduced dry matter intake during the dry period significantly contributes to the pathogenesis, methods to avoid this decrease in voluntary intake remain unclear, as some cows experience reduced intake even in the absence of social stressors. Although feeding cows individually can eliminate competition for bunk space and potentially improve intake, overcrowding affects feeding behavior, but there is currently no evidence indicating that the stocking rate affects metritis incidence (Proudfoot et al., 2009; Silva et al., 2014). Herbs such as Echinacea (Echinacea purpurea) and Goldenseal (Hydrastis Canadensis) are known for their immune-stimulating and anti-inflammatory properties, which may aid in combating bacterial infections associated with puerperal metritis (Wulff et al., 2011). Homeopathic remedies like Pyrogenium and Belladonna may be considered for their potential to stimulate the body's natural healing mechanisms (Grubb et al., 2020), as summarized in Table 01.

Table 1: Summary of predisposing factors and treatment approaches for cattle reproductive disorders

Disease	Cause	Treatment	Reference
Retained Fetal Membranes (RFM)	Specific infections (Brucella, Leptospira, etc.), twin births, nutritional deficiencies (selenium, vitamin E, A)	Adequate diet, avoid social stress, ensure selenium and vitamin E, nutritional strategies to prevent milk fever, feeding monensin, homeopathic remedies (Arnica montana, Sabina), herbs (Chamomile, Echinacea)	Abdisa and T 2018
Puerperal Metritis	Retained fetal membranes, obstetric complications, twin births, over conditioned or under conditioned cows, feeding urea to dry cows	Antibiotics (e.g., ceftiofur), supportive care, herbs (Echinacea, Goldenseal), homeopathic remedies (Pyrogenium, Belladonna)	Wittrock et al., 2011
Pyometra	Pathogenic bacteria in the uterine lumen, early ovulation during uterine infection	PGF2α or its analogs, herbs (Echinacea, Hypericum perforatum), homeopathic remedies (Pyrogenium, Belladonna)	Santos and Bicalho, 2012
Cervicitis and Purulent Vaginal Discharge	Cervical trauma during parturition, primary vaginitis	Cytology for diagnosis, treatment of underlying infection or trauma	Deguillaume et al., 2012
Prolapse	Increased intra-abdominal pressure, relaxation of pelvic girdle, excessive force during delivery, uterine inertia	Gentle repositioning, calcium gluconate, oxytocin, surgical interventions, herbs (Shepherd's purse, Yarrow), homeopathic remedies (Nux vomica, Aesculus hippocastanum)	Kumar and Yasotha, 2015

Pyometra

Pyometra is typified by the accumulation of purulent or mucopurulent material within the uterine lumen, resulting in distension of the uterus, and is typically observed in the presence of a closed cervix and an active corpus luteum (Sheldon et al., 2008). Postpartum pyometra is relatively rare, with an incidence rate of less than 2%, and is believed to arise from the proliferation of pathogenic bacteria in the uterine lumen following the formation of the first corpus luteum on the ovary. While there is functional closure of the cervix, complete occlusion of the lumen does not always occur, and pus may occasionally discharge from the cervix into the vaginal lumen. Ultrasonography findings in pyometra typically reveal mixed echo density fluid in the uterine lumen with uterine distension, along with the presence of a corpus luteum in one ovary (Sheldon et al., 2006).

A delayed luteal phase may be attributed to elevated concentrations of luteotropic prostaglandin PGE2 associated with bacterial infection of the endometrium. Pyometra can occur if ovulation takes place too early in the postpartum period, leading to the formation of a corpus luteum during uterine infection. The preferred treatment for pyometra is PGF2α or its analogs. This treatment induces luteolysis, behavioral estrus, expulsion of accumulated exudate, and bacterial clearance of the uterus in approximately 90% of treated cases. Recurrence of pyometra after a single treatment occurs in 9% to 13% of cases (Sheldon et al., 2008). Herbal medicine offers a natural approach to combating uterine infections, with herbs like Echinacea purpurea and Hypericum perforatum known for their antimicrobial and immune-stimulating properties, demonstrating the efficacy of herbal formulations in reducing uterine inflammation and promoting bacterial clearance in dairy cows with pyometra (Chen et al., 2023). Furthermore, homeopathy remedies such as Pyrogenium and Belladonna show potential in resolving uterine infections and reducing associated symptoms (Wang et al., 2024).

Cervicitis and Purulent Vaginal Discharge

Though visible purulent discharge from the vagina may be associated with more severe cases of endometritis, it has been observed that cows may exhibit such discharge without having endometritis. Primary cervicitis is identified as the primary cause of vaginal discharge when endometrial inflammation is absent. An increased cervical diameter three weeks postpartum, along with purulent vaginal discharge, predicted a reduced likelihood of pregnancy. The enlargement of the cervix was previously recognized as an indicator of poor fertility (LeBlanc et al., 2002).

It appears likely that these cows have experienced cervical trauma during parturition, which is separate from endometritis, though the two conditions can coincide. Dubuc et al. (2010) discovered that endometritis and purulent vaginal discharge have independent and cumulative negative effects on reproduction, with distinct risk factors. Recent evidence from Deguillaume et al. (2012) provides direct support for the existence of cervicitis, diagnosed through cytology, independently of endometritis. In their study, the prevalence of endometritis alone was 13%, cervicitis alone was 11%, and both conditions coexisted in 32% of cows. Both cervicitis and endometritis contributed to a reduced likelihood of pregnancy, with cows experiencing both conditions faring worse than those with either one alone (Deguillaume et al., 2012). While identifying cervicitis as a common postpartum ailment, it doesn't fully elucidate the origin of purulent vaginal discharge. Approximately half of cows with cervicitis also exhibit purulent vaginal discharge, and vice versa. In some instances, purulent vaginal discharge might indicate more severe endometritis. Nevertheless, in certain cases, the source of exudate remains unresolved and may signify primary vaginitis in some animals (LeBlanc, 2014).

Prolapse

Uterine prolapse, a non-hereditary complication, refers to the expulsion of the uterus through the vulva following parturition, sometimes occurring immediately but occasionally several hours later (Kumar et al., 2014). It protrudes with or without the vagina and cervix through the vulva, typically shortly after calving, hanging externally with the inner surface exposed. Factors contributing to prolapse include increased intra-abdominal pressure due to the enlarged pregnant uterus, intra-abdominal fat, or rumen distension, as well as relaxation and softening of the pelvic girdle, excessive force during delivery, or uterine inertia resulting from metabolic issues like milk fever. Uterine prolapse is a prevalent obstetrical issue, affecting cattle's productive and reproductive performance by diminishing postpartum estrus return, conception rates, and calving intervals in dairy cows (Kumar and Yasotha, 2015).

Prolapse, whether partial or complete, involves the organ turning inside out, with its inner portion protruding through the vulva's lips and hanging down, sometimes reaching as far as the hocks (Ward and Powell, 2018). It is deemed a medical emergency, particularly in cows, as it can be life-threatening. Without prompt treatment, the affected cow may go into shock or succumb to blood loss. Proper repair of the uterine prolapse can enable the cow to maintain normal reproductive function. However, a secondary infection in the repaired uterus may delay rebreeding or render the cow unable to breed altogether (Ward and Powell, 2018). Herbs like Shepherd's purse (Capsella bursa-pastoris) and Yarrow (Achillea millefolium) may have astringent properties that could potentially help in reducing swelling and promoting tissue healing in cases of prolapse (Papatsiros et al., 2014). Homeopathic remedies such as Nux vomica and Aesculus hippocastanum may be used to support the overall health and healing process in cases of prolapse in cattle. Nutritional deficiencies and management issues can sometimes contribute to prolapse, which can be addressed by washing the everted part with KMNO4 and gently pushing it back inside. Therapeutic agents like calcium gluconate and oxytocin may be utilized, along with surgical interventions if necessary (Kayne and S.B., 2009).

Conclusion

Reproductive diseases in dairy cattle, including retained fetal membranes, puerperal metritis, pyometra, cervicitis, purulent vaginal discharge, and uterine prolapse, significantly impact herd health and farm productivity. These conditions arise from a complex interplay of factors such as infections, nutritional deficiencies, and management practices. While various treatments exist, their efficacy varies, and the reliance on antibiotics raises concerns about resistance. Effective management practices and preventive measures are crucial but challenging to implement consistently. Future research should focus on developing better diagnostic techniques, validating alternative therapies like herbal and homeopathic remedies, and enhancing nutritional strategies to prevent these diseases. Emphasizing preventive care, early detection, and sustainable farming practices can improve reproductive performance, reduce economic losses, and promote dairy cow welfare.

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Chapter 27

Role of Nutrition in Prevention of Liver Ailments in Animals

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ABSTRACT

The liver is the most important metabolism and detoxification organ in animals. The animal's food and nutritional composition can be affected in many ways and cause serious diseases. It should be as balanced as possible so as not to burden or harm the mind. This chapter describes some of the common liver diseases and emphasizes the importance of diet in preventing liver disease. We will discuss the role of different nutrients in treatment of hepatic ailments. Good liver health is the basic requirement for a healthy and a productive animal. Malnutrition or malnutrition can cause problems that can lead to serious diseases such as fatty liver disease, tetany, milk fever, ketosis, polio, absent muscle disease, and many more. Milk production is important for farmers. When the liver is affected or liver disease occurs, milk production increases and other negative effects on the animal's health occur. So, prevention of liver diseases by good nutrition management leads to better animal output and better production of the dairy herd.

KEYWORDS		
Liver, Fatty Liver Syndrome, Nutrition, Prevention, Mycotoxicosis, Clostridia spp.	Received: 19-May-2024 Revised: 12-July-2024 Accepted: 21-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Health nutrition and management cleaning, maintenance, development, production goes parallel to each other. Animals get nutrients from food such as proteins, carbohydrates, lipids, mineral, vitamins, and water. Foods containing all of the necessary nutrients are needed for maintenance, health, milk production and reproduction (Heinrichs, 1993). Malnutrition or malnutrition can cause problems that can lead to serious diseases such as fatty liver disease, tetany, milk fever, ketosis, polio, absent muscle disease, and many more (Burns, 2019). Liver health tends to play a necessary role in the nutrition of cows. A healthy heart means a healthy herd. Liver dysfunction can cause many metabolic diseases in cattle. The liver performs many functions such as glucose synthesis, ammonia detoxification, digestion, metabolism, and storage of vitamins and minerals. The rumen microbiota synthesizes volatile fatty acids, which enter the liver and are converted to glucose. This sugar is then used to meet the body's energy needs and produce milk. Energy needs to be increased during the lactation period, the animal's dry matter decreases in the new period, thus the liver plays a vital role in this period. It metabolizes stored fat to synthesize glucose used by the body. If liver health is affected during this period, subclinical or clinical ketosis, fatty liver syndrome, hepatic lipidosis, etc. may occur in animals (Bezerra et al., 2014). Milk production is important for farmers. When the liver is affected or liver disease occurs, milk production increases and other negative effects on the animal's health occur. As mentioned above, the liver helps with metabolism, food processing, milk production, and other functions in the body. If there is a problem with the liver, these activities can be seriously affected, including loss of appetite, weight loss, and infection. Proper nutrition, clean water and stress management can reduce liver disease (Li et al., 2015).

Common Liver Diseases in Cattle

Liver diseases such as liver disease, fatty liver, liver disease, mold poisoning, poisoning (copper, iron, zinc), cobalt deficiency and other disease problems.

a. Fatty Liver Syndrome

Fatty Liver Syndrome occurs in the period of non'esterified fatty acids (NEFA) in cow's milk. This is due to negative energy balance (Adewuyi et al., 2005). In the new period when the energy need is high and the animal's dry matter is low, the liver metabolizes the stored fats to meet the body's needs. Therefore, triglycerides are produced and these then start to be stored in the liver and cause the liver to turn into fat, therefore this condition is called fatty liver syndrome and can cause the liver to not work anymore. The role of nutrition in the treatment and prevention of fatty liver syndrome is very important (Bobe et al., 2004). Diet programs and other management methods using these methods have been tested. Increasing the spraying rate by increasing the NCF level or adding oil will not prevent the disease (Montgomery et al., 2005). Two nutrients, choline (which protects the rumen) and propylene glycol have been shown to be effective in preventing liver disease (Ahmadzadeh-Gavahan et al., 2021). The choline may increase hepatic VLDL secretion while propylene glycol can reduce fat loss from adipose tissue (Bjerre-Harpøth et al., 2015). Short dry period is also a control method that reduces poor energy balance after calving and triglyceride accumulation in the liver.

b. Liver Abscess

Also called liver abscess, it is defined as an acid containing lump in the cow's liver. These abscesses are caused by certain diseases or injuries. Liver disease can occur in cattle of all ages and breeds. However, most of the cattle are in feedlots due to the high wheat content of their feed (grain-based diet) (Mir et al., 2008). Inefficiencies and reduced carcass yield greatly reduce the operational efficiency of commercial slaughterhouses. These abscesses are light yellow in color, generally spherical in shape, and their tip size reaches 15 centimeters. Most of these diseases are caused by *Fusobacterium necrophorum* (anaerobic, Gram-negative, non-motile, non-sporulating, rod-shaped (pleomorphic) bacteria and *Mythobacterium pyogenes*) (Tamai et al., 2023). Treatment of liver abscess is medication, (Mir et al., 2008). Inform beef cattle managers that sunflower seed supplementation lowers the rate and intensity of liver abscess. The incidence of liver abscess has decreased. However, the full fat corn germ that is used in the study was soaked and therefore often produced anti-Maillard end products, including brown melanoid pigment. Remember, melanoidins are associated with usual proteolytic process and are also known for their anti-microbial activity, so the reduction in liver abscesses is associated with *Fusobacterium spp*. It appears to be due to the indirect effect of the intervention on by inhibiting its proteolytic activity. In animals fed low, moderate and high protein and energy diets, the incidence of liver abscess was shown to be related only to energy intake, but not to the high protein diet. Therefore, more investigation is needed to better know the effect of a high protein diet and some other nutrients on the rate and intensity of bovine liver abscesses.

c. Mycotoxicosis

Food or concentrates (grains) of toxic metabolites produced by certain fungi. Fungi need warmth, humidity and moisture to release toxins (Awuchi et al., 2021). Mycotoxins can accumulate in grain, damaged grain and improper storage. Mycotoxins can produce toxins in many ways, including harming metabolism, nutrition, or endocrine function. Many mycotoxins can cause liver damage, reduce average daily intake, growth and feed quality. Some of the mycotoxins are anti-inflammatory, while others are carcinogenic (Gallo et al., 2015). Digesting nutrients and then absorbing the end products of digestion allows cells and tissues to use them to function properly. Effective use of these macronutrients is important for animal feed production. Mycotoxins reduce the activity of macronutrients. Most of the consequences will be chronic or subacute due to long-term consumption of minor toxic substances (Xu et al., 2022). In this case, there may be various signs of toxicity, apart from loss of appetite, poor growth, and strong susceptibility to other diseases. Severe infections may have more pronounced and different symptoms with each different mycotoxin. Overall, data shows that mycotoxins negatively affect food intake, digestion and absorption, making it difficult for animals to use nutrients for production (Gallo et al., 2015). The diagnosis of chronic mycotoxicosis is often difficult because the symptoms are less pronounced and unclear. When mold poisoning is detected, the victim's bait is often collected and eaten without being stored for analysis.

This also requires proper cleaning and maintenance of feeding equipment. Grain cleaning and grading, milling, thermal methods, mixing of bacteria and non-bacteria, irradiation, use of medications can all reduce mycotoxins in feed (Kolosova and Stroka, 2011). Some mycotoxin detoxification agents are also used as food additives; these are mycotoxin biotransformers (BA) and adsorbents (AA). Biotransformation agents (BAs) are bacteria or fungi that have enzymes that convert mycotoxins into smaller metabolites (Saldarriaga-Hernández et al., 2020). Adsorbents (AA) can reduce the bioavailability of mycotoxins, thereby reducing the absorption and distribution of mycotoxins into the blood and target organs such as the liver and kidneys (Li et al., 2018). Give energy to farm animals. Animals need good breeding in order to reach the production level for which they have been genetically selected. Some mycotoxins and their combinations can cause food spoilage, reduce livestock energy and food utilization, and reduce or increase performance. However, it should be noted that nutritional value should not be the sole measure in assessing all mold toxicity in food-producing animals because there is good evidence that mycotoxins can cause other severe effects in many organs and systems such as the intestine and liver or kidneys, for example, the brain of animals, growth and immunity sometimes do not affect growth (Zain, 2011). These can damage the liver in many ways.

d. Hepatic Encephalopathy

Hepatic encephalopathy occurs in bovine, equine and swine. It can lead to acute and also chronic liver disease that leads to liver failure (Riet-Correa et al., 2013; Chileski et al., 2021). The severe the disease will progress, the faster the liver failure will be. The clinical signs often seen in hepatic encephalopathy are depression, lethargy, circling, head pressing, ataxia, pics, seizures and coma (Salgado and Cortes, 2013). Respiratory collapse also occurs in equines. Secondary photosensitization occurs with acute or chronic liver failure, which can result in skin inflammation and damage (Minervino et al., 2010). As we are discussing role of nutrition in hepatic diseases prevention, so we will discuss the dietary management of hepatic encephalopathy. Dysphagia is a common problem in these animals, so they should be fed with care and be given small amounts of food frequently. The energy requirements of the animals are met with carbohydrate sources, animals should be fed with relatively normal protein in feed, not too high protein. The feed should contain enough starch so that animal can combat the glucose deficiency. Feed additives such as molasses should be added to enhance the palatability of feed. Soya bean and linseed are used as protein sources. Beet pulp is a commonly used ingredient in dairy feeds and should be dried to prevent esophageal obstruction. The legume products such as alfalfa should not be used, as it has too high protein content. The vitamins A, D, E and K should be supplemented as they are fat soluble vitamins and are not readily stored. So, they should be provided to animals through diet. Vitamin K is indicated in the animals with hepatic coagulopathy (Wojciechowski et al., 2017). Also, avoid feeding animal with excessive fat to prevent animals from fatty liver. A process of transferring the ruminal fluid (containing rumen microflora) of healthy animal is placed into diseased animal is termed as transfaunation. It also improves the appetite of animal.

e. Acute Hepatic Necrosis in Cattle

Acute hepatic necrosis occurs due to toxins insult in liver. Hepatic necrosis can occur after mastitic or metritic animals or animals in endotoxemia. The kupffer cells start producing lysozymes, collagenases etc. that result in hepatocytes damage and ultimately liver failure. Anorexia, weight loss, very low milk production, icterus and photosensitization occur in this disease. Liver enzymes such as AST, GGT are increased but fatty liver does not occur in this condition. Its diagnosis includes history of endotoxemia and increased liver enzymes. Its differential diagnosis includes other liver disease (such as hepatotoxins, hepatic lipidosis) and conditions that cause weight loss and low weight loss (Furlan et al., 2014; Perosa 2023). Its nutritional management is much successful and often gives better results with fluid therapy as endotoxemia is also present. To treat acute hepatic necrosis, protein sources with almost 15% protein content (alfalfa meal) should be forcefully fed to animals. Beet pulp and potassium chloride are also fed in this condition (Njidda et al., 2022). Transfaunation can also be helpful in this disease (Sweeney et al., 1988).

f. Copper Poisoning

In ruminant animals, copper metabolism that occurs in animals' rumen, which is probably the best striking example of healthy nutrition (Gupta, 2018); It is the reaction between copper, molybdenum and sulfur (Cu-Mo-S) that may affect animal health. Ruminant bile has a very low copper-releasing capacity; only a small portion of copper binds to metallothioneins in the liver (Elmes et al., 1989). Since the copper intake is higher than necessary, it does not seem to increase the excretion of copper through bile, which causes more copper to accumulate in the liver. When the storage capacity is exceeded, abrupt and often deadly accidents occur. Copper toxicosis occurs mostly in dry cows and is associated with liver catabolism caused by changes in the social groups and body weight loss, sudden discontinuation of concentrates, and are considered the main stressors. It is low in texture but food composition and dry matter differ, making it difficult to measure mineral intake. The standard for copper should include the most commonly used food, where these different factors (maintenance, production, reproduction and growth) are duly collected. The absorption coefficient of copper, in the ruminant, changes much which depends on the concentration of molybdenum and sulfur, the major copper antagonists, and this should be taken into account when we calculate the copper requirement. If the food contains approximately 0.4% sulfur (such as sulfur in water), the copper concentration in the food should be increased by 1.3 to 1.5 times. The concentration of the major copper antagonists (sulfur, molybdenum and iron), the type of food (forage, silage, haylage, concentrated TMR) and many other factors must be taken into account (Arthington, 2003).

g. Iron Poisoning

Iron poisoning is seen in cattle. Tremors, colic and seizures are observed in iron toxic calves. Often the liver is brittle and swollen or has atrophyed. The heart is light tan or mottled reddish brown. Iron-containing foods must be measured accurately to prevent poisoning. Chronic malnutrition causes liver disease, biliary hyperplasia, and periportal fibrosis (Payne et al., 2015).

Cattle Infectious Diseases Affecting the Liver and their Nutritional Management

Here are some infectious diseases and feed management that can damage the liver in various ways. How much food can prevent animals from contracting these diseases? It is called phytotoxic hepatitis. In the worst-case scenario, cows older than six months can die quickly. Visible symptoms in cows that do not die immediately are photosensitivity, which occurs when the plant's explosives cause sunlight on the skin. Animals are stressed, itchy, and have heat in their mouths and pale skin, with white faces and white patches. It affects animals, is then treated quickly, and death often occurs before symptoms appear. Fewer animals produce beautiful images and some cause heart failure. However, the important point here is that Setaria scabs are found all over the world and are not thought to cause pain in cattle. Fungal infections are now considered the cause of ABLD because the symptoms of this infection are similar to those of fungal infections. In addition to the acute or chronic toxicity, the mycotoxins can change nutrition, yield (animal milk production or their growth rate), utilization of nutrients, reproduction ability, and other quality products (such as residues in milk and meat). Diseases from aging rough foxtail grass can be shifted to nearby beautiful areas by natural or mechanical processes. Acute necrosis, bleeding in the necrotic area. ABLD is frequently associated with the presence of *C. echinatu*s and *Drechslera spp.* of fungi are present in grasslands and pasture systems, but still it is not clear why. The *Delbrueckii spp.* can produce toxic spores that can spread to rough setaria and new plants in pastures and can then be eaten by cattle. *Delbrudium spp.* favorable conditions for spore formation is caused by changes in humidity and temperature. This provides a general overview of the currently published information about ABLD. This can also lead to extensive research and unknown data on fungi and mycotoxins that may cause ABLD. The risk factors for ABLD include min. temperature >12°C, precipitation >4 months, high humidity, and calmer conditions than the previous day. Other cases of ABLD may also occur that are unrecognized or unreported. This has led to speculation about the cause and pathogenesis of the disease. Autumn weather can encourage the formation of mycotoxins, or lethal bacteria, to which animals get exposed while growing grass. The specific venom and its location remain speculative, and its stability to survive or reside in the environment is still unknown. Thus, even if there are too many toxins in the feed ingredients, analysis of tissues taken from dead animals will give an idea on this issue. Think simply, every suspicious thing can indicate the nature of poison. Additionally, the presence of Setaria roughness and *Despermia spp*. Therefore, *Drechslera spp.* Rough foxtail may be a source of toxins associated with weed. hours to months) "poisonous". It is still unclear that "toxic" paddocks will remain "toxic" for years to come or they will be free of toxins (Quan et al., 2020).

The management options for paddocks are as follows:

(1) Sheep eating out in paddocks reduce the amount of dry standing material

(2) Processing of the high risk pastures

(3) Do not place animals in pastures with dry material collected for long periods of time

(4) Give the animals another try, but just in the first test to check the "toxicity" of some animals test it. If any abnormalities are detected, cattle should be removed from the paddock immediately.

Clostridial Diseases

Clostridium species causes liver damage in domesticated, wild and in lab animals also. *C. novyi* (type B) can cause infectious necrotic hepatitis (INH) in sheep and occasionally in other animal species. *Clostridium novyi* (type B) spores are commonly found in soil; After damaging the liver of animals, usually caused by parasites migration, locally occurring anaerobic environment allows *Clostridium* spores to germinate and then produce toxins. *Clostridium novyi* (type B, toxin alpha) can cause severe necrosis of liver and widespread edema, congestion in organs, and bleeding in various organs. *C. haemolyticum* causes hemoglobinuria in sheep, bovine and sometimes in equine. The main virulence factor of *Clostridium haemolyticum* is Beta toxin and can cause necrosis in liver and RBCs breakdown. *C. trichomes*, which is the causative agent of Teisel's disease (TD), are Gram-negative and obligative intracellular disease causing *Clostridium* species. Teisel's Disease occurs in many species but it is more common in foals, in some wild animals and lab animals. The mode of transmission is by fecal and oral route, that is, oral intake of spores in an environment contaminated with feces. In diseased animals, *C. trichomes* proliferates in the mucosa of small intestine, causing necrosis and spreading to the liver and to other vital organs. To date, the adverse effects of these diseases are not been identified. Given the hyper-acute or severe nature of animal Clostridial hepatitis, treatment is rarely effective. However, Infectious necrotic hepatitis and TD are preventable and should be managed through vaccination and hepatitis prevention. So far, there is no vaccine against TD. In China, the use of antibiotics in dairy and cattle farming has been banned due to antibiotic resistance (Shao et al., 2021). The aim of cattle breeding is to reach live weight at first mating or calving by feeding a fiber-rich diet, thus increasing economic performance.

Because *Clostridium spp.* The digestive system of ruminants is quite old and useful for nutrition. But when it turns into opportunism, it attacks the same gut and destroys the heart. *Clostridium* can be used as an alternative to antibiotics to improve intestinal health and nutrition in animals. A better option to improve gut health is to use live bacteria called probiotics. Clinical study evaluating the effect of *Clostridium butyricum* (*C. butyricum*) supplementation on aniaml growth, ruminal fermentation and gut flora and some parameters of blood in Dutch cows. Good endophytes that have the properties of probiotics and which have the ability to produce short chain unsaturated fatty acids, specially butyrate. An important thing of this species is that, unlike *Lactobacilli* and *Bifidobacteria*, it produces endospores and can survive in high bile and low pH, thus making them available in the cow's rumen. Now-a-days, *Clostridium butyricum* is excessively being used in aquatic and livestock sector. Many studies have shown that consumption of butyrobacter can increase the growth rate of shrimp, tilapia *Miicthys miiuy* and increase resistance to diseases or diseases. It is also used as a probiotic diet in broiler chickens to provide an immune effect and, more importantly, to adjust the intestinal balance. Additionally, the addition of *C. butyricum* non-digestible diets to weaned piglets has been shown to have a positive effect on their growth. Therefore, we expect Butyrobacteria to have similar beneficial effects in heifers fed a high-fiber diet. The investigation of Butyric acid in cow's milk is mainly aimed at preventing diseases, improving milk components and milk volume; However, there is not very much knowledge on the growth and development in different growth stages such as cows and growing heifers. Research studies show that microbes used as feed additives like yeast improves the gut performance of ruminant animals by increasing the activity and growth of rumen bacteria (Aronoff and Kazanjian, 2018).

We can hypothesize that *Clostridium butyricum* may influence rumen fermentation of feed by controlling the overall composition of the ruminal microflora, thereby enhancing the growth of young heifers. So, the aim of doing this study was to know the nutritional supplement *Clostridium* effects of butyric acid on growth rate, ruminal digestion, ruminal microbes and the blood parameters in Dutch heifers. According to the experiments, *Clostridium butyricum* is an effective microbial food for heifer production. It plays an important role in heifer production. It is involved in all major and minor processes and metabolism in the animal body (Awuchi et al., 2021; Li et al., 2021).

Conclusion

Good nutrition and nutritional strategies can allow animals to grow well, but at the same time, excessive or unexpected use of certain ingredients in the feed can also lead to animals suffering from serious diseases such as mold poisoning. Feed consumption and production for animals will be higher. The appropriate amount of protein, fat, carbohydrates and other components in the feed should be controlled, and supplements that will promote animal development should be added to the feed. Food plays an important role in preventing liver disease, as in some of the conditions previously described. Nutritional management is based on the animal's life stage to ensure adequate nutrients.

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Chapter 28

Effect of Minerals on Dairy Cow's Fertility

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ABSTRACT

Healthy dairy animals are important for providing good quality nutritional products to human beings. Optimum production and fertility of dairy cows need a balanced nutrition in order to get these parameters to the desirable levels. Along with recommended levels of proteins, carbohydrates, fats and vitamins, minerals should also be provided as they play an important role in the general metabolic activities and reproduction. The minerals are generally divided into macro and micro minerals. Calcium (Ca), phosphorus (P), potassium (K), magnesium (Mg), sodium (Na), sulphur (S) and chlorine (Cl) are among the macro minerals while copper (Cu), zinc (Zn), cobalt (Co), iodine (I), iron (Fe), manganese (Mn), molybdenum (Mo), selenium (Se), chromium (Cr), boron (B) and fluorine (F) are micro minerals. Among these the micro minerals are more important in reproductive activities, especially Se and Mn and their deficiency can cause reduction in the fertility parameters. This chapter focuses on the information regarding the effect of various minerals on the reproductive performance of dairy cows.

KEYWORDS
Minerals, Fertility, Dairy Cows, Reproduction

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INTRODUCTION

Importance of Dairy Industry

It is acknowledged that dairy industry is a significant source of nutrition and income globally. According to Food and Agriculture Organization (FAO) over 245 million dairy cows are distributed worldwide. The dairy industry has an important impact on sociological values, domestic economics, public health and food security of the human beings. Millions of jobs are directly or indirectly supported by this industry. Dairy milk and its products are a healthy component of a balanced diet. Emerging nations perform poorly in milk production because of energy and mineral deficient low cost nutrition available to their dairy animals (Fadlalla, 2022). Dairy industry is mainly based on production by cows worldwide along with fewer numbers of buffaloes in some Asian countries.

Nutritional Requirements of Dairy Cows and Challenges

The cow's general health, its milk production and fertility are dependent on quality of nutrition provided to them, so balanced nutrition is a key factor for better health and fertility of dairy animals. But mostly dairy animals receive low cost nutrition which is deficient in emery, proteins and essential minerals.

Importance of Minerals for Metabolism and Fertility

Minerals are inorganic matter, so their synthesis inside the body through metabolism is not possible but they play important role in the formation of body as structural units, the general body metabolic process, they act as cofactors or activators in many biological reactions as integral parts of enzymes and hormones. Besides, they play their role in cellular biology and hence the growth of animal's body is affected by these minerals as they control cellular replication and differentiation. Depending upon the bodily requirements in diet minerals are divided into macro and micro minerals. The macro minerals are required in concentration more than 100ppm (mg/kg diet) whereas, those required less than this concentration are called as micro minerals are trace minerals. The Ca, P, K, Mg, Na, S and Cl are among the macro minerals while the Cu, Zn, Co, I, Fe, Mn, Mo, Se, Cr, B and F are micro minerals (Sharma et al., 2007). Studies have revealed that excesses and deficits in minerals in plants and soils can cause productivity losses, reproductive issues as well as clinical manifestations of mineral deficiencies, including diarrhea, anemia, anorexia, tetany, low fertility, wasting diseases, hair loss, depigmented hair, skin disorders, and pica (McDowell et al., 1986). The dairy cows' diets contain minerals because they are necessary for controlling the biological processes like development, reproduction, and production. In tropical climates, animals do, nevertheless, consume a little amount of minerals through feed and fodder. The reproductive issues and subpar milk production are two common reasons for money losses by the farmers. A prolonged dry season and fewer calving and hence lactations over an animal's life cause substantial financial losses in terms of reduced calf crops and less milk production. So fertility is important factor determining the yield by this sector (Barui et al., 2015). The minerals make up about 5 percent of an animal's body weight and animals get these minerals from soils through forages.

The average intake of Cu exceeded the National Research Council's (NRC) recommended levels by forty percent. Ovulation intervals and postpartum uterine involution were reduced by increasing Cu intake ($r = -0.31, -0.32$; $p < 0.01$). Consuming Zn and Cu have positive impacts on blood levels of macro minerals and certain reproductive factors (Garg et al., 2003).

Given their roles in the synthesis of the body's structural components as well as the appropriate operation of enzymes, hormones, vitamins, and cells, macro and trace minerals are equally significant (Balamurugan et al., 2017). The body's structural elements, minerals are essential for the production of hormones, enzymes, bodily fluids, tissues, and regulators of cell division and replication. Minerals are required for all physiological processes in the animals, including reproduction (Elrod and Butler, 1993).

Provision of Minerals to Animal in Nutrition and Mineral Deficiency

Minerals are provided to dairy animals' nutrition through forages and as mineral supplements. The tropical forages do not fully meet all mineral requirements, as grazing cattle typically receive common salt as a mineral supplement and must rely almost entirely on forage for their total mineral needs. Many forages around the world have been reported to have inadequate amounts of specific nutritional components. The tropical cattle that graze on poor quality soil and forages have long been blamed for low productivity and other issues regarding reproduction. Plants take up necessary components from the soil solution in large enough quantities to meet both their own needs and the needs of many grazing livestock. In addition to the necessary elements for plants, grazing ruminants also require the elements such as Se, Co, and I, which plants also withdraw (Fadlalla, 2022). Nearly all tropical locations of the world have been documented to have mineral imbalances and deficiencies. Beginning in the early years of this century, numerous African reports have demonstrated the advantages of mineral supplementation on overall performance, fertility performance calving percent, and mortality reduction (Fadlalla, 2022).

Sources of Minerals in Cattle Diet

In beef cattle operations, oral TM supplementation is a fundamental management technique. Compared to inorganic forms, organic sources of trace minerals (TM) have been shown to improve performance and health during times of high stress and low feed intake (Rabiee et al., 2010).

Forages

Forages are important mineral source for animals but are unable to fulfil all requirements especially in tropics. The minerals in frequently used fodder, cereals, cereal by-products, and concentrates made from vegetables are insufficient to provide farm animals with the optimal level of nutrition. The soil, plant type, maturity stage, yield, pasture management, climate, and other factors all affect the concentrations of mineral elements in forages. To meet their own needs, plants remove necessary components in large amounts from the soil solution like Se, Co, and I, necessary for grazing animals' need as well (McDowell, 1996). Forages provide ruminant production with all of the nutrients they need in various parts of the world. Mineral imbalances in soil and feed are widespread, with forages often lacking in important trace minerals (McDowell and Valle, 2000). It is often acknowledged that grasses are not as rich in various mineral elements as plants and legumes due to their natural dilution process and movement of nutrients to the root systems. Moreover as plant ages, its mineral levels decrease. Phosphorous P, K, Mg, Na, Cl, Cu, Co, Fe, Se, Zn, and Mo concentrations typically decrease as plants get older. Grazing pressure drastically alters the leaf/stem ratio, which directly affects the plant's mineral content. Minerals from the soil are removed from it more quickly when crop yield increases. Overlining increases the concentration of these elements in plants, which can accumulate Se or Mo toxicity in cattle (McDowell, 1996). The chikori green and lucerne were found to contain large amounts of cobalt (>0.35 ppm) (Bhanderi et al., 2015). With the exception of cottonseed cake, all varieties of straws and concentrate ingredients had Cu contents below the essential threshold (<8 ppm). With the exception of paddy straw, the Zn content in all the straws was below a threshold level (<30 ppm). Crushed grains were shown to be a worse supplier of zinc than greens and cakes (Maradal et al., 2004). The district's Mn levels were found in straws at 36.47–478.12 ppm, green fodders at 62.64–132.99 ppm, and concentrate ingredients at 13.18–75.74 ppm. These results were consistent with the observations made by Mandal et al., Yadav et al., and Youssef et al. The range of cobalt levels detected in feed and fodder resources were 0.18 ppm to 0.71 ppm. The roughages and concentrates comprised 0.06–0.20% and 0.25–0.67 Phosphorus, respectively (Yadav et al., 2002).

In most parts of the world, deficiencies in certain minerals, such as those of the major elements Ca, P, Mg, Na, S, and the trace elements Co, Cu, I, Mn, Se, and Zn, can affect the productivity of grazing animals at pasture (Khan et al., 2007). The Co^{2+} insufficiency is the most prevalent mineral shortage in grazing animals, aside from P and Cu. and soil, can influence the probability of Zn^{2+} absorption and hence their shortage in the ruminants (Nasrullah et al., 2003).

Soil the Enrich Source of Minerals

An examination of the soil may occasionally show that animals are deficient in certain critical minerals. The amounts of Co, Mo, and I in the soil somewhat mirror the amounts of these elements in the plants. Forage mineral uptake from the soil is influenced by a number of factors, such as plant yield, maturity stage, deficits in certain species and strains, seasonal and climatic circumstances, chemical forms of minerals, and soil characteristics like pH and aeration level and water logging (Fadlalla, 2022).

Animal's malnutrition is mostly caused by a shortage of feed and micro- and macro minerals in the soil (Hegde et al., 2018).

All soil microminerals, with the exception of zinc, showed seasonal variations; pasture iron, zinc, and selenium also did. With the exception of cobalt and selenium, all soil mineral levels were high enough to meet plant needs for normal growth in both the winter and the summer (Sunder et al., 2007).

Role of Minerals in General Metabolic and Reproductive Activities

Role of Trace minerals (TM) in Cattle Immunity

The superoxide dismutase (SOD) is an antioxidant enzyme that contains copper, zinc, and manganese, while glutathione peroxidase (GPx) contains selenium. The leukocytes are shielded by these enzymes from free radical damage to their membranes. These TM are involved in several critical processes, including leukocyte movement, phagocytosis and bacterial death, antibody secretion, cytokine synthesis, and cell-mediated immunity (CMI) (Palomares, 2022).

Role of Calcium

The major functions include the development of bones and teeth, nerve and muscle functioning, blood coagulation, cell permeability, and an important component of milk. Both active and passive absorption (diffusion) occur through the duodenum. The necessary amount of vitamin D and the Ca : P ratio are crucial factors for absorption from gut. Its loss through urine is negligible, with feces serving as the primary route of excretion. The vitamin D plays a role in both bone deposition and absorption; too much P and Mg inhibit absorption; the Ca : P ratio shouldn't be less than 1:1 or greater than 7:1 (1:1 to 2:1 for monogastric) for proper absorption (McDowell and Arthington, 2005). The Ca deficiency causes many metabolic problems or disease conditions like milk fever, osteodystrophic diseases, direct or indirect infertility through disturbed Ca: P ratio which disturbs pituitary and ovarian action. A prolonged Ca deficiency causes painful joints, lameness, long bone fractures backbone arching and posterior paralysis (Sharma et al., 2007).

Role of Phosphorus (P)

The main processes include the production of bones and teeth, phosphorylation, high-energy phosphate bonds, maintaining acid-base balance, and a part of DNA, RNA, and many enzyme systems. The duodenum is the site of absorption; vitamin D is necessary for absorption, and a 1:1 ratio of calcium to phosphorus is crucial. Excretion occurs primarily through the feces and urine. Too much calcium and magnesium reduce its absorption (Fadlalla, 2022). The phosphorus deficiency is most widespread among all minerals and effects the reproduction critically as it causes delayed onset of puberty, depressed or irregular estrous and delayed conception. Poor feed conversion in pregnant beef cows and stunted growth of calves and hence delay in sexual maturity of these heifers. The phosphorus can be given directly by mixing within feed or given in drinking water up to 5g/head/day for growing cows and its double for breeding stock (Miller et al., 1990).

Role of Cobalt

The cobalt is used by rumen microorganisms to synthesize vitamin B_{12} and to support the growth of rumen bacteria, which are essential for the production of methyl and adenosyl cobalamin. It is absorbed in the lower section of the small intestine as a component of vitamin B_{12}. This is excreted mostly by urine and feces, with a 1-12% possibility of milk excretion (Fadlalla, 2022). Its deficiency has negative impacts on the reproductive performance of cows like delay in puberty, delayed uterine involutions and decreased conception rates. The levels of Co can be directly correlated with the concentration of vit B_{12} in the circulation (Sharma et al., 2007).

Role of Magnesium

An important component of bone that is necessary for healthy skeletal development, this enzyme activator works mainly in the glycolytic pathway to reduce tissue irritability. It is taken-up principally through reticulorumen part of digestive system. This is excreted primarily by the urine, feces, and milk pathways. Magnesium carbonate, magnesium oxide, magnesium sulfate, and magnesium chloride are its important sources. The excessive interactions and toxicities disrupt the metabolism of calcium and phosphorus; its toxicity is unlikely (McDowell and Arthington, 2005). The Mg is also an important mineral which effects reproduction negatively if provided in less than required quantities, very high levels of potassium and phosphorus negatively affect the availability of Mg. In cows, the required magnesium level is 10-15 mg/kg body weight (Miller et al., 1990).

Role of Copper

Many enzymes and proteins involved in the synthesis of mitochondrial energy and other metabolic pathways need copper. Its main contribution to immunity comes from its participation in the metalloprotein enzyme Cu-SOD, which causes neutrophils to produce hydrogen peroxide radicals for killing of bacteria. The myeloperoxidase system uses these free radicals to produce potent oxidizing agents like hydroxyl radicals (Maywald et al., 2017). Furthermore, because it scavenges superoxide radicals, this enzyme is crucial for reducing oxidative stress. By doing this, Cu-SOD stops superoxide free radicals from building up too much and damaging leukocyte membranes. Additionally, copper is a part of ceruloplasmin, an acute phase protein that plays a significant part in bovine immunity, particularly in animals under stress (Puertollano et al., 2011).

The consumption of pastures high in molybdenum or low dietary amounts of copper might result in copper insufficiency. Similar to this, feeding ethanol coproducts like distillers' grains or providing high sulfate water to cattle might have a detrimental effect on their ability to absorb copper. Acute phase protein response and neutrophil phagocytic activity are both impaired by copper deficiency (Enjalbert et al., 2006). Overall, calf health and performance have been linked to copper deficiency (mostly diarrhea, growth retardation, and death); this is probably due to weakened innate immunity, unsuccessful passive transfer, lower antibody formation, and compromised cell-mediated immunity. The cattle suffering from severe Cu deficiency may pass quite suddenly from heart failure (Bonham et al., 2002). The Cu plays important role in reproduction, bone and connective tissue growth, pigmentation of skin appendages. The Cu concentrations are significantly raised on the day of estrus than from other reproductive stages. Its deficiency cause reduction in ovarian activity and postpartum estrus along with reduction in reproductive performance of dairy animals. The hypocuperosis is also responsible for early embryonic mortality, reduction in growth, feed conversion efficiency, fertility parameters, conception rates and increased incidence of placental retention. The cows grazing on soils which are deficient in Cu gave birth to weak calves which face incoordination, stiff gait and opisthotonus. And such the cows experience depressed estrous, delay puberty and infertility. The Cu deficiency causes embryonic losses and their resorption, placental retention and its necrosis. When Cu is given orally or in injectable form to an animal facing Cu deficiency it improves breeding performance. The cow in late gestation should get 2mg of absorbable Cu (Miller et al., 1990).

Role of Zinc

In tissues that go through mitosis, such as lymphoid tissue, skin, testicular seminiferous tubules, and mucous membranes, zinc is crucial. The Zn strengthens the mucosal lining of the gut and respiratory systems. Additionally, it contributes to epithelial integrity and mucosal tissue repair (Maywald et al., 2017). It plays role in nucleic acid replication. It is also essential for the synthesis of cytokines by lymphocytes and macrophages during both innate and acquired immunity due to its role in mRNA expression and subsequent translation into proteins (Puertollano et al., 2011). As a structural element of superoxide dismutase (Zn-SOD) zinc is a potent antioxidant and its deficiency affects both innate and adaptive immunological response negatively (Wang et al., 2013). Reduced birth weight, congenital abnormalities, extended labor, preterm or post term deliveries, and poor maternal zinc status have all been linked to these outcomes. Maternal zinc supplementation was found to reduce preterm births in a minor but meaningful way, according to a 2007 meta-analysis (Chaffee et al., 2012).

Role of Selenium

The enzyme glutathione peroxidase (GPx), which catalyzes the reduction of hydrogen peroxide to water and oxygen, has selenium as a structural component. The Se deficiency has been linked to decreased GPx antioxidant functions, decreased neutrophil migration and killing activity, and the impaired B-cell and antibody synthesis (Enjalbert et al., 2006). The white muscle disease is a type of muscular degeneration that can affect calves lacking in selenium. The myocardial degeneration associated with this syndrome may cause instant death. Calves that are marginally Se-deficient may show signs of frailty and low energy. A retrospective study conducted in France found that cows with low and marginal Se status had a higher chance of infectious abortion, as well as high calf morbidity and mortality from a weakened immune system, which may be connected to changes in iodine metabolism. Furthermore, a higher incidence of retained fetal membranes has been linked to vitamin E and selenium deficiencies in cows (Enjalbert, et al., 2006).

The Se is very important in reproductive process of both male and female most probable due to metabolic pathways which underwent through glutathione peroxidase GPx. High as well low levels of Se have impact on reproduction its higher levels cause fetal resorptions and abortions while its long-term deficiency causes abortions still births and neonatal mortality, placental retention, cystic ovarian diseases and silent heat. In male's sperm viability and maturational process in epididymis is also affected by low levels of Se (Sharma et al., 2007). The recommended level of Se in diet is 0.2-0.3 ppm it is given in the form of mineral mixtures or Se/ vit E injections (Sharma et al., 2007).

Role of Manganese

Several enzymes, including pyruvate carboxylase, arginase, and SOD, contain manganese. It also serves as an enzyme activator for several kinases, transferases, and hydrolases. Since manganese is a structural element of the Mn-SOD enzyme, it plays a crucial role in scavenging ROS generated by phagocytic cells (Tomlinson et al., 2008). The only really significant impact of dietary manganese deficiency on immunity is a weakened humoral immunological response. Abortion, long bone congenital abnormalities (including swollen joints, stiffness, twisted legs, shorter bones, and general physical weakness) in newborn calves, and tongue neuromuscular dysfunction in cows have all been linked to manganese deficiency (plasma Mn < 76 nmol/L) (Palomares, 2022). The manganese is an important component of the skeleton of the animals that's why manganese deficient calves are born with skeletal deformities. The manganese deficiency causes negative impacts on reproduction of animals like compromise on conceptions and delayed estrous in postpartum cows as well in heifers, silent estrous, cystic ovarian diseases and abortions. In case of Mn deficiency supplementation with 7-17mg/kg DM should be provided to compensate. And if diet have less than 30-40 ppm Mn it is considered as deficient in this mineral (Sharma et al., 2007).

Role of Chromium

In tissues like muscle and the liver, chromium is necessary to stimulate the functions of insulin and insulin-like growth factor I. As a result, it is connected to several metabolic pathways that are related to growth and homeostasis, such as glucose tolerance and clearance rate. Furthermore, under extremely stressful conditions, Cr seems to lower circulating cortisol concentrations. Multiple immune mechanisms are impacted by chromium. The Cr has a biphasic pattern of action on lymphocytes, acting as an inhibitor at high doses and as a stimulant at low ones. After *in-vitro* mitogen stimulation in nursing Holstein cows, chromium decreased the levels of immunomodulatory cytokines, such as IL-2, IFN-γ, and TNF-α (Faldyna et al., 2003).

Role of Iron

The average human ferritin content is 3.4–4 g, or roughly 40–50 mg of ferrous iron per kilogram of body weight. The hemoglobin contains the majority of the iron in the body. The Fe is a necessary part of myoglobin. In addition, growth, development, regular cellular activity, the creation of certain hormones, and the formation of connective tissue all require iron. The major sites of absorption in the gastrointestinal tract are the jejunum and duodenum (Al-Fartusie and Mohssan, 2017). The excretion through sweat, hair, urine, and feces can result in significant loss from bleeding. The ferrous sulfate, ferrous carbonate, meats, legume seeds, green vegetables, and cereal grains are sources. The Cu is necessary for the healthy metabolism of Fe. An excessive amount of Fe could negatively affect P, Cu, and Se metabolism (Ross, et al., 2020). Iron is the 2^{nd} most abundant metal and it is very important in the body especially for its role in transport of oxygen in the body. The Cu in small quantities is required along with Fe for Hb synthesis. In adult cattle Fe deficiency is not common but in young calves it mostly occurs in calves which are fed on only milk or milk replacer deficient in iron face anemia. To avoid its deficiency it should be added to milk replacers at 100mg/kg DM (Sharma et al., 2007).

Effects of Minerals on Reproductive Processes

The cows are polyestrous animals with 21 days long estrous cycle, the first postpartum oestrus used for breeding occurs after 42 days, duration of the oestrus is 18 hours, and the average age at first service is 14 to 22 months (Fadlalla, 2022). Reproductive efficiency of the animals is an important factor in the life of a dairy animal as it determines the overall production from an animal in terms of milk and meat production and it is influenced by many factors including a balanced diet, weight gain, healthy environment and level of production (Patterson et al., 1992).

The reproductive events are important metabolic processes which are highly specific and needs an optimum microenvironment. It has been observed that micro minerals play important role in proper functioning of reproductive process of dairy animals. The deficiencies of minerals cause cessation of oestrus, conception failure and embryonic deaths due to change morality of fluid in fallopian tubes repeat breeding (Joshi, 1994). The optimum fertility is very important for better sustainability in dairy sector. There are many reasons for decreased fertility. It has also been closely related to mineral deficiencies like low phosphorus consumption has been linked to delayed sexual maturity, low conception rates, and inactive (anaestrous) ovaries. Abortions, silent anestrous, and decreased ovarian function have all been linked to deficiencies in other minerals like copper, manganese, and cobalt (Fadlalla, 2022). The duration between parturition and the first oestrus in tropical cattle is influenced by a variety of factors, including as internal and external parasites, heat and humidity, diet, management, endocrine events, and genetic-environmental interactions. Prolonged postpartum anoestrus and infertility are further consequences of nutritional variables that lead to lower hemoglobin levels, such as deficits in trace minerals and parasite infestations. The best indicator for tracking the reproductive condition of a herd is the calving interval.

Low productivity and issues with reproduction have been attributed to mineral shortages in soils and forges among tropical cattle that graze. The ovarian steroid secretion is disrupted by molybdenum, which delays puberty in heifers by interfering with the production of luteinizing hormone (LH) (McDowell, 1993). The zinc is important for spermatogenesis and plays a synergistic function in spermatozoa's uptake of vitamin A; this is especially important because vitamin A is necessary for puberty and for maintaining the integrity of the testicular cell epithelium as well as libido. According to research by Master and Moir, lambs born to ewes fed on a zinc diet of 4 mg/kg weighed 17% less than lambs born to ewes on an adequate zinc diet of 50 mg/kg (Masters and Moir 1983).

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Chapter 29

Use of Hay Protein to Improve Cattle Health

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ABSTRACT

Economic viability and animal welfare are impacted by the health and production of cattle, making them the most important considerations in livestock management. Conventional methods of improving cow health frequently concentrate on elements like diet, immunization, and illness control. However, recent studies indicate that robust health and performance in cattle are significantly influenced by the quality of dietary protein especially that comes from Hay. The purpose of this chapter is to clarify the possible advantages of supplementing cattle with hay protein to enhance their health. We examine the nutritional makeup of hay protein, including its digestibility and talk about how it supports different physiological processes in cattle. Additionally, we investigate the impact of hay protein on reducing prevalent health issues in cattle, including immunological suppression, metabolic abnormalities, and ruminal acidosis. We have highlighted new developments in feed technology and processing techniques that improve effectiveness of hay protein supplements. We have discussed how to include hay protein supplements into cow feeding schedules in a realistic manner, taking into account factors like time, dosage, and compatibility with other nutritional ingredients. In summary, the present chapter highlights the possibility of supplementing hay proteins as a viable approach to enhance the well-being of cattle.

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INTRODUCTION

One way to preserve fodder for animal feed is with hay, which, when stored correctly, may be preserved for extended periods of time with little nutritional loss. Hay is one way that fodder can be preserved for use in animal feed. If stored correctly, hay can be kept for extended periods of time with minimal nutritional loss (Marsalis et al., 2009). One of the main reasons alfalfa hay is popular as animal feed is because it has high protein content. The alfalfa hay typically has a crude protein content of 15% to 20%. This means you should anticipate to find about 0.15-0.20 pounds of protein for every pound of alfalfa hay. Dried grasses, legumes, or other herbaceous plants make up the majority of hay, a common feed for cattle. It is commonly known for its ability to give animals energy and fiber. For the animals that eat hay, the protein plays a crucial function in growth, muscle development, and general health (Brown and Jones, 2020). Higher concentrate diets and diets supplemented with protein are generally associated with improved performance in recently weaned or received cattle. On the other hand, limited data indicate that higher concentrate and protein diets in receiving diets are associated with an increased rate and severity of subjectively determined BRD morbidity. There is a need for research on the relationship between humoral and cell-mediated immune function and diet concentrate/protein level, as well as performance and health markers. Although the effects of supplementing with B vitamins in receiving diets have been inconsistent, it is likely due to variations in stress and the corresponding feed intake responses. More dose titration studies are required, however on vitamin E supplemented to receiving meals to provide ≥ 400 IU/animal daily is advantageous for improving growth and lowering BRD morbidity (Galyean et al., 1999). The Zn, Cu, Se, and Cr supplements can change the immune response of recently received calves, and some field trials have demonstrated that supplementing lowers the BRD morbidity rate. It is important to consider that highly stressed, recently acquired beef cattle have lower feed intakes, and that there may be nutrient deficiencies. However, it is challenging to justify, based on current data, fortifying such diets with trace minerals above and beyond what is necessary to offset these effects (Galyean et al., 1999).

When evaluating the nutritional value of protein for animals, factors like digestibility and amino acid composition are critical. Livestock producers who want to feed their animals a balanced diet, maximize production efficiency, and support animal health and welfare must comprehend the protein content of hay and its nutritional importance (Smith and Johnson, 2019). When creating a sustainable diet, protein is one of the components that needs to be taken into account. These issues underscore the necessity of using ruminants responsibly in order to maximize land utilization and produce sufficient protein. Any suggestions for agricultural reforms must take the environment into account while emphasizing the best possible use of available natural resources to produce wholesome diets (Smith and Johnson, 2019).

Preservation of Green Fodder as Hay

Harvested forages can be stored as hay to feed the animal during a lean phase after they reach the right nutritional content. Stopping the microbial activity is best achieved at a moisture content of 10–12%. Grass and fodder can be stored as either silage (wet fodder) or hay (dry fodder), based on the resources that are available and the weather. Low input farmers have, however, only seldom been included in the silage and hay-making process (Mojumdar, 2009). Making hay is a good way to keep these grasses and fodders preserved. This method of conservation can also be used to feed at a later stage obligate plants, which are an important source of protein. Its flavors can be effectively kept, particularly if drying doesn't take a long period. Dry matter is lost during the fermentation and handling phases of any feed conservation technique. In addition, more labor and materials are used in the preparation of green feed than in its direct feeding (Mojumdar, 2009). The fundamental idea behind haymaking is to gradually lower the amount of moisture in the green forages so that they may be kept without going bad or losing more nutrients. At the time of storage, the moisture content of hay must be less than 15%. Therefore, since they dry faster than crops with thick, pitiful stalks and few leaves, those with thin stems and many of leaves are more suitable for creating hay (Brown and Jones, 2020).

Importance/Benefits of Hay Protein in Cattle

Dairy cows are interested in proteinaceous meals made from by-products since some of them have a high crude protein content and low ruminal degradability. A number of factors are covered that impact the amount of protein in distillers grains, distillers grains with soluble, brewers grains, corn gluten feed, corn gluten meal, meat meal, meat and bone meal, blood meal, and fish meal which can be broken down in the rumen. Additionally, these feeds may be able to supply additional amino acids that lactating dairy cows require. In regard to total amino acid transit to the small intestine, the significance of optimizing microbial protein production and organic matter digestion in the rumen is highlighted (Brown and Jones, 2020). These feeds should give complementary amino acids to other amino acids that pass through the small intestine and be reasonably priced, according to a reliable source, in order for them to be used as effectively as possible. The successful usage of by-product feeds should result in lower costs per unit of milk produced due to the elimination of costly supplemental protein and enhanced milk production from feeding proteins with higher ruminal escape potentials (Smith et al., 2018).

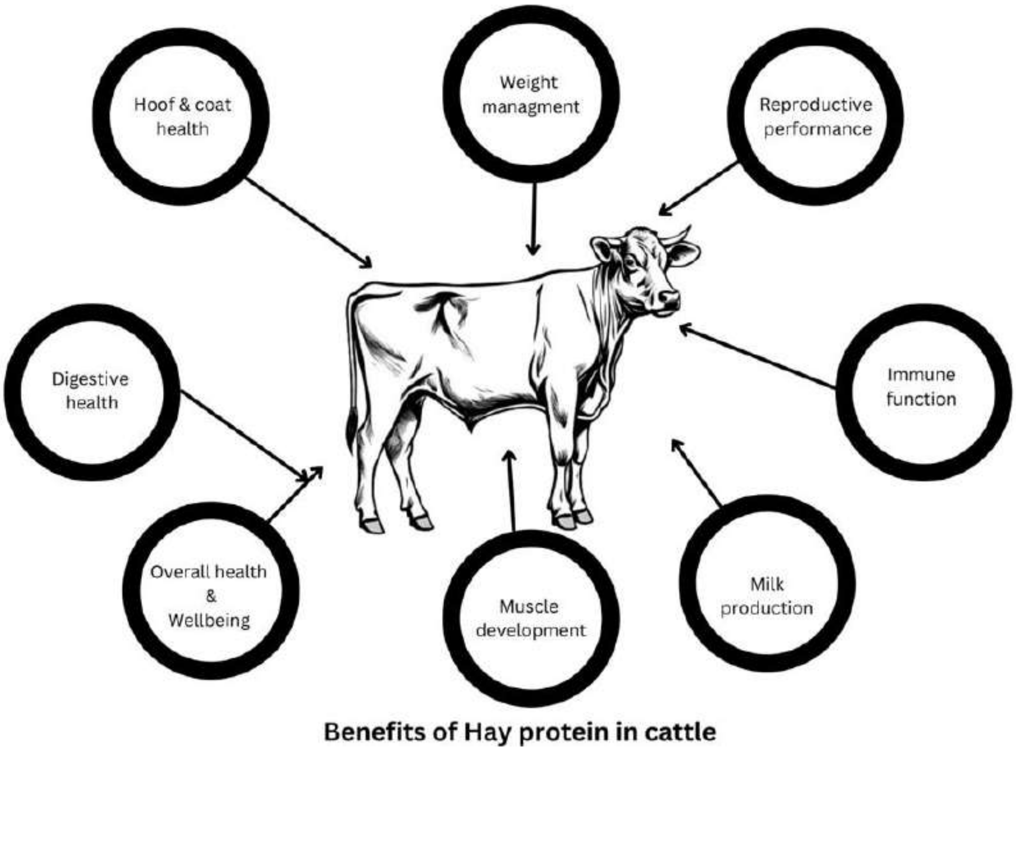

Fig. 1: Benefits of hay protein in cattle

Muscle Development

Farmers and agricultural scientists have made significant efforts to improve the muscle mass of animals that produce meat. In the past, conformation was subjectively evaluated in order to choose superior breeding stock. In the recent past, therapeutic growth promoters have been used to artificially boost muscle mass during the finishing phase of cow production. Many generations of intense selection have produced a number of cattle with enormous muscle (Johnson, 2020).

Milk Production

Although the amount of protein required in the diet for both body maintenance and milk production is known, there has been inconsistent research on the effects of different dietary protein percentages on milk production during the early stages of lactation. While some reports of high-producing cows have showed no response to protein supplementation over 12 to 13% crude proteins in dry matter of total ration, other research have found a rise in the milk yield. Researchers are now looking into how age affects milk production and how adding more protein to the diet during early lactation affects the distinctive lactation curve and growth requirements of heifers during their first lactation compared to multiparous cows (Wu, 2022).

Immune Function

For many years, it has been known that a diet rich in protein and vitamins can enhance both immune system performance and general health. In the Southeast, forages that may be deficient in protein for ideal health are mostly used to rear beef cattle. Subclinical protein deficiencies are more prevalent and harder to identify, but they can still cause larger economic losses. Clinical protein deficiencies cause the characteristic signs that are common to various nutrient deficiencies (e.g., poor growth and unthrifty appearance) (Crook et al., 2020).

Reproductive Performance

A cow's milk output can be increased by increasing its dietary protein intake, but doing so may also lower its fertility. Although the impacts are very different, they can impact any point in the reproductive cycle, from the embryo's survival to the return to cyclicity following parturition. Uncertainty exists on the underlying reason for the association between fertility and protein intake. One possible explanation for the decreased fertility is the extra energy required for the metabolism of breakdown products of protein, which can also have a direct harmful effect. Additionally, unknown is the impact of protein degradability (Cardoso et al., 2020).

Weight Management

More precisely, the growth and repair of tissues, enzymatic activity, molecular transport, genetic storage, immunological function, and cell differentiation are all impacted by the amino acids. Although amino acids are the substances that animals need, as was previously stated, the phrases "amino acid" and "protein nutrition" will be used interchangeably. Minimal dietary crude protein (CP) and sufficient ruminally degraded protein (RDP) are the two main objectives of protein nutrition for ruminants in order to maximize the ruminal efficiency and microbial CP generation (Wu, 2022).

Hoof and Coat Health

An important component of good hoof horn growth is nutrition. In order to guarantee proper horn growth and the structural binding of keratin proteins, a few minerals, amino acids, and vitamins are required for the keratinization process. Laminitis is a significant illness affecting the hooves of cattle. Both bleeding and ulceration on the feet are seen as signs of subclinical laminitis. A feed plan with too much protein may cause issues since it promotes rapid horn growth. The maintenance of the hoof's structural and functional integrity depends on the amino acids cysteine and methionine (Cardoso et al., 2020).

Digestive Health

One of the main things that determines a cow's productivity and general well-being is the state of its digestive system. Both overfeeding and underfeeding are widespread practices in the dairy and beef industries, which have a detrimental effect on the environment, welfare, and financial gains. Minimal dietary crude protein (CP) and sufficient ruminally degraded protein (RDP) are the two main objectives of protein nutrition for ruminants in order to maximize ruminal efficiency and microbial CP generation (Wu, 2022).

Overall Health and Well-being

An adequate diet must include protein. The 'building blocks' of chemistry known as amino acids comprise proteins. Your body requires amino acids to create hormones, enzymes, and to build and repair muscles and bones. They are also useful as a source of energy. Hay's protein content helps guarantee that cattle receive the nutrients they need for optimal health and productivity (Cardoso et al., 2020).

Effects of Hay Protein on Cattle Health

It is essential to provide premium hay to ruminants, such cows and goats. Hay of high quality increases salivation, encourages chewing and rumination, and gives the animals all the nutrition they need. Furthermore, higher feed intakes are made possible by high-quality hay because it has less lactic acid, which inhibits feed, than silages made of lower quality. Sugar, crude proteins, and crude fibers are the three main ingredients of hay. Dairy cows need roughly 90 g of crude proteins per day, which include amino acids, proteins, and proteiods in addition to the building blocks of protein. Hay is mostly composed of sugars, which are short-chained, quickly digested carbohydrates (Johnson and Smith, 2021).

Strategies for Optimizing Hay Protein Content

Hay is a highly versatile stored forage due to its ability to be stored for extended periods without losing much of its nutrients if kept out of the weather; (2) it can be produced and fed in small or large quantities using a variety of crops; (3) it can be harvested, stored, and fed manually or it can be fully mechanized; and (5) it can provide the majority of nutrients required by various types of livestock. Hay is one of the most commonly used feeds, thus it's critical to comprehend the aspects influencing its quality as well as how to identify it (Garcia and Patel, 2022).

Animal performance is the ultimate gauge of hay quality. When animals eating the hay perform as expected, the quality can be deemed satisfactory. There are three variables that affect an animal's performance: Consumption: Hay needs to taste good in order to be eaten in sufficient amounts; (2) digestibility and nutrient content: Hay needs to be digested in order to be turned into animal products; and (3) toxic factors: High-quality hay needs to be devoid of substances that could harm animals who eat it (Dal Prà et al., 2023).

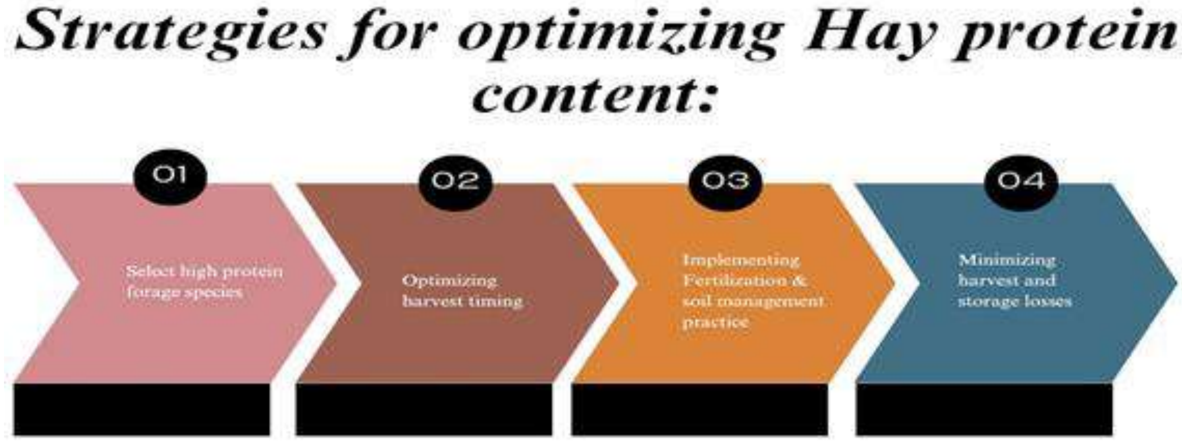

Fig. 2: Strategies for Optimizing Hay Protein Content

Selecting High-Protein Forage Species

In order to produce seed that would provide beneficial qualities in the following crosses, forage breeders carefully pick plants exhibiting strong features, such as resilience to drought, winter hardiness, or shade tolerance. Grain crop breeding is easier than forage crop breeding. The variety of fodder crops, including grasses, legumes, forbs, and sedges; they can be annual or perennial; grow in warm or cool climates; produce bunches or sods; are single species or mixtures; and have cross- or self-pollinating traits, all add to the complexity of forage breeding (Dal Prà et al., 2023).

Optimizing Harvest Timing

A set time in the fall was used to determine the fodder quality and availability in this experiment. In these examples, the same locations where alternative cutting dates were conducted in September were used to estimate the availability of forage and crude protein. It's noteworthy that when cutting dates grew in September, the quality of forages rose as well. That is to say, the crude protein level of the forage collected in September in the June 1 (9.10% CP) region was lower than that of the August 1 (16.53% CP) area. Upon closer inspection, this makes sense because, in September, the fodder that was cut in that location on June 1 is more mature than the forage that was originally gathered on August 1 and then recut in September (Soufan and Al-Suhaibani 2021).

Implementing Fertilization and Soil Management Practices

All green plants, including forages, need light, heat, nutrients, and moisture to grow. In order to increase output and ensure high-quality finished hay, a healthy diet is necessary. Temperature and light levels control when springtime plant growth begins. The formation of new root systems, the synthesis of new cell walls, the metabolism and conversion of energy, and the creation of new enzyme systems are all aided by phosphorus and potassium, which together make up half of macronutrients required by plants. When physically feasible, these two nutrients should be administered to the field in accordance with the findings of the soil test. If deficiencies are found, sulfur and boron should be added in spring (Zhang et al., 2020).

Minimizing Harvest and Storage Losses

To maintain the protein content of hay, losses must be kept to a minimum throughout harvest and storage. More than 20% harvest moisture increases the likelihood of mold growth, which increases the amount of dry matter lost due to microbial activity. Hay should be stored under cover if you want to minimize storage losses (Rotz et al., 2020).

Addressing Common Health Challenges with Hay Protein Supplementation

Introduction to Common Health Challenges in Cattle

Over the past few decades, the developed world's dairy business has experienced significant transformations. Herd size has increased while the number of farms has dropped significantly. Because of this, a growing percentage of dairy farms rely on hired labor from outside their families (Sharma and Koundal, 2018). The use of new technology is growing more widespread. Even though access to pasture is restricted in some nations, fewer farmers in those historically engaged in seasonal grazing allow their dairy cows to graze throughout the summer. The percentage of organic dairy farms has grown worldwide, and conventional farms might be able to learn from well-run organic farms given the push to reduce usage of hormones and antibiotics. There are a lot of opportunities for diagnosing and tracking diseases with milk, and organizations dedicated to improving dairy herds will keep adding to the array of tests available for pregnancy and disease detection (Sharma and Koundal, 2018).

Understanding the Role of Nutrition

The goal of fundamental nutrition is to measure the flow of nutrients through diverse tissues and organs during their digestion and processing, as well as to explain the intricate biochemical events that underlie these processes. At every level of biological organization, including the entire animal, organ systems, tissues, cells, and molecules, significant progress has been made. At the whole-animal level, advances have been made in understanding metabolism in late pregnancy and the lactation transition, as well as in the whole-body utilization of amino acids and energy-producing substrates for growth in young calves (Grazioli, 2016).

Ruminal Health and Hay Protein

Hay is necessary for a ruminant's diet to be healthy. Hay quality needs to be given special consideration. This is because they have specific tastes and require leaves and herbs for good health. It is advised to employ mechanical hay drying for fodder plants since conventional ground drying results in significant losses of leaves and buds from crumble and flake formation. Technical hay drying with a heat pump is ideal because herbs need to be dried slowly and since drying air and herbs have different temperatures. Nonetheless, it is imperative to give enough protein and energy. High hay quality is ensured by technical hay drying, which is necessary for animal cleanliness and health. There's also a risk of listeriosis for small ruminants using typical hay drying methods if the silage quality is low (Klevenhusen et al., 2019).

Mitigating Metabolic Disorders

Enzyme, coenzyme, or cofactor deficits as well as malfunctioning biochemical pathways are the causes of metabolic disorders, which include metabolic diseases that are hereditary. Galactosemia, ruminal acidosis, ruminal bloat, horse exertional myopathy, hepatic and muscular glycogenosis, diarrhea in lactose-fed chicks and newborn pigs given sucrose, and hypoglycemia are among the disorders brought on by aberrant carbohydrate metabolism. Conditions brought on by aberrant lipid metabolism include pregnancy toxemia, yellow fat disease, obesity, fatty acid deficiency syndrome, ketosis in dairy cows, fatty cow syndrome, fatty liver hemorrhagic syndrome in laying hens, and fatty liver and kidney syndrome in chickens. Hay protein is helpful during these diseases (Xue et al., 2021).

Enhancing Immune Function

For many years, it has been known that a diet rich in protein and vitamins can enhance both immune system performance and general health. In the Southeast, forages that may be deficient in protein for ideal health are mostly used to rear beef cattle. Subclinical protein deficiencies are more prevalent and harder to identify, but they can still cause larger economic losses. Clinical protein deficiencies cause the characteristic signs that are common to various nutrient deficiencies. Hay may also contain certain proteins with immunomodulatory properties that boost cattle's immune systems, reducing disease risk and improving overall health (Sharma et al., 2014).

Improving Reproductive Performance

A cow's milk output can be increased by increasing its dietary protein intake, but doing so may also lower its fertility. This study examines the impacts of consuming more protein in the diet on dairy cow fertility as well as potential causes. Although the impacts are very different, they can impact any point in the reproductive cycle, from the embryo's survival to the return to cyclicity following parturition. One possible explanation for the decrease in fertility is the extra energy required for the metabolism of breakdown products of protein, which can also have a direct harmful effect. A higher body condition score is also associated with effective reproduction and cow fertility, and this could be achieved with protein supplementation (Chahine et al., 2019).

Case Studies and Practical Applications

Case studies prove the efficacy of hay protein supplementation in managing predominant health fears among cattle. India's vast diversity in terms of temperature, geography, water resources, flora, fauna, and ethnicity has a significant impact on the way land is used and produced. On the other hand, all production methods involve production of livestock. Livestock constitutes backbone of the production system in certain regions, particularly the arid and semi-arid zones of Rajasthan, Gujarat, and cold deserts of Ladakh, Lahaul, and Spiti; trees and food crop waste serve as important sources of feed (Serrano et al., 2020).

Considerations for Integration

With sophisticated hydraulic drive systems, robust diesel engines, and large disc mower-conditioner heads, today's self-propelled windrower models are well-equipped. The productivity of self-propelled windrowers depends critically on speed. That being said, operating conditions have a limit to how much speed can increase output before production starts to slow down. To fully utilize power offered by today's potent models, it is imperative to eliminate any rough places (Hay et al., 2023).

Future Directions and Implications

Improved nutritional quality can be achieved by providing cattle with diverse grazing pastures or blended feeds. Alfalfa, for instance, can be cultivated alone or in combination with a variety of other grass species because it is the highest-yielding perennial forage legume and generates more protein per unit area than other forage legumes (Ntakyo et al., 2020). The optimization of hay protein content has become a priority in fodder production due to the growing strain to sustainably meet the nutritional needs of livestock (Ntakyo et al., 2020).

Technological Advancements in Forage Production

Agriculture must overcome the negative consequences of climate change in the twenty-first century while protecting the environment. In order to attain this equilibrium, improved use of natural resources and efficient management of agricultural practices are essential. A new problem regarding increased fodder biomass production during drought conditions is formation of legume-grass associations as a result of increasing global warming. One novel way to sow in the year of establishment is to employ cover crops to create perennial herbaceous combinations (Ntakyo et al., 2020).

Enhancing Nutrient Management and Soil Health

The difficulties facing agriculture today in achieving greater resource use efficiency are attributed to this measurement. With a short growing season and mechanical farming, specially developed energy crops produce large amounts of biomass or vegetable oils. Energy crops are categorized into three groups based on their biological traits and intended use to produce specific energy products: 1) Wood in short rotation (Paulownia, Poplar, Willow); 2) Grassland energy crops for the production of bioethanol or methane (Miscanthus, Bamboo, Corn, Sorghum, Wheat); and 3) Grassland energy crops for the production of biodiesel (Sunflower, Rape, Soybean) (Silveira and Kohmann 2020).

Exploring Alternative Protein Sources

In the past few years, interest in protein sources as substitutes for animal products has grown dramatically. Although there is a need, there are a variety of reasons why consumers may be motivated, such as allergies, claimed health benefits, worries about animal cruelty or climate change. Enhancing the protein content and overall feed efficiency of cattle may be achieved by incorporating these substitute protein sources into diets based on hay (Li et al., 2023).

Addressing Environmental Sustainability

Environmental and financial benefits are obtained from sustainable agricultural growth. In addition, as nitrogen is essential nutrient putting greatest strain on the environment, modern agriculture aims to increase the efficiency with which nutrients are used. The study illustrated necessity of lessening agriculture's detrimental effects on the environment and addressed the potential for introducing innovative techniques in sustainable agriculture. The concentration of crude protein and digestibility of feed materials were key factors that prompted special attention to low-emission options. Economic elements of animal husbandry were also given special consideration, as were conventional and unconventional sources of protein (Scheurich et al., 2021).

Future Perspectives in Hay Protein Research for Cattle Health

The changes in the enhancement of feed resources and animal nutrition, both past and present, are examined in this study. Global cattle output has been steadily improving over the previous few decades. Growing populations, urbanization, wealth growth, more efficient production systems, and environmental sustainability have all contributed to the majority of the advancements. The job that animal nutritionists were assigned was to optimize feed efficiency in order to produce more livestock products from less feed, in order to fulfill the growing demand for livestock goods worldwide (Tona, 2018).

Nutritional Enhancement

For the dairies, hay is the most economical, highly nutritious source. Hay is the most affordable way to provide native, hybrid, and exotic animals with nutrients, as many people in the area have questions regarding feeding, animal behavior, and the impact on milk yield. But in perennial fodder such as Alfalfa and Rhodes grass, hay varies greatly from field to field and year to year. Numerous factors can significantly vary nutritive value of hay crops, including weather during growth and harvest, harvest timing, variety, and age at harvest. Following harvest, the quality of hay can be impacted by mechanical equipment, temperature, drying time, and hay color (Te Pas et al., 2021).

Functional Feed Additives

By boosting digestibility and preserving and stabilizing the beneficial microbiota in the gut, natural additives in animal feed can increase productivity and performance. Prebiotics, advantageous microorganisms, bacteriocins, phytogenic chemicals, and organic acids are examples of natural feed additives that can meet customer desire for natural products while also offering possibilities for use in nutrition and animal health research. For a variety of reasons, including bettering digestibility, boosting medicinal action, and improving nutritional profile, they are regarded as unique useful chemicals. Antibiotics are the most often used additives because of their preventive properties (Gutierrez-Reinoso et al., 2021).

Precision Feeding Technologies

Precision in livestock feeding necessitates measuring vital data about the feeds and animals before figuring out the ideal feed nutrient concentration. This allows the feed to be automatically fed to animals in accordance with the predetermined production goals, both in terms of quantity and composition (Sejian et al., 2022).

Alternative Protein Sources

Vegan and plant-based proteins are substitutes for animal protein in food technology. These comprise foods derived from algae, insects, fungi (like mushrooms), plants (including grains, legumes, and nuts), and even cultured (lab-grown) meat (Mee et al., 2022).

Genomic Selection and Breeding

Using molecular genetic markers to create innovative breeding programs and new marker-based models for genetic evaluation, genomic selection (GS) is a promising strategy. Fast rates of genetic advancement have been brought about by genomic selection (GS), particularly in developed countries' dairy cattle, where a greater percentage of young bulls with confirmed genomic makeup are now used in breeding. Well-established conventional genetic evaluation systems have served as the foundation for this success (Gutierrez-Reinoso et al., 2021).

Sustainable Forage Management Practices

Sustainable forage management strategies, such as rotational grazing, intercropping, and agroforestry, not only enhance soil health and biodiversity but also improve the quality of hay protein and cattle health. These integrated approaches improve forage systems' resilience to environmental stressors including climate change, promote the natural cycle of nutrients, and reduce reliance on external supplies (Niderkorn and Jayanegara, 2021).

Economic and Policy Considerations

There is a pressing need to support livestock systems that are both economically and environmentally sustainable because the cattle industry faces significant challenges in all areas of sustainability. Furthermore, the majority of European nations consume far more animal protein than is recommended by dietary guidelines. Rebalancing animal and plant proteins in diets is known as the "protein transition," and it is promoted as both a way to encourage healthier eating habits and a way to lessen the negative environmental effects of cow rearing. It is yet unknown, though, how such a shift will affect livestock farmers today (Te Pas et al., 2021).

Conclusion

In conclusion, using hay protein offers a viable way to improve cow health and herd performance as a whole. Hay protein provides important support for several physiological processes essential to cow health through its rich nutritional content, which includes essential amino acids and superior digestion. By addressing significant hurdles such as immuno-suppression, metabolic irregularities, and ruminal acidosis, producers can increase resilience against common health issues by supplementing cow diets with hay protein. Additionally, giving cattle hay protein supplements may improve their immune systems, muscular growth, and reproductive health, all of which will increase their productivity and profitability. Hay protein supplements are now more beneficial and successful in cow feeding regimens due to recent improvements in feed technology and processing procedures that have increased their bioavailability and effectiveness. Research clearly supports benefits of supplementing with hay protein; nevertheless, more studies are required to completely understand the mechanisms underlying these benefits and to optimize their application in a variety of production settings. As part of comprehensive herd management strategies, hay protein supplementation can help producers prioritize cow health while maximizing financial benefits. By using this cutting-edge method, livestock companies may maintain sustainability and profitability while building healthier, more robust herds in the ever-changing agricultural world.

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Chapter 30

Flavors and Microbes: Exploring the Interaction between Diet, Microbiota and Health

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ABSTRACT

The accelerated pace of today's societies, in addition to modifying the ways of communication and coexistence, has wreaked havoc on an aspect that is fundamental for survival: food. The increase in the consumption of ultra-processed foods, with high sugar, sodium and fat content, and the eventual displacement of homemade, fresh and nutritious foods, is progressively increasing the number of people suffering from overweight and obesity around the world, and along with them, the risk of developing metabolic and cardiovascular diseases. The fact that bad eating habits mark the origin of many diseases highlights the importance of taking care of your diet. To ensure health and well-being, the diet must include foods that optimally maintain the microbiota, which contributes to proper intestinal functioning. Like other conventional medicines, such as homeopathy or phytotherapy, which make use of natural products to prepare the extracts with which they treat different conditions, nutrition, by integrating natural foods into a healthy diet, plays a determining role in both care of health, as in the prevention of diseases.

KEYWORDS		
Nutrition, Intestinal microbiota, Probiotics, Prebiotics, Healthy living	Received: 17-May-2024 Revised: 10-Jul-2024 Accepted: 05-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Health is a fundamental aspect for the development of people. The damage to health is not only an impediment for people to develop fully, but also impacts the economy, health systems and society in general, due to the costs involved in their care (Ramírez et al., 2004).

The insistence on following a healthy lifestyle reflects the importance of taking care of the body to have a full life. A nutritious and balanced diet, which provides the body with adequate nutrients to be able to carry out daily activities, is essential. Nevertheless, so are other aspects such as frequent physical exercise, adequate hydration, respecting sleep cycles, maintaining personal hygiene, reducing stress and avoiding toxic habits of alcohol, drug or tobacco smoking, among other aspects, will contribute to this objective. In addition to this, it is important to pay attention to mental health to maintain personal emotional needs and strengthen social coexistence relationships. A healthy life contributes to developing health habits that, in addition to improving our quality of life, prevent or significantly reduce contracting diseases (Cáez and Casas, 2007; Astaraki, 2016).

Despite trying to raise awareness among the population about these measures, dietary patterns worldwide show few changes. Consequently, the problem faced is widespread malnutrition, which includes both deficiencies, excesses, and imbalances in nutrient/energy consumption, increasing the number of people with malnutrition, overweight and obesity, at an alarming rate. Insufficient and/or deficient consumption of nutrients mainly affects growth, representing a great risk to the health and life of those who suffer from it. Underweight (weight less than what corresponds to age), wasting (weight less than height) and insufficiency or lack of nutrients characterize this condition. In contrast, overweight and obesity reflect an energy imbalance: More calories are consumed than expended (Maza-Ávila et al., 2022).

Eating habits associated with overweight and obesity, resulting from the imbalance between food consumption and energy expenditure, today represent a high risk factor for developing diseases. Especially metabolic and cardiovascular types such as high blood pressure, hypercholesterolemia, fatty liver, diabetes, among others (Olatona et al., 2018; Reynoso et al., 2018).

The Pan American Health Organization (PAHO) highlights that in Latin America the increase in the sale and consumption of ultra-processed foods, with high percentages of sugar, sodium and fats, and the eventual displacement of homemade, fresh and nutritious foods, is being decisive in the increase in the frequency of the number of people suffering from overweight and obesity (PAHO, 2019).

Magnitude of the Global Nutritional Problem

Recent estimates project that of the 2.6 billion people with obesity in 2020, the figure may reach 4 billion in 2035. By 2020, the number of people over 5 years of age, totaling those who were overweight (BMI ≥ 25kg/m^2 and obese (BMI ≥ 30kg/m^2) was 2,603 (38% of the population). The proportion of people with obesity (including all age groups) was 985 (14%), with an economic impact of 1.96 trillion US$ globally (Lobstein et al., 2023). (Table 1) shows the most recent data on obesity at a global level, with a differentiation by regions and age groups.

Table 1: Number and proportion of people with obesity by region in 2020*

REGION	Children and Adolescents (5-19 years)				Adults (> 20 years)				Economic Impact (Billions US$)
	NIÑOS		NIÑAS		HOMBRES		MUJERES		
	PREV (Mill)	PROP (%)	PREV (Mill)	PROP (%)	PREV (Mill)	PROP (%)	PREV (Mill)	PROP (%)	
African[1]	6	3	10	5	18	7	50	18	23
Americas[2]	24	20	18	16	111	32	135	37	870
Eastern Mediterranean[3]	14	11	13	11	43	20	60	30	70
European	11	13	7	8	89	26	103	28	516
South-East Asian	14	5	8	3	28	4	51	8	65
Western Pacific	36	19	16	9	58	8	62	9	412
Total prevalences	105		72		347		461		1,956

[1] Sub-Saharan Africa; [2] North, Central and South America; [3] North Africa and Middle East; PREV: PREVALENCE (Number of cases, in millions). PROP: PROPORTION (Percentage of the population); * Prepared from the data reported in (Lobstein et al., 2023).

The above data show the dimensions and economic impact associated with obesity; in infants, it affects more males and in adults, it affects more females. The study recently carried out by *GBD Diet Collaborators* shows the background of this problem. In this study, they evaluated the consumption of the main nutrients and foods in 195 countries, to quantify their impact on morbidity and mortality from non-communicable diseases. The risk factors included the analysis of low diets and diets rich in different components. Diets low in: fruits, vegetables, legumes, whole grains, nuts and seeds, milk, fiber, calcium, omega-3 fatty acids and polyunsaturated fatty acids. Diets rich in: red meat, processed meat, sugary drinks, trans fatty acids and sodium (GBD, 2019).

With the results obtained, they determined that worldwide the consumption of the vast majority of nutrients and healthy foods is suboptimal. The average consumption of milk, nuts, seeds and cereals (combined) was 12%. Only 16% milk and 23% for whole grains. In comparison, the intake of unhealthy foods was higher, compared to the maximum recommended consumption. For sugary drinks (95% higher than the optimal amount), red meat (18%), processed meat (90%) and sodium (86%). Likewise, they determined that food intake (both healthy and unhealthy) is higher in men than in women aged 50-69 and lower for young adults (25-49 years), although the latter consume more sugary drinks. Although they conclude that at a global level the consumption of healthy foods is less than optimal, some exceptions by region stand out. For healthy foods, a high consumption of legumes for the eastern and western regions of Sub-Saharan Africa, the Caribbean and South Asia. High consumption of vegetables in Central Asia and seafood rich in omega-3 in the Asia Pacific region. Regarding unhealthy foods, they determined that worldwide consumption of sodium and sugary drinks exceeds the estimated optimal. The highest consumption of red meat corresponds to Australia, South America and Tropical Latin America. For processed meat, North America was the largest consumer, followed by Western Europe and the Asia Pacific region. Regarding the consumption of Tran's fats, the highest records correspond to North America, Central America and Andean Latin America. Regarding the association with the number of deaths, they report that the risks associated with diet were responsible for 11 million deaths. Cardiovascular diseases were the main cause of diet-related death, as well as type 2 diabetes mellitus (GBD, 2019).

The set of these results makes it evident why nutrition care is currently acquiring greater relevance throughout the world. In this regard, the World Health Organization (WHO) identifies unhealthy diets and lack of physical activity as the main risk factors for health. Therefore, it highlights the importance of consuming a healthy diet from the beginning and throughout life, to improve health and quality of life, as well as to avoid malnutrition and associated non-communicable diseases. Among its recommendations are to ensure that caloric intake is balanced with caloric expenditure (exercise). Do not exceed fat consumption of 30% of caloric intake, free sugar consumption of 10% and keep salt consumption below 5g/day (WHO, 2018).

Like other conventional medicines, such as homeopathy or phytotherapy, which make use of natural products to prepare the extracts with which they treat different conditions, nutrition, by integrating natural foods into a healthy diet, plays a determining role in both care of health, as in the prevention of diseases. Likewise, it can contribute as a complementary or alternative therapy to the improvement of patients with various diseases, and for whom adequate nutrition is essential for their recovery (Caminal, 2005; Meza, 2015).

Role of the Intestinal Microbiota in Health

To ensure health and well-being, the diet must include foods that optimally maintain the intestinal microbiota, made up of highly beneficial microorganisms that digest complex polysaccharides, produce vitamins, recover nutrients and energy, as well as protect the body against pathogens. Taxonomically, 9 phyla of bacteria are identified in the microbiota. The greatest diversity corresponds to the phylum Firmicutes, followed by Bacteroidetes and Proteobacteria. Due to its diversity, a high proportion (~90%) of the microbiota includes bacteria from the phyla Firmicutes and Bacteroidetes, although the most numerous is the former with about 64% of the bacteria present in the intestine. Firmicutes are gram-positive bacteria, whose most representative genera are *Clostridium, Enterococcus, Ruminococcus, Peptostreptococcus* and *Faecalibacterium*, some of which are probiotics. In the Bacteroidetes, gram-negative bacteria are included, including species that are important glycan degraders (*Prevotella, Bacteroides*). Other representative bacteria of this phylum are *Panabacteroides, Alistipes, Butyrimonas, Paraprevotella* and *Odoribacter* (Guarner, 2007; Kim et al., 2017; Sánchez-Tapia et al., 2019).

The microbiota performs the following functions (Guarner, 2007; Garza-Velasco et al., 2021):

1. Nutritional and metabolic: They participate in the metabolism of substrates or residues incorporated into the diet that the intestine cannot digest, thanks to the enzymes and biochemical routes that follow in the degradation of food. These processes, in addition to generating the energy necessary for the proliferation of bacteria, benefit the body both through the energy recovered from the diet and through the absorption of ions such as Fe, Ca and Mg in the colon. They also participate in the synthesis of amino acids and vitamins (folic acid, biotin, pantothenic acid, vitamins K and B12.
2. Protection: They generate a protective barrier that prevents foreign bacteria, which enter along with contaminated food, from implanting, thanks to the ability to secrete bacteriocins, (antimicrobials). These substances control harmful species that generally produce diarrheal symptoms, such as colicins produced by *Escherichia coli*, which act against other variants with enterotoxigenic, enterohemorrhagic or inter-aggregative effects. In this protection, the microbiota to maintain its populations in balance, but in adverse conditions, such as competition for nutrients when they are scarce, this balance is broken.
3. Trophic: Participates in the control of the proliferation and differentiation of intestinal epithelial cells, principally enterocytes, whose role is to prevent the passage of microbiota bacteria from the lumen of the intestine to the submucosa, to prevent the generation of an immune response. It also has a fundamental role in brain development, memory, learning and mobility, due to its participation in the synthesis of neurotransmitters such as GABA (γ-aminobutyric acid) and serotonin. Serotonin participates in peristalsis, although synthesized in the brain; is produced in the intestine from the degradation of plant fibers by the microbiota. In addition, bacteria such as *Ruminococcus* and *Clostridium sporogenes* produce serotonin from the decarboxylation of tryptophan. While GABA, with antidiabetic, diuretic and analgesic effects, is produced by bacteria such as *Bifidobacterium* and *Lactobacillus* through the decarboxylation of glutamic acid (Guarner, 2007; Garza-Velasco et al., 2021).

Despite the importance of these functions of the microbiota for the well-being of the organism, under certain conditions the intestinal environment undergoes changes that alter bacterial functioning. The greatest effects are associated with the regular consumption of medications, antacids, anti-inflammatories, laxatives, and particularly, antibiotics. Incorrect, prolonged and/or excessive use of antibiotics can generate negative impacts on the diversity, functioning and density of the microbiota. These changes generate vitamin K deficiencies, an increasing the intestinal dominance of pathogenic bacteria over beneficial bacterial diversity, mainly. Consequently, the loss of the natural protection conferred by the intestinal microbiota harms the body, leaving it exposed to the colonization of exogenous pathogenic bacteria, thereby increasing the risk of developing diseases. These alterations lead to *Dysbiosis*, which is both a quantitative and qualitative alteration of the bacterial microbiota. Among the extrinsic factors that alter the microbiota are the consumption of chlorinated water, stress, environmental microbial load, but especially due to the type of eating habits (Shirakawa et al., 1990; Salinas, 2013; Kim et al., 2017; Yan et al., 2022).

Influence of Diet on the Intestinal Microbiota

Various research has generated evidence of the close relationship between diet and intestinal microbiota. Ley et al. (Ley et al., 2009) carried out a research in which they did a network-based analysis of sequences of the bacterial 16S rRNA gene of the fecal microbiota of humans and 59 species of mammals, free-living and others, which live in captivity. From these sequence networks, they mapped the composition and structure of the microbiota in the phylogeny and diet of the studied mammals. The purpose was to correlate the evolution of mammals with their microbes. One of the conclusions they reached is the establishment of a coevolutionary pattern between the animal species and its microbiota. This makes mammal's metagenomic, since in addition to their own genetic load they are composed of that of all the genomes of their associated microbes (microbiome). They determined that the adoption of a new diet generates physiological changes and activates adaptation and evolutionary mechanisms. Likewise, the different diets of herbivorous, carnivorous and omnivorous animals introduce significant variations in the composition of the intestinal microbiota.

In another study, they compared two groups (Dedauko and Sengele) of hunter-gatherers from Hazda, Tanzania. One of the last communities that currently preserve a foraging lifestyle. They do not practice agriculture, nor the domestication of plants or animals. They found that due to the type of diet they eat, there is a greater diversity of Bacteroidetes and Actinobacteria. They explain this fact by less dependence on antibiotics and a greater consumption of unrefined foods, since they feed on what they can collect in each season of the year. Their diet includes berries, tubers, baobab, meat and honey.

They determined that the Hazda share a higher density of populations of *Succinivibrio*, *Prevotella* and *Treponema* with other African tribes. Their findings confirm that the microbiome is a diverse and receptive ecosystem in constant adaptation as another component of the person who carries it (Schnorr et al., 2014).

Finally, in a research that compared the fecal microbiota of European (EU) children from Florence (Italy), against children from a rural African village in Burkina Faso (BF). The diet of European children was in line with the developed world. Rich in proteins of animal origin, carbohydrates, starch, fats and low in fiber. The diet of the village children was similar to that consumed by Neolithic farmers. Predominantly vegetarian, low in animal proteins (chicken or termites) and fat, rich in fiber, polysaccharides, starch and vegetables. In BF, they determined a significant presence of Bacteroidetes and a significant reduction of Firmicutes, with the presence of *Prevotella* and *Xylanibacter*, capable of hydrolyzing cellulose and xylan, both absent in EU. With a significantly higher amount of short chain fatty acids in BF than in UE. *Shigella* and *Escherichia* showed low presence in BF, while in EU it was significantly high. They concluded that in BF, the coevolution of the microbiota allows maximizing the intake of foods rich in fiber (De Filippo et al., 2010).

Research such as the ones mentioned above shows the clear influence that diet has on the intestinal microbiota. Different contributions developed in this regard highlight the following:

1. Dietary habits are one of the main factors that contribute to diversifying the intestinal microbiota (Bäckhed et al., 2005).
2. The composition of the microbiota depends on dietary habits, in the same way that health depends on microbial metabolism (De Filippo et al., 2010).
3. The consumption of proteins and fats of animal origin establishes a relationship with the phylum Bacteroidota, while carbohydrates with the phyla Bacteroidetes and Firmicutes, which implies that there is an association with dietary patterns (Wu et al., 2011).
4. The intestinal microbiota varies depending on diet, lifestyle and environment (Schnorr et al., 2014).
5. The quantity, quality, type and balance of carbohydrates, proteins and fats contained in the diet have a great impact on the intestinal microbiota, essentially due to the degradation products that are generated (Walsh et al., 2014).
6. Diet alters the metabolism of the intestinal microbiota. Foods not digested by the body are the substrate for bacterial metabolic activities (David et al., 2014).
7. The type of diet influences intestinal transit time; it is faster with diets of plant origin and slower with diets of animal origin (Shen et al., 2014).
8. The microbiota provides additional potential for adaptation to different lifestyles and directly influences health (Schnorr et al., 2014).
9. A diet that includes foods of animal origin promotes greater microbial diversity and an increase in bile-tolerant bacteria (Bacteridota), while Firmicutes decreases (David et al., 2014).
10. Diet produces changes in the composition of the intestinal microbiota, which alter the homeostasis of the body, with repercussions for health (Basain et al., 2015).
11. Foods integrated into the diet influence the structure and composition of the microbial communities of the intestine (Álvarez et al., 2018).
12. Diet is crucial in modulating the intestinal microbiota (Sánchez-Tapia et al., 2019).
13. Diet can generate imbalances in the intestinal microbiota that result in the generation or exacerbation of chronic diseases (Garza-Velasco et al., 2021).
14. Dietary changes show important effects on the intestinal microbiota in short periods of time (Tinahones, 2023).

Based on this knowledge, different diets seek to promote these changes in the microbiota for the benefit of health. Among them:

Vegetarian Diet

This diet make distinctions, depending on what each group consumes. Strict vegetarians or vegans (they do not consume foods of animal origin), lactovegetarians (vegetables and dairy products) and ovolactovegetarians (vegetables, dairy products and eggs) (Santana and Carbajo, 2016). (Table 2) integrates the benefits that this type of diet.

Mediterranean Diet (MedDiet)

It integrates the foods and lifestyles of the Mediterranean region. Includes a high consumption of fruits, vegetables, cereals and seeds. Also, minimally processed, fresh in season and locally grown. High consumption of extra virgin olive oil, as the main source of fat. Dairy products in moderation. Red meat, poultry and fish in low-moderate quantities. Herbs and spices. It includes a high consumption of nuts and olive oil, and moderate wine with meals. Considered one of the diets that provides the greatest benefits to the intestinal microbiota (Sofi et al., 2013; Guasch-Ferré and Willet, 2021). (Table 3) integrates the benefits that the Mediterranean diet brings to the microbiota and health.

Milpa Diet ("Dieta de la Milpa")

Diet identified for the Mesoamerican region (from central Mexico to Central America). It incorporates four basic foods (beans, corn, pumpkins and chili), produced in the region. In adittion, locally grown foods during the rainy season. Includes tomatoes, starchy vegetables, legumes and whole grains, water, fish. Avoid red meat, artificial sweeteners and processed foods. Low dairy consumption. Food animal origin includes game animals (rabbit or deer) and insects as a source of animal protein (Biruete et al., 2024). (Table 4) integrates the benefits that the Mediterranean diet brings to the microbiota and health.

Table 2: Microbiota and health benefits of vegetarian diets

VEGETARIAN DIET	
Benefits to the microbiota	Health benefits
* Promotes the development of more diverse and stable microbial systems * Significantly high Bacteroidetes counts * Polyphenols increase the amount of *Bifidobacterium* and *Lactobacillus*, with antimicrobial, anti-inflammatory and vascular protection effects The fiber: * Increases the number of lactic acid bacteria (*Ruminococcus*, *E. rectale* and *Roseburia*) * Reduces the number of *Clostridium* and *Enterococcus* * Promotes the growth of species that ferment it to form short-chain fatty acids	Improvements in: * Immunity against pathogens * Integrity of the blood-brain barrier * Supply of energy substrates * Intestinal peristalsis Reduces Incidence of: * Reflux * Irritable bowel syndrome * Lower incidence of obesity * Coronary heart disease * Hypertension * Type 2 diabetes

(Santana and Carbajo, 2016; Tomova et al., 2019)

Table 3: Microbiota and health benefits of the Mediterranean Diet (MedDiet)

MEDITERRANEAN DIET	
Benefits to the microbiota	Health benefits
* The fiber in foods, favors the metabolic and fermentative processes of bacteria. * The consumption of probiotics contributes to strengthening the balance of the intestinal microbiota. * Antioxidants in foods enhance bacterial growth * Phytosterols contained in cereals, nuts, dried fruits, legumes and olive oil contribute to lactic acid bacteria with HSB activity (Lactobacillus acidophillus) reducing cholesterol levels through interaction with bile. (Márquez-Villalobos et al., 2017; Urquiaga et al., 2017)	Reduction of: * Incidence of cardiovascular events. * Risk factors for obesity, hypertension, metabolic syndrome and dyslipidemia. * Incidence of diabetes. * Age-related cognitive dysfunction. * Incidence of neurodegenerative disorders (Alzheimer's). * Visceral fat. * Glycosylated hemoglobin in newly diagnosed patients * Fasting plasma glucose * Serum insulin levels * Insulin resistance * Central adiposity Improvements in: * Glycemic control * Oxidative stress * Insulin sensitivity * Lipid profile * Intestinal microbiota

(Guasch-Ferré and Willet, 2021; Muscogiuri et al., 2022)

Table 4: Microbiota and health benefits of the Milpa Diet ("*Dieta de la Milpa*")

MILPA DIET	
Benefits to the microbiota	Health benefits
* Promotes acid-alkaline balance * Fiber increases the number of beneficial bacteria (Bifidobacteria and Lactobacilli). * Phytosterols help lactic acid bacteria reduce cholesterol levels through interaction with bile * Omega-3 EPA and DHA promote the restructuring of the composition of the intestinal microbiota, reducing inflammation and improving neurotransmission	Reduction of: * Progression of kidney disease * Risk of insulin resistance * Risk of metabolic syndrome * Risk of developing diabetes mellitus * Risk of kidney problems * Bone demineralization * Risk of cardiovascular diseases Promotes: * Cardiometabolic Health * Appropriate values of renal acid potential * Regulation of blood glucose levels, by incorporating complex carbohydrates

(Dawson-Hughes et al, 2008; Almaguer et al., 2018)

The Role of Prebiotics and Probiotics in Intestinal Health

The consumption of prebiotics and probiotics is essential for strengthening the intestinal microbiota. *Prebiotics* are food components made up of oligosaccharides or polysaccharides, indigestible for the body, but very useful for the microbiota. A prebiotic must meet the following requirements:

a) It should not be absorbed or hydrolyzed in the upper portion of the digestive tract. It must be resistant to the action of gastric acids, enzymatic hydrolysis, or absorbed in the small intestine.

b) Susceptible to fermentation by the beneficial bacteria of the intestinal microbiota.

c) Induce beneficial effects for the health of the organism (Corzo et al., 2015).

During the prebiotic digestion process, microorganisms produce micronutrients, metabolites and energy useful for the body. Prebiotics participate actively, modulating the activity and composition of the microbiota. By contributing to their nutrition, they also favor the multiplication of beneficial bacteria, mainly increasing the populations of Bifidobacteria and lactobacilli (Sánchez-Tapia et al., 2019).

They include a wide group of compounds, although the best known are inulin, galacto-oligosaccharides, oligofructose, lactulose and fructo-oligosaccharides. They are present in foods such as legumes, wheat, oats, garlic, onion, honey, among others. Its benefits are diverse; in addition to directly benefiting the microbiota they promote the health of those who ingest them. They increase the number of beneficial bacteria and strengthen the absorption of minerals and the production of short-chain fatty acids. They modulate lipid metabolism decreasing the synthesis of triglycerides and lipoproteins, thereby reducing cholesterol and triglyceride levels in the blood (Hutkins et al., 2016; Sánchez-Tapia et al., 2019; Peña-Montes et al., 2022).

On the other hand, Probiotics are organisms that, when consumed in adequate quantities, produce benefits to the body. They contribute to the modulation of the intestinal microbiota, controlling the pathogens that have entered the digestive tract, thereby reinforcing immune defense mechanisms. Probiotic cells are classified into: a) True probiotics (TP), the cells are live and active, b) pseudoprobiotics (PP), with live but inactive cells (vegetative bodies or spores) and c) ghost probiotics (GP) the cells are lysed, dead and not viable (Márquez-Villalobos et al., 2017; Zendeboodi et al., 2020).

The beneficial effect of different probiotics is associated with their metabolic, immunological and neuroendocrine properties. The positive effect they generate on the development of the intestinal microbiota stands out, helping to regulate the homeostasis or functioning of the intestines, by maintaining the necessary balance between beneficial and pathogenic bacteria (Schachtsiek et al., 2004; Quigley, 2019).

Genetic and molecular studies have identified the following mechanisms involved in the beneficial effects of probiotics: a) Immunomodulatory activity that they exert on the host. b) Antagonistic activity, expressed by the production of substances that destroy pathogenic organisms. c) Participation in the inhibition of toxins from pathogenic bacteria and d) Competition against pathogens for nutrients and epithelial adhesion sites. These mechanisms are essential in the maintenance of the microbiota, prophylaxis and treatment of diseases (Khalesi et al., 2014; Markowiak-Kopeć and Śliżewska, 2017; Mazziotta et al., 2023).

Conclusion

One of the problems in all regions of the world is associated with food. In some regions, environmental and geographical conditions significantly reduce the possibilities of having enough food to meet the population's demand. Socially, a significant number of people suffer from hunger, not because of lack of availability, but because they do not have the means to access them. Regardless of the conditions, the truth is that currently there are many options to take care of your diet. We must overcome the idea that talking about diets means submitting to a restrictive regime where prevented from eating what we like. Rather, it is about understanding food from that very common expression in Mexico of "we are what we eat." Changing eating habits to achieve a healthy diet does not imply thinking about making large investments to purchase certain foods. It is integrating into our diet foods that are locally within our reach, in the necessary quantities and in a balanced way, based on dishes that combine flavors with good nutrition, to keep our intestinal microbiota in good condition, which guarantee a good state of health.

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Chapter 31

Exploring the Synergy: Alternative Approaches in Nutrition with a Focus on Soybean Functional Products

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ABSTRACT

New plant-based products have emerged due to a high demand for non-dairy products and new plant-based milk and meat product categories. Soya beans have also been identified to have health-enhancing qualities, especially for those who have had a high soy protein intake in recent decades. Products made from soy are very popular among the growing population with special requirements for their diet and health conditions. From the present evidence, it can be concluded that soy products decrease the probability of developing several age-related chronic diseases, with epidemiological studies suggesting that individuals who eat soy products have a significantly reduced prevalence of these diseases than those who rarely incorporate soy products in their diets. The benefits of soy components mostly relate to lower cholesterol levels, the treatment of menopausal symptoms, and the prevention of chronic ailments including cancer, heart ailments, and osteoporosis. Soy products come in various flavors and textures and they may be incorporated to form low-fat meals that are nutritiously balanced. The main objective of the chapter is to explore the alternative nutritional practices and the functional benefits of soybean products. The growing market of soybean functional products represents a major turn toward consumer demand for health, sustainability, and personalization. In response to changing tastes and increasing consumer demand for functional, health-promoting foods, including soybean-based probiotics, protein powders, and other products in the meat analog category — the industry has made important strides forward. These also satisfy needs like gut, protein boost, and sustainable eating which resonate well with the larger wellness trend. Planning; and use of environmentally sustainable packaging like soybean-based ‘bioplastics’ also offers a compelling roadmap for sustainable leather manufacturing. Such undertakings assist in the fight against the existing issue of plastic pollution in real-time while also signaling a commitment toward more sophisticated and sustainable aspects of production.

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INTRODUCTION

New concepts of nutrition include new food choices including plant-based diets, functional foods, and nutraceuticals that enhance the body's health other than giving it nutrients. These call for enhanced intake of more nutrients that would help avert diseases and improve the standard quality of life. This chapter describes why soybeans contain high nutritional values such as proteins, vitamins, minerals, and biochemical compounds such as isoflavones. It has been credited with various positive effects and these are reduced incidence of cardiovascular diseases (CVD), enhanced bone status, and anticancer properties. Soybeans are part of the complementary food sources because they are rich in proteins besides containing other essential amino acids. They include functional soybean products, soy protein isolates, soy flour, fermented soy products, etc, all of which offer better nutrition and functionality. They are employed for leavening foods, to create distinct textures, as well as to enhance specific health benefits. Soybean or soy is an ingredient that is used in a variety of products and all these products are discussed in this chapter. It is confirmed that the incorporation of soybean products in other meal patterns can enhance health benefits. For instance, plant-based diets can be supplemented with soy protein to meet the required intake of protein while at the same time, deploying the health benefits of isoflavones.

The combination of soy-based products and other functional meals can have synergistic benefits that improve overall health. This is covered in detail in this chapter. Several case studies demonstrate the effective incorporation of soybean products into a variety of dietary habits. These examples demonstrate how soy-based ingredients have been employed to create nutritionally superior bakery products, meat alternatives, and health supplements. Practical applications show the feasibility and benefits of adding soybeans to daily meals, all are covered in this chapter.

Overview of Alternative Nutritional Approaches

Sustainable, tasty, safe, nourishing, readily available, and reasonably priced products are what consumers want. Developing new sources and ingredients requires careful consideration of several factors. In this sense, there is still room for improvement in the manufacturing of meat substitutes like cultured beef. There is also a lot of potential in other biotechnology processes, such as microalgae cultivation, fermentation, or the addition of microorganisms, such as those that create vitamin B12. It is important to note that certain plant-based products may be appropriate for people with specific needs; particularly those who are allergic to components found in animal-based meals or have chronic illnesses that have been shown to improve with more vegetable consumption and less animal-based food. As a result, keeping the ecosystem healthy should be consistent with sustaining a healthy human population, because humans, animals, and plants are all part of it (Alcorta et al., 2021).

Plant-based milk alternatives are water-soluble extracts from legumes, cereals, pseudo-cereals, nuts, and seeds that mimic cow's milk. These plant materials break down in water, resulting in homogenized milk-like fluids similar to cow cheese. The primary reasons for using these milk substitutes include vegetarian or vegan diets, medical conditions like lactose intolerance, or cow's milk protein allergies (Silva et al., 2020).

Plant-Based Diets: Benefits and Challenges

The plant-based diet, even though nontraditional, aims to modify the diet to incorporate only raw, unprocessed, or minimally processed plant-based foods instead of processed and animal products. A vegetarian diet might be chosen for health for ethical, political, religious, or just economic reasons. Scientifically, there is increased interest in plant-based diets concerning their nutritional and medicinal values. There are several variations of vegetarian diets such as vegan, lacto-vegetarian, ovo-lacto-vegetarian, semi-vegetarian, and pesco-vegetarian. It is to be understood that a vegetarian diet is safe at any age when properly planned and properly managed (Corrin and Papadopoulos, 2017).

The main motivations for a vegetarian diet are the favorable health advantages of a plant-based diet which lowers body fat and obesity rates and decreases factors that are leading to diseases. Benefits of happiness and well-being (better standard of living and optimistic impacts on the person and social environment, and even on the advancement of health) come after those linked to health. Lastly, there are advantages related to ethics and the environment, more effective use of financial resources encourages the preservation of all life on Earth (Rosenfeld, 2018).

The preference for meat and the challenge of giving it up are the primary roadblocks to a vegetarian diet. The second most common reason is health concerns, for which the most common deficiency is in specific constituents (nutrients), such as essential vitamins. Evidence indicates that meal preparation takes too much time; therefore, a plant-based diet could get monotonous and unpalatable in terms of convenience and time. Vegetarian cuisine options at restaurants are typically not very great. Furthermore, if the person's family does not adhere to the vegetarian diet's guidelines, it could become bothersome (Ruby, 2012).

This could potentially impede the shift to a plant-based diet, as there doesn't seem to be a lot of trustworthy information accessible regarding this kind of eating. Living a vegetarian lifestyle might result in social restrictions, discrimination (negative connotations and the possibility of eating disorders developing as a result), and imitation-based motivation. In addition, budgetary restrictions may occur because some plant-based diet ingredients are too costly to buy (Feher et al., 2020).

Functional Foods

Functional foods are food products that offer health benefits and can be differentiated from basic nutritional and nutraceutical products containing high bioactive compounds. This hypothesis has received much attention from scientists and business people because of its contribution to health promotion and disease avoidance. Nutraceuticals are dietary supplements that contain concentrated bioactive constituents in a non-food format to support health at higher levels as compared to traditional foods. These supplements come in tablet, capsule, and extract forms which are reminiscent of a pharmaceutical product. The consumer interest in the beneficial aspects of foods with altered nutrient composition and unchanged taste is highly promising for functional foods. Functional foods are products that are designed with health-promoting benefits other than the basic nutritional value of regular foods (Jooyandeh, 2011).

Health Benefits of Functional Foods

Livestock eating patterns are closely aligned to the promotion of health and well-being through the consumption of foods. In recent years these substances have been given more attention by researchers, consumers, and food suppliers because finding foods with health benefits is one of the best ways to enhance health in the community. Several epidemiologic investigations conducted over the past five decades have also conclusively demonstrated the benefits of the consumption of fruits, vegetables, and products with plant-based fibers in the reduction of the risks of chronic diseases including cardiovascular diseases, diabetes, obesity, and other related diseases and enhancement of overall quality of human health. This discovery has made people around the world aware that foods derived from plants possess health qualities since the scientific world has found plant bioactive compounds to have positive health impacts. Consumption of fruits, vegetables, and whole grains has been indicated to reduce risks of chronic diseases, such as cancer and cardiovascular diseases that are some of the leading causes of death in Europe and the US (Balsano and Alisi, 2009; Cencic and Chingwaru, 2010).

Table 1: Types of Functional Foods

Types of foods	Explanation	Examples
Basic	These have naturally bioactive init	• Carrots are full of beta-carotene • Oat bran cereals are rich in beta-glucan
Bioactive added processed	During the processing of foods bioactive added additional	• Calcium added orange juice Omega-3 added milk
Enhanced naturally present bioactive compounds	Degree already naturally existing bioactive is adjusted (for example, by genetic engineering or breeding).	• Fortified yogurt with prebiotic • Increased lycopene in tomatoes • Higher omega-3 fatty acids eggs

(American Dietetic Assocaition (ADA); Gul et al., 2016)

Plant-based Functional Foods

An epidemiology data set provides compelling facts that a plant-based diet is capable of lowering the incidence of chronic illnesses, especially cancer. According to research by Block et al. (1992), the risk of cancer was only half that of persons who consumed a diet high in vegetables and fruits compared to those who consumed fewer of these items. It is now evident that a plant-based diet can lower cancer risk in ways other than just consuming traditional nutrients. These physiologically active plant compounds are now referred to as "phytochemicals," having been identified by Steinmetz and Potter in 1991. Phenolics and carotenoids found in vegetables and fruits, as well as lignans, β-glucan, as well as inulin found in cereal-based goods, are the most significant phytochemicals. Plant-based diets have several essential preventive effects, including lowering blood pressure, heart disease risk, cholesterol, tumor incidence, slowing gastric emptying, and preventing cancer and CVDs (Szabo et al., 2016).

Soy is rich in nutrients, high in fiber, and a strong source of protein, and have garnered attention recently for their possible role in the avoidance and cure of degenerative diseases through diet (Singh et al., 2008). Isoflavones, specifically genistein and diadzein, are found only in soybeans and serve a variety of biological purposes. It is believed to have therapeutic and preventive effects on osteoporosis, cancer, cardiovascular disease, and the reduction of menopausal symptoms (Jabeen, 2016).

Nutritional Composition of Soybean

Soybean is scientifically called Glycine max and it belongs to the legume family of plants. It contains about 40% protein, 20% oil, and 35% carbohydrates which include both soluble and insoluble dietary fiber and sugars such as sucrose, raffinose, and stachyose and 5% ash. Green soybeans have approximately 14% moisture content. Soy protein products can be easily digested in human digestive systems and have a digestion coefficient of 92-100%. Historically, soybeans have been referred to as the "meat of the field". Soybeans primarily contain two key components: lipids and proteins. Soybean oil contains important fatty acids, has a low level of saturated fatty acids, and is a source of vitamin E. Soybean contains 15% saturated fatty acids, 61% PUFA, and 24% MUFA. Soybeans are also one of the few plant sources of omega-3 fatty acids, particularly alpha-linolenic acid, in addition to omega-6 fats (Jooyandeh, 2011).

A well-balanced spectrum of amino acids can be found in soybeans. Soybean protein is of an equivalent quality to animal protein sources such as milk and meat. Cereal proteins, which are usually low in lysine, are a suitable match for soy proteins' high lysine level. Recent research suggests that selective tumor retardation (seen in rat trials) may be facilitated by the decreased methionine level of soybean proteins relative to casein. The main components of soy protein are glycinin (11S globulin) and β-conglycinin (7S globulin). These two important proteins' physicochemical processes—emulsification, foaming, gelation, and the capacity to bind water and fat—depend on the makeup and structure of their amino acids (Hawrylewicz, 1995).

Bioactive substances known as phytoestrogens or isoflavones are found in soy protein products; genistein, daidzein, and glycitein are the primary types. Depending on the techniques used for processing, such as dehulling, flaking, and defatting, the concentration of these isoflavones in soy products might differ significantly. While textured soy protein keeps more of these components, soybeans can generate a comparatively pure protein with little isoflavone concentration. In textured soy protein, soy flour, and soy granules, isoflavone levels range from 2mg/g protein to 0.6 to 1.0 mg/g protein in isolated soy protein (Cenic and Chingwaru, 2010). Depending on the processing technique, soy protein concentrates have varying amounts of isoflavones; in general, alcohol-extracted soy products have less isoflavones than concentrates that have been water-washed. Soy flour contains a fairly high quantity of isoflavones, but soy sauce and oil usually contain very little of these substances. Miso, tofu, tempeh, and soy milk have smaller but still significant amounts of isoflavones (Dwyer, 1994; Anderson and Wolf, 1995).

Isoflavones have the potential to lower the risk of several cancers, such as those of the breast, lungs, colon, rectal, stomach, and prostate. Although genistein is the subject of most studies on the anticancer effects of soy isoflavones, research indicates that daidzein is more bioavailable. By interfering with enzymes that promote cancer, inhibiting hormone function, and obstructing the flow of nutrients and oxygen to tumors, genistein is thought to protect against cancer (Broihier, 1997).

Health Benefits of Soy Consumption

Although soy products have been consumed for more than a millennium, they have just become more widely accepted in Western diets in the last 20 years. Because of their high protein and isoflavone content, soybeans are now known to have health advantages, especially in the prevention and treatment of chronic disorders. Frequent use of soy products can reduce the chance of developing long-term illnesses like cancer, heart disease, and stroke. Foods made from soy provide a variety of healthy nutrients, such as fiber, vitamins, and minerals. Several clinical experiments have investigated the possibility of soy as a preventative measure against chronic illnesses (Martini et al., 1999).

Osteoporosis

Because of the loss of calcium and other minerals, osteoporosis is an illness marked by porous and brittle bones. Foods containing soy may help both, prevent and treat osteoporosis. Several researchers are looking into how isoflavones could slow down the rapid bone loss that comes with menopause because their structures are comparable to those of estrogen. Soybeans and soy-based products include large levels of isoflavones including genistein and daidzein, which may help prevent bone resorption. Asian women who consume a lot of soy protein are thought to have higher bone mineral density (Messina, 2002), according to epidemiological studies. The body absorbs soy quite efficiently when combined with calcium. Foods made from soy may also provide additional advantages for bone health. The use of 40 grams of isolated soy protein each day for six months enhanced both mineral content and density considerably, according to a study by Erdman and Potter, 1997. Soy milk with added calcium is an excellent source of calcium as well (Erdman and Potter, 1997).

Diabetes

Due to low glycemic index, legumes—especially soybeans—are beneficial in a diabetic diet. Frequent soy protein ingestion may help reduce the symptoms of type 2 diabetes. Studies have indicated that soy can decrease glycosylated hemoglobin levels, enhance glucose tolerance, and lessen postprandial hyperglycemia (Bhathena and Velasquez, 2002).

Excessive Weight

Obesity is associated with aberrant lipid metabolism, insulin resistance, and hyperinsulinemia. It also involves an imbalance in the management of energy. It is a significant risk factor for atherosclerosis, cardiovascular disease, Type II diabetes, and some types of cancer. Fat cells, or adipocytes, play a critical role in preserving lipid homeostasis. When energy is abundant, they store it as triglycerides and release it as free fatty acids when needed (Bhathena and Velasquez 2002).

Consuming too much fat might cause preadipocytes to differentiate into mature adipocytes and existing adipocytes to grow to meet the body's increased requirement for storage. Important regulators of gene expression and lipid content in adipose cells include several transcription factors (Harp, 2004). The regulation of adipogenesis is greatly aided by hormones such as insulin, glucagon, thyroid hormone, estrogen, growth hormone, and insulin-like growth factors. The most common estrogen, 17 β-estradiol, is important in controlling the quantity and development of adipocytes in both males and females. Isoflavones exhibit mild estrogenic effects in different tissues due to their structural resemblance to endogenous estrogens. They compete with 17 β-estradiol for binding to intranuclear estrogen receptors, which can result in either estrogenic or antiestrogenic actions. Regular soy protein consumption was linked, according to Bhathena and Velasquez, to lower fasting insulin levels, a lower body mass index, and greater levels of HDL cholesterol in postmenopausal women (Orgaard and Jensen 2008).

Mental Processes

According to recent research, soy isoflavones may influence metabolism in the hippocampus and frontal cortex of the brain by activating estrogen receptor β, which is widely distributed in these regions. In the hippocampus and frontal cortex, isoflavones may also raise the mRNA levels of neurotrophins and choline acetyltransferase (Singh et al., 2008). While the frontal cortex is critical for working memory, sifting out irrelevant information, and other executive cognitive processes, the hippocampus, and nearby cortex are critical for the explicit acquisition and consolidation of linguistic and visual-spatial memories (Gazzaniga and Mangun, 2002).

Conventional Soy Food Items

Soybeans have been used more and more in the feed and food industries; their present global production stands at 219.8 million metric tons. Soybeans contain low fat and calories, no cholesterol, rich in fiber, high biological quality protein, and polyunsaturated fatty acids. Soy foods are classified into fermented soy foods and non-fermented soy foods, and the latter is made from whole soybeans. Non-fermented soy products are soy milk, fresh green soybeans, whole dry soybeans, soy nuts, soy sprouts, whole-fat soy flour, and tofu. Soy nuts are usually eaten roasted as a snack while soy sprouts are used in soups, salads, and on the side in the United States and as vegetables in many Asian countries. Soybeans are soaked, rinsed, ground, and filtered to make soy milk and tofu. The leftover material, known as okara, can be fermented to create tempeh or used in recipes. The filtered soybean liquid is processed further to create soy milk, which is coagulated to create tofu. Soy is a staple in Asian fermented cuisines. Compared to unfermented soy, traditional fermented soy products including tempeh, natto, and soy sauce have higher concentrations of total and aglycone isoflavones (Jooyandeh, 2011). The section that follows will cover these products.

The Use of Soy in a Variety of Fermented Food Products

Many consumers are opposed to soybean products because of their inherent flavors, which are commonly described as beany, grassy, or astringent, as well as their ability to produce flatulence. Fermenting soybeans can help to address these difficulties by lowering beany flavor, chalkiness, and anti-nutritional components like phytate and oxalate, which block the absorption of key minerals including calcium, magnesium, iron, copper, and zinc. Fermentation also reduces the flatulent sugars, stachyose, and raffinose, by utilizing microbial cultures, particularly lactic acid bacteria. Furthermore, changes or processing procedures, such as applying heat, soaking in ethanol or alkali, and acid grinding during soymilk manufacture, can enhance the appeal of soybean products (Golbitz, 1995).

Soy is regarded as a great substrate for functional meals because probiotic fermentation can: (1) lower carbohydrates that can result in intestinal gas; (2) raise levels of free isoflavones; and (3) encourage advantageous changes in the bacterial populations of the gastrointestinal tract. As proteins decompose into amino acids and peptides, oligosaccharides change into monosaccharides, and phytic acid decreases to inorganic phosphates during fermentation, soy products acquire functional characteristics. The way proteins behave in food systems throughout processing, manufacture, storage, and preparation is influenced by these physicochemical alterations (Champagne et al., 2009).

Miso, tempeh, natto, fermented tofu, and soy sauces (shoyu) are examples of common fermented soy products. There are several types of miso, a fermented bean paste that is used as a seasoning or in soups. Some of the variations are rice, barley, and soybean miso. To produce it, rice, barley, or soybeans are soaked, cooked, cooled, and inoculated with Aspergillus strains. This is followed by fermentation and mashing. Tempeh is a main course or meat substitute in Asian and vegetarian diets. It is manufactured from dehulled, cooked soybeans that have been fermented by *Rhizopus oligosporus*. The result is a cake-like product with a yeasty scent. The texture and flavor of deep-fried tempeh are crispy and nutty, and it smells good (Pablo et al., 2010).

Asia is a major consumer of soy sauce or soya; Japan leads the world in yearly per capita consumption with over 10 liters eaten annually. Preparing soybeans, soy meal, or soy flakes, mixing with koji (an enzyme source), mashing, fermenting, pressing, refining, and pasteurizing, are the stepladders in its manufacturing. Fermented tofu comes in two varieties: sour and pungent. Pickled tofu is made by soaking the dry tofu cubes in vinegar, salt solution, Chinese wine, and chopped chilies or a mixture of ground soybeans, bean paste, and rice. Stinky tofu is primarily prepared using a brine of fermented milk, vegetables, and meat, although ingredients such as dried shrimp, amaranth greens, mustard greens, bamboo shoots, and Chinese herbs may be included. This tofu is particularly notorious for its odor which is said to resemble the stench of rotting feces (Gandhi, 2009).

Dairy Type Products

Issues with intolerance and allergies, a desire for vegetarian options, and other causes are driving up demand for dairy-free alternatives, which is driving up interest in soy-based meals. For those who are allergic to milk protein, soybeans offer an alternative source of protein. All of the necessary amino acids are present in soy protein, which has a high digestibility rate (92% to 100%), however, it has a low methionine content compared to its high lysine content. Dairy-free goods made from soy are devoid of lactose, high in healthy fats, and cholesterol, and have little to no saturated fat (Singh et al., 2008; Granato et al., 2010)

Many dairy-free soy products include soy milk, soy cheese, soy yogurt, soy sour cream, soy cream cheese, and soy milk-based frozen desserts. Soy products are rich in high-quality protein, B vitamins, potassium, iron, dietary fiber, and some bioactive agents like isoflavones. Soy milk is a traditional product from China and other Asian countries which is famous for its nutritious and cheap protein value. Soy-based cheeses, prepared from tofu, soy milk, or a mixture of soy milk and tofu with soy protein isolates, are available in different types of flavors and consistencies and can be in slices, shreds, or blocks. There are also soy-based parmesan cheese and cream cheese as well as soy-based sour cream. Tofu or soybean curd is a food product that is made by adding a coagulant to soy milk which is obtained from soaked soybeans ground into a paste. Raw tofu can be categorized as soft/silken, firm, or dried. Tofu is one of the few foods that are calcium-fortified, offering calcium contents that are similar to that of milk per the same portion (Sethi et al., 2016).

Cereal Based Products

Soy protein components are also incorporated in cereal-based products because of their nutritional and functional properties. It is useful in lowering fat content, raising protein levels, and enhancing the baking characteristics of products like bread, crackers, doughnuts, cakes, pies, muffins, and other bakery products. Also, soy protein is a good source of lysine, which is usually a limiting amino acid in most cereal proteins.

Meat and Seafood Products

Products made from soy are used in food preparation to replace meat, fish, or poultry products due to their cheaper price. Soy protein has benefits to meat products as it acts as a binder, emulsifier, and humectant which helps in improving the flavor, color, texture, shelf life, slice ability and yield as well as making the end product juicy. Soy protein can also lower the fat content of products like hot dogs, ham, sausage, and luncheon meats. Since soy concentrates are known for their water binding and retention characteristics this product is incorporated into textured soy protein as an extender for fish, especially surimi. Soy protein also provides a fibrous matrix that improves the texture and mouthfeel of poultry rolls. Today soy protein has few uses in household foods including coarse ground meats like ground beef patties, and emulsified meats like frankfurters (Jooyandeh, 2011).

Beverages

The application and promotion of soy proteins have been gradually accepted by the beverage industry. Soy protein can be conveniently consumed through beverages. Soy protein concentrates and isolates offer highly digestible protein for beverages. It should also dissolve with low viscosity without affecting flavor into a clear, flavorless solution and should be stable at wide pH, ionic strength, and temperature. The ability of soy proteins to interact with water influences expressions like dispersibility, water absorption, swelling, viscosity, and gelation as well as the surface active properties of the proteins that qualify them for nutrient-enriched liquid products including infant formulas, creamers, milk substitutes, and spray dried products. Furthermore, soy isolates can be lecithinated to improve dust reduction and dispersion in these applications (Hawrylewicz et al., 1995).

Daily Intake

The Food and Drug Administration (FDA) states that a diet high in soy protein may reduce the incidence of coronary heart disease. The FDA suggests ingesting four servings of at least 6.25 grams of soy protein per day, or at least 25 grams every day, to reap these heart-healthy advantages. Consuming up to 50 grams of soy protein per day has been shown in numerous clinical studies to be safe as well as potentially helpful in lowering risk factors for chronic illnesses like diabetes, cancer, and cardiovascular disease. Even though soy's functional and nutraceutical qualities are widely valued, flavor continues to be a major factor in customer preference and a major obstacle to product development. Despite this, about 31% of American consumers are aware of the unique health benefits of soy, and about 33% actively seek out goods containing it. Customers are primarily aware of soy's health benefits when it comes to helping them regulate their weight (31%), lowering their risk of heart disease (27%), and preventing certain types of cancer (20%). 84% of consumers think soy products are helpful, and over 34% of customers are aware of the FDA's claim that consuming 25 grams of soy protein per day can lower the risk of coronary heart disease (Jooyandeh, 2011).

Future Trends

Consumers are drawn to healthier eating options more often. Because they may help lower the risk of heart disease and other diseases, soy products and beans have drawn a lot of interest. Apart from soy proteins and isoflavones, soybeans are extremely versatile and contain a high concentration of essential nutrients for instance fiber, minerals, polyunsaturated fats, and vitamins. Informing consumers about the health advantages of soy components may also increase the perceived sensory quality of soy products.

Soy-based foods containing probiotic strains will be considered a viable alternative to probiotic dairy products. The next food category to benefit from beneficial bacteria will be soy beverages and yogurts. Oriental soy items, together with non-fermented and fermented, are staples of many people's diets around the world. The dairy and meat industries, which have traditionally been conservative, will see a revolution in product formulation as new foods are designed around ingredient availability. Because soy protein products can mimic the textural properties of traditional foods, they will provide the necessary balance of protein in formulated foods.

New developments will also create opportunities for the soybean protein sector. For example, similar to milk proteins (particularly whey proteins), the soy industry is conducting extensive research to separate proteins into specific peptides with specific functional and bioactive properties. The use of non-thermal processing is another example of these improvements. Heat treatment has unfavorable impacts on soy protein solubility and water absorption properties. On the contrary, softly heat-treated products produce significant off-flavors, which is the primary issue when manufacturing soy protein foods. Designing unique soy foods or a range of new food compositions employing cutting-edge methods like high hydrostatic pressure is therefore essential.

The future trends in the market are likely to be shaped by innovations in functional soybean products that will appeal to current trends in consumer diets and health needs. An example is the use of soybean for the production of microencapsulated probiotics through fermentation to meet the increasing market for solutions for gut health. Likewise, soybean protein powders that can be customized according to dietary preference through sophisticated techniques address everyone’s need for Personalized Nutrition. Soybean-based plant protein burgers have come in to meet the rising demand for meat substitutes while energy drinks augmented with soybeans offer a natural and lasting energy boost. Soybean oil and its compounds are currently being used in skincare for their moisturizing and anti-aging efficacy while satisfying consumer trends toward clean and natural products.

Conclusion

Traditional soy products like soy crisps and bars are developed to be tasty and healthy meal supplements that can be consumed on the go. Additionally, there is an increasing demand for dietary supplements that use soybean isoflavones for brain function amid rising interest in the topic. Biodegradable packing materials consisting of soy-based bioplastics solve many ecological issues of traditional plastics. Soybean-enhanced functional beverages and culinary kits are more functional and nutrition-enhanced, mirroring an adoption of more utilitarian products. Altogether, these innovations accentuate how soybean functional products can dominate the health, sustainable, and personalized customer domain.

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Chapter 32

The Role of Functional Foods in Preventive Medicine

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ABSTRACT

Individuals are increasingly realizing that functional foods play a role in preventive medicine and can improve their well-being. Functional foods include a diverse range of nutrient-dense foods that offer health benefits beyond basic nutrition. This chapter addresses prevalent health issues such as cardiovascular disease, cancer, diabetes, and the prevention of neurodegenerative diseases. Functional foods are key in this effort. Classic functional foods include fruits and vegetables, while modified functional foods include nuts, seeds, fish, and fortified commodities. These foods have bioactive components that can lower cholesterol, decrease inflammation, and defend against free radical damage. Studies indicate that some functional foods rich in carotenoids, flavonoids, omega-3 fatty acids, and probiotics have the potential to reduce the risk of cancer. Functional meals can reduce the likelihood of cardiovascular disease and stroke by influencing biomarkers associated with cardiovascular health. A Mediterranean diet rich in fruits, vegetables, whole grains, and healthy fats has been linked to improved glucose regulation and a lower risk of complications from diabetes. Functional foods are important in preventing neurodegenerative illnesses, lowering oxidative stress, and promoting cognitive function. The lack of scientific proof and transparency, together with regulatory concerns and consumer skepticism, are impediments to the broad acceptance of functional foods. Meal planning, a balanced diet, and the inclusion of foods that promote health are the practical guidelines for incorporating functional foods into the diet. Future research on functional foods should focus on environmentally sustainable production methods, innovative technologies, evidence-based recommendations, and well-designed clinical trials to better understand their health benefits. Functional foods integrated into preventive medicine show the potential to reduce chronic disease and promote optimal health outcomes.

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INTRODUCTION

Functions of food advancement as a possible solution for better health and disease risk reduction have been encouraged in the present preventive medicine. This chapter investigates many functional foods that are explained in detail by their mechanisms and importance to human health to understand their essential role in the prevention of illnesses.

Preventive medicine, which is part of science, aims at the research of functional foods, which are characterized by their ability to offer health effects above and beyond the routine basic nutrition. The effects of these foods on the body are physiological, which is why they are good or even better when enriched with other nutrients. For the authors, the aim is to study in a thorough scientific way, the intricate functioning of foods in disease prevention and health promotion through a specific focus on functional foods.

The chapter starts with a description in detail of the various functional foods known today from the traditional staples like honey to the latest inventions. For each food group, there exist bioactive substances that can impact metabolic processes and cut the risk of disease. Whenever it is, veggies and fruits containing antioxidants, and whole grains with fiber-rich are the first thing that you will find. The researchers in their paper gives a general description of functional foods and kick off with a systematic review of the available literature, which ultimately terminates the role of functional foods in preventive medicine.

Not only the chapter looks into the distinction between nutraceuticals and functional foods but also it shows how they can be used to enhance health promotion and decrease the risk of diseases. The term "nutraceuticals" refers to concentrated bioactive ingredients found in such functional foods, which have unique health benefits. The aim is to demonstrate that dietary interventions can be a cohesive part of medicine for preventive care by studying their joint ways of action and mechanisms of work.

Additionally, this chapter discusses integration considerations and challenges in functional foods into prevention efforts in health. Regulatory barriers and the unwillingness among the consumers for such preventive functional foods are also examined. The intent of this scientifically grounded resource is to assist individuals and healthcare professionals in improving their nutritional choices with references on the means of including functional foods in daily meal plans.

The developments in functional food studies and innovations of the future could lead to the creation of novel dietary approaches and treatment strategies for preventing diseases. The potential of functional foods can include better health outcomes, the prevention of diseases, and overall well-being when studies are done scientifically and through interdisciplinary collaboration.

Functional Foods

Functional foods are a wide variety of foods that have a purpose more than just providing nutrition; they also have health advantages. Vitamins, minerals, probiotics, and fiber-containing foods fall under this group, whether they contain these nutrients naturally or have been fortified. Incorporated into regular diets, functionally improved meals seem extremely similar to regular foods. In contrast to processed foods, they have physiological benefits that reduce the likelihood of chronic diseases and help keep the digestive tract healthy (Cenic and Chingwaru, 2010). When components are used in cooking or preparation with scientific acumen, without knowing how they work or what effects they have, the idea of "functional food" arises. According to Centic and Chingwaru (2010), functional foods provide essential elements that the body needs to stay healthy, including vitamins, lipids, proteins, and carbs.

Types of Functional Foods

Functional foods can be broadly classified into two types: traditional and modified.

Essential nutrients such as vitamins, minerals, antioxidants, and heart-healthy fats are abundant in conventional functional foods' natural, unprocessed components. Some examples of traditional functional foods are berries, oranges, and kiwis; a variety of veggies like broccoli and spinach; nuts and seeds like almonds and cashews; legumes and whole grains like oats and barley; seafood and fermented foods like tempeh and kefir; and herbs and spices like ginger and turmeric (Alkhatib et al., 2017).

Nevertheless, modified functional foods have been supplemented along with additional elements including vitamins, probiotics, minerals, or fiber to enhance their health benefits.

Fortified juices, dairy products (milk, yogurt, etc.), cereal, granola, eggs, and substitutes of milk (almond, coconut, etc.) are all examples of modified functional foods.

Difference Between Functional and Nutraceutical Foods

In the field of nutrition and health, nutraceuticals and functional foods are two separate but connected ideas.

By fusing "nutrition" and "pharmaceutical," Stephen DeFelice coined the term "nutraceutical" in 1989 for characterization of foods or dietary components that include medical or health-promoting properties, such as helping in the prevention or treatment of specific disorders. A nutraceutical is a functional food that goes beyond just nutrition to treat or prevent diseases other than anemia (Brower, 1998). Importantly, there is no regulatory definition for the term nutraceutical, despite its extensive use in marketing. Nutraceuticals are different from dietary supplements because they help to prevent illness and also aid in treatment in addition to supplementing the diet. They can be eaten like regular foods or used as a standalone supplement.

Conversely, functional foods are those that do more than just meet nutritional needs. The biologically active compound in them allow them to improve health, which are often sourced from animals or plants. While it's true that all foods have a purpose, there's been a recent uptick in demand for those that boast particular health benefits. It is significant to note that functional foods cannot replace unhealthy eating habits. Moreover, there are no foods that are fundamentally "good" or "bad"; what matters is the diet as a whole (Laparra and Sanz, 2010).

Functional foods and nutraceuticals work hand in hand to promote health and lower the danger of chronic ailments including cancer, dyslipidemia, type 2 diabetes, and stroke. Functional foods are those that have passed the rigorous testing required by regulatory bodies such as the FDA, EFSA (Bresson et al., 2009), and ANVISA. These guidelines usually call for proof that the food is safe to eat, that it can be obtained without a doctor's prescription, and that it has health advantages when eaten in moderation.

The Role of Functional Foods in Preventing Common Health Conditions

Cancer

About one in eight fatalities are caused by cancer globally, and this makes it one of a major cause of mortality. Around 25% of Americans may face cancer at some point in their lives, adding to the enormous global burden of the disease. Radiation therapy, chemotherapy, and pharmacological treatments are common and often unpleasant parts of the treatment process. In 2010, there were 13.3 million new instances of cancer, costing an estimated US$ 290 billion (Chen et al., 2014). According to projections made by the World Economic Forum in 2011, this figure is expected to rise to US$ 458 billion by 2030. Surprisingly, about 50% of cancer incidences and deaths globally can be avoided (Aghajanpour et al., 2017).

An important factor that contributes to about 30% of all cancer cases is nutrition. The potential of functional meals to lower cancer risk has been the subject of substantial investigation. Researchers in the field of cancer biology are increasingly looking to natural remedies to help prolong the lives of cancer patients. Incorporating nutritional veggies, medicinal herbs, and extracts or components of these into cancer preventive and treatment strategies is becoming more popular in Europe, Japan, and the United States (Wu et al., 2013).

In recent years, manufacturers of food goods have taken a health-conscious tack by creating "functional foods," or meals with extra beneficial health effects. The vitamins, lipids, proteins, and carbs found in these seemingly ordinary meals are vital to good health and constitute a regular part of most people's diets (Terpou et al., 2019).

Functional foods cover a wide range of products, including natural components and substances found in regular, fortified, improved, and upgraded foods. Some naturally occurring substances in food have shown promise as chemopreventive agents; they include essential oils, chemicals with antioxidant properties found in plants or plant extracts, and other similar substances (De Martel et al., 2012). One theory suggests that antioxidants can help to reduce DNA damage, which is a major factor in cancer growth. Astaxanthin and other phytonutrients have been effective in reducing inflammation in both animals and humans.

There has been research on the possible cancer-preventive effects of phytochemicals, such as carotenoids, xanthines, and other pigments. Functional foods may also benefit from the addition of growth factors, conditionally required nutrients (such as amino acids and PUFAs), and substances that promote or inhibit the growth of beneficial bacteria (such as prebiotics, probiotics, and synbiotics) (Aghajanpour et al., 2017). Table 1 below summarizes the cancer-preventive potential of certain functional foods.

Table 1: Some functional foods and their anti-cancer effects.

Functional Foods	Dietary Sources	Function	Effects	References
Alpha-carotene	Yellow-orange and dark-green vegetables	Antioxidant	Enhances gap junctional intercellular communication in moderate doses	(Rutovskikh et al., 1997)
β-Carotene	Green leafy vegetables and orange/yellow fruits	Antioxidant	Similar to α-Carotene	(Rutovskikh et al., 1997)
Lycopene	Tomatoes, watermelon, apricot, peaches	Antioxidant	Potent inhibition of cell growth in various human cancer cell lines	(Levy et al., 1995)
Lutein	Dark green leafy vegetables	Antioxidant	Efficient in cell cycle progression; inhibits growth of various cancers	(Hyang-Sook et al., 2003)
β-Cryptoxanthin	Orange fruits	Antioxidant	Anti-inflammatory effects; reduces cancer risk	(Tanaka et al., 2012)
Astaxanthin	Green algae, salmon, trout	Antioxidant	Modifies gap junction communications	(Kurihara et al., 2002)
Canthaxanthin	Salmon, crustacea	Antioxidant	Scavenges free radicals; quenches reactive oxygen species	(Tanaka et al., 2012)
Fucoxanthin	Brown algae, heterokonts	Antioxidant	Anti-cancer and anti-inflammatory properties	(Tanaka et al., 2012)
Isothiocyanates	Broccoli, cauliflower, kale	Antibacterial	Reduces risk of lung, breast, liver, esophagus, stomach, and colon cancer	(Kurahashi et al., 2017; Conaway et al., 2022)
Flavonoids	Synthesized in plants	Antioxidant	Effective in preventing or treating many cancers	(Kurahashi et al., 2007; Plochmann et al., 2007)
Probiotics	Yogurt and fermented foods	Anti-allergy	Alleviates cancer symptoms	(Kumar et al., 2010)
Phyto-estrogens	Soy products	Anti-cancer	Competes with endogenous estrogens for estrogen receptor binding	(Limer, 2004)
Fiber	Found in most foods (vegetables, cereals, etc.)	Cholesterol-lowering	Reduces risk of colon and prostate cancer	(Wakai et al., 2007)
Omega-3	Fish or fish oil	Cholesterol-lowering	Reduces risk of breast and prostate cancer	(Bidoli et al., 2005; Shannon et al., 2007)

Cardiovascular Diseases

When it comes to alleviating the heavy load of cardiovascular diseases (CVDs), the creation of functional meals that support cardiovascular function is crucial. Heart disease, stroke, peripheral vascular disease, rheumatic heart disease, heart failure, cardiomyopathies, hypertension, and a host of other illnesses affecting the heart and blood vessels are collectively referred to as cardiovascular diseases (CVDs) by the World Health Organization (WHO, 2017).

Cardiovascular diseases (CVDs) become a cause of death of about 17 million individuals each year, with a large number of these casualties being caused by heart attacks and strokes. Eighty percent of all deaths from CVD and thirty-two percent of all deaths in the world are caused by these diseases. Despite being leading causes of mortality globally, the World Health Organization (WHO) emphasized in 2017 that 80% of preventable deaths from cardiovascular disease and stroke could be achieved by decreasing hazardous features such as cigarette smoking, poor consumption habits (including excessive alcohol consumption), and an absence of physical movement.

Traditional techniques for preventing cardiovascular diseases and related inflammatory illnesses include eating a balanced and healthy diet, exercising regularly, limiting alcohol consumption, and not smoking. But in 2016, the American Heart Association found that almost 25% of the world's population had metabolic syndrome, which is a major health problem that includes obesity, dyslipidemia, hypertension, hyperglycemia, or diabetes (Granato et al., 2020).

Atherosclerosis and other illnesses and morbidities caused by fatty deposits in the walls of arteries are much more likely to occur in people with metabolic syndrome. Overweight and obesity, lack of physical activity, inherited susceptibility, and getting older are all elements that might lead to metabolic syndrome. Even in young adults and teenagers, metabolic syndrome can be triggered by unhealthy eating and lack of physical activity.

Nutritionally sound food products that also offer targeted protection against cardiovascular diseases have been the focus of intense research and development efforts during the last 20 years. Consumption of foods with functional properties has been shown in multiple studies to modulate particular biomarkers, hence reducing CVD-related morbidity and mortality. It is clear that comprehensive programs for the prevention and management of cardiovascular illnesses must include continuing efforts to create and promote functional foods (Baumgartner et al., 2020).

Davis, (2019) argues that creating processed diets with lower content of sodium is a viable way to prevent salt-induced high blood pressure in people. The fact that these meals are considered "foods for special needs" rather than "functional" is worth noting, though. Bioactive peptides derived from a variety of sources are one example of the novel components that have recently emerged as having the ability to fight CVDs. Possible uses for these peptides in food have been investigated (Gallego et al., 2018).

Peptides display a wide range of functional characteristics; they typically consist of 2–20 amino acids. One example is the antihypertensive and antioxidant properties of microalgal bioactive peptides (Ejike et al., 2017). According to Amorim et al., (2019), hydrolyzed peptides from brewer's yeast inhibited the activity of angiotensin-I converting enzyme (ACE-I) and exhibited antioxidant characteristics. Also, hypertensive rats' blood pressure was normalized by peptides produced by probiotic bacteria during milk fermentation (Ahtesh et al., 2018). Antioxidant and cholesterol-inhibiting properties were demonstrated by cowpea peptides (Marques et al., 2015).

Important processes in peptide identification, such as hydrolysis, purification, and testing in food matrices, were outlined by Arnoldi et al., (2019). In vivo and in vitro screens guarantee safety, and clinical trials, particularly multicentric randomized controlled trials (RCTs), are suggested for validation. Nutraceuticals, which are concentrated chemical compounds, have recently gained popularity as a way to increase fruit and vegetable consumption, since many people don't eat enough of these foods already.

According to Mak et al., (2018), classical investigations have consistently highlighted the fact that chemical compounds included in food can modulate endothelial, cardiac, and vascular functions, which in turn can lower the risks of cardiovascular diseases (CVDs). The carotenoids are the utmost prevalent and widely used nutraceuticals among these chemicals (Yeung et al., 2018).

Also, linked eating habits and cardiovascular disease risk variables were investigated in cross-sectional research of Japanese people who were not overweight (Higuchi et al., 2015). According to the research, there was a negative relationship about levels of serum β-carotene, smoking status, insulin resistance, and poor insulin sensitivity. According to Facchini et al., (2000), β-carotene can reduce responsive species that root insulin resistance and malfunction in pancreatic β-cells, according to its known antioxidant and anti-inflammatory properties.

The possible function of carotenoids in regulating lipid metabolism and reducing the hazards of cardiovascular diseases (CVDs) was suggested by the correlation between increased intake of green/yellow vegetables, dairy products, and fruits and elevated serum β-carotene levels.

Neurodegenerative Diseases

Improving one's information processing capabilities, either internally or externally, is the goal of cognitive improvement, often known as intelligence enhancement (Bostrom and Sandberg, 2009). The brain depends on complex networks of billions of linked neurons to manage both cognitive and physiological activities (Pushpalatha et al., 2013). According to Colovic et al., (2013), the proper coordination of bodily activities depends on the regulation of neurotransmitters and the management of oxidative stress. Morris et al., (2006); Joseph et al. (2007); and Caracciolo et al., (2014) cite experimental and epidemiological research that suggests a lower risk of several neurodegenerative illnesses is associated with a diet rich in foodstuffs, beverages, herbs, spices, and teas.

The acetylcholinesterase (AChE) enzyme neutralizes acetylcholine (ACh) in cholinergic synapses, releasing choline and acetate as its byproducts. According to Akter et al., (2011) and Kim and Feldman, (2015), hypoinsulinemia and insulin resistance may be associated with the relationship between diabetes mellitus and Alzheimer's disease (AD). Additionally, stroke, Alzheimer's disease, diabetes mellitus, and other central nervous system diseases can be precipitated or exacerbated by oxidative insults that affect AChE activity (Mushtaq et al., 2015).

Adefegha et al., (2016) found that extracts of shea butter and bread alkaloids inhibited cholinesterase, lipid peroxidation and monoamine oxidase in vitro. Further research revealed that protocatechuic acid affected rat cholinergic, antioxidant and Na+/K+-ATPase activities.

Type 2 Diabetes

Fruits, vegetables and legumes make up the majority of the Mediterranean diet (MD), which also calls for moderate amounts of dairy products and fish and low amounts of red meat and wine. On this diet, you can substitute herbs and spices for salt as well (Esposito et al., 2017). Westernized diets have reduced adherence to the MD, even Although the Mediterranean diet (MD) is most commonly eaten in areas bordering the Mediterranean, its components are not limited to this region. Its application in non-Mediterranean regions has also yielded encouraging outcomes (Alkhatib et al., 2017).

Over the long term, compared to a low-fat diet, MD is associated with a 14.7 percent and a 5.5 percent decrease in pharmaceutical dependence, respectively, after one and five years after diagnosis (Esposito et al., 2014). Another study that found an inverse association between MD consumption and type 2 diabetes mellitus incidence rate compared to a low-fat diet was the PERIMED (Prevención con Dieta Mediterránea) prospective analysis (Perona et al., 2006; Salas-Salvado et al., 201). Supporting the idea that MD can lessen the impact of obesity on type 2 diabetes risk, recent meta-analyses have demonstrated that sticking to MD components like legumes, fruits, and vegetables lowers incidence rates over a 9.5-year follow-up, regardless of changes in obesity (measured by Body Mass Index; BMI). Some of the most important components of MD, such almonds and olive oil, are quite high in energy, thus it is not a calorie-restrictive diet (Esposito et al., 2015).

The beneficial impacts of the Mediterranean diet (MD) on Type 2 Diabetes Mellitus (T2DM) are attributed to specific nutraceuticals included in MD foods. Oily fish provide eicosatetraenoic acid (EPA) and docosahexaenoic acid (DHA), while walnuts and olive oil include alpha-linolenic acid, which is an omega-3 polyunsaturated fatty acid. Whole grains and cereals with a low glycemic index are high in fiber. The fruits and vegetables in the Mediterranean diet are abundant in antioxidants and flavonoids (Alkhatib et al., 2017).

Studies have shown that phytosterols such as beta-sitosterol, antioxidants like alpha-tocopherol, and polyphenols present in plants can enhance micro- and macrovascular function by reducing inflammation and oxidation. An example is the fatty acids included in olive oil. These effects can help partially avoid type 2 diabetes and cardiovascular disease (CVD). An appropriate consumption of fruits and vegetables is associated with a lower risk of type 2 diabetes, whereas an insufficient intake is connected to a higher risk of disease and death (Ezzati et al., 2013).

It is challenging to ascribe the advantages of decreasing the risk of type 2 diabetes to a single functional food or nutraceutical in the Mediterranean diet. Epidemiological studies investigating the association between specific components of the Mediterranean diet and a reduced incidence of type 2 diabetes have produced varying and inconclusive results (Ley et al., 2014). As an example, only Asian cultures were found to have a lower incidence of type 2 diabetes when they consumed omega-3 fatty acids from shellfish and fish (Wu et al., 2014). Neither European nor North American groups showed this association. In women who had gone through menopause, sticking to a low-fat diet over time did not reduce their risk of type 2 diabetes or cardiovascular ailment (Tinker et al., 2008). However, in high-risk people, some functional components of MD, such as tree nuts and extra-virgin olive oil, have demonstrated metabolic protective effects by lowering blood IL-6, C-reactive protein, and other adhesion factors between endothelial cells and monocytes (Peyrol et al., 2017).

The polyphenolic content of MD, particularly the flavan-3-ols found in many MD foods and drinks like coffee, tea, red wine, and cocoa, is responsible for its protective effects against type 2 diabetes, which include better glucose control, insulin resistance, and other cardiometabolic risk factors. Foods high in polyphenol lignans, such as flaxseeds, have been shown to improve insulin resistance, lower glucose and insulin levels, and decrease C-reactive protein levels in clinical trials (Guasch-Ferre et al., 2017).

Olive oil's primary polyphenol, hydroxytyrosol, has antioxidant and anti-inflammatory properties while also improving lipid profiles, glycaemia, and insulin sensitivity (Peyrol et al., 2017). Among the many advantages for the inhibition and regulation of type 2 diabetes is resveratrol, which is present in grapes and grape products. It improves intracellular glucose transport while reducing insulin release (Szkudelski et al., 2011). In several groups, consumption of polyphenol-rich beverages such as coffee and tea is also inversely associated with the risk of type 2 diabetes (Matusheski et al., 2012).

To summarize, each of the many components of MD has its own special properties and ways of protecting against type 2 diabetes. Thus, it is recommended to use a comprehensive strategy and incorporate the components of the MD diet to manage the diabetic lifestyle.

Obesity

The World Health Organization (WHO) defines obesity as an excess of body fat and states that it is associated with a number of social, physical and psychological problems; consequently, it is a major public health concern. A body mass index (BMI) of 30 kg/m^2 or more is considered obese and is associated with an increased risk of chronic diseases, disorders and death (Materko et al., 2017).

While it's true that portion control is key to weight management, recommending that you completely eliminate certain foods may not be the best strategy. The potential health consequences of bioactive chemicals, which are present in minute amounts in many foods, are an area of ongoing research. People who eat a lot of natural functional foods, such as specific vegetables and fruits that are rich in bioactive compounds, have a lower risk of developing chronic diseases, according to epidemiological evidence (Konstantinidi and Koutelidakis, 2019).

These diseases such as obesity, Type 2 Diabetes, Metabolic Syndrome, Cancer and cardiovascular disease are among them. Individual bioactive compounds from natural sources like resveratrol, epigallocatechin, curcumin, oleuropein, sulforaphane, quercetin, ellagic acid, anthocyanins, and β-glucans have been the subject of ongoing research for their possible direct or indirect molecular action which counteracts the pathophysiology of cardiovascular disease, diabetes, etc.

Some experimental studies can be considered as guidelines based on which the researchers can start. They also point out the need for further clinical and epidemiological investigations to confirm their possible effects. An influential stilbene that is in human diets is resveratrol (RSV), and it is based in red wine, pomegranates and grapes.

Curcumin (CUR) was identified to have anti-inflammatory, antioxidant, and cancer-preventing properties. The polyphenol in ginger is the main part of C. longa L,. which is the source herb. The polyphenol ellagic acid (EA) which is known for its antioxidant ability provides potent free radical scavenging activity. Ellagiatannins, which are found mainly in nuts and berries, make it what it is. Red Onion, blueberries, strawberries, and grapes are all high in anthocyanins (AC), which are water-soluble pigments that come in different shades of red, purple, and blue. According to Cianciosia et al., (2018) the anthocyanins are very effective components as they have been researched to have anti-inflammatory, antioxidant, and chemoprotective benefits.

Sociated with an epidemic of metabolic disease, obesity has become a global and European pandemic. Metabolic issues, inflammatory disorders that are chronic and degenerative diseases are connected to one with it (Ntigriou et al., 2019). Food addiction, in terms of the frequent consumption of foods high in sugar and fat because of a feeling of high desire or a strong compulsion to take food while having the phenomenon of overweight, is a global epidemic caused by several reasons, including increased food consumption, decreased physical activity, and a balance between them (Masheb et al ., 2018).

There has been a significant deal of evidence from empirical as well as health research showing that functional foods can have positive impacts, therefore, they are gradually being accepted as a part of scientific knowledge. When they are added to a nutritious diet whether the functional foods is naturally occurring or a modified version, they have a great potential in improving health and weight management (Elmaliklis et al., 2019; Ntrigiou et al., 2019). For instance, a recent research showed lower BMI indices among healthy participants who fed on functional foods like pomegranates, goji berries and cranberries. Besides this, researches have proved that beta-glucan, glucomannan and the foods low in fat and sugar together with the other functional foods and bioactives can help obesity and reduce its effects on metabolism.

Challenges and Considerations

People who are confused, skeptical, or cynical may resist functional food promises. Understanding the science behind functional foods, honing one's critical thinking skills, and making informed selections can empower consumers to make healthier dietary choices.

Consumers, healthcare providers, researchers, legislators, and industry stakeholders must work together to resolve these conflicts and restrictions. To ensure the continued advancement and effective contribution to preventive medicine, the field of functional foods must solve regulatory issues, improve scientific evidence, ensure product quality, promote transparency, and consider ethical and social consequences.

Recommendations for Incorporating Functional Foods into Diet

Siro et al., (2008) discovered a notable trend in the functional food sector: individuals with higher levels of education and wealth appear to be the primary customers in both the United States and Europe. Knowledge and a substantial cost are required to join this private club catering to sophisticated tastes. Hilliam, (1996) suggests that the privileged class not only has the financial means to purchase pricey functional foods but also takes pride in understanding the health benefits of these foods. They appear to have knowledge of numerous health benefits (Kustor and Vidal, 2017).

Sääksjärvi et al., (2009) further explore the economic puzzle and discover a direct correlation between income level and awareness of functional foods. Picture a hierarchy of knowledge with the bottom tier representing individuals earning less than 10,000 euros annually, and the top tier representing those earning more, introducing them to the functional food enlightenment package. Financial resources are not the sole determinant; education also plays a vital role. Regarding functional nutritional knowledge, the author asserts that college graduates surpass persons with lower levels of formal education (Kustor and Vidal, 2017).

Wait a moment, there's a surprising development ahead! Allow the successive generations to enter. The Institute of Food Technologists (IFT) found in 2014 that millennials, individuals born between 1982 and 2005, are the primary advocates for functional foods. They believe that functional meals can combat stress, enhance eye health, maintain cognitive abilities as they age, and serve as an alternative to medicines for fatigue. Every new nutrition label represents a revision of the wellness guidelines.

There is a notable age difference, especially in terms of covering health benefits, as indicated by the Nielsen Company (2015). Baby boomers are more hesitant to spend money on functional foods that claim to prevent diseases and enhance health compared to younger generations such as millennials and individuals from their country of origin. The world of functional foods is experiencing a confrontation between different generations and views.

Highlighting Meal Planning and Dietary Strategies for Optimal Preventive Health Benefits

Optimizing the well-being advantages of functional foods for disease prevention can be achieved through careful meal planning and dietary management. Some important points and suggestions are presented here.

Dietary Balance by incorporating a wide range of nutrient-dense foods into meals, such as fresh produce, whole grains, lean meats, and healthy fats is necessary. To promote health and wellness all over, one must eat a balanced amount of carbs, proteins, and fats.

Adding health-promoting functional foods to diet is necessary. Making sure to include functional foods in meals and snacks every day will help to prevent many diseases (Nataraj et al., 2020). To maintain healthy muscles and a full stomach, lean proteins such chicken, tofu, fish, beans, legumes, and lentils should be eaten. Eating foods with anti-inflammatory properties is essential as inflammation is a hallmark of many long-term health problems; reducing inflammation can help alleviate these symptoms.

Future Trends and Research Directions

There is a crucial necessity to investigate ecologically viable production techniques and sustainable sources of functional foods in light of rising worries about food insecurity, environmental degradation, and the effects of climate change. Green methods of food production, less food waste, and more support for regenerative farming techniques might be the subjects of future studies.

Technological and scientific developments in the food industry bode well for the creation of innovative functional food ingredients, recipes, and delivery methods. Enhancing the bioavailability and efficacy of functional chemicals may be investigated in future studies using nanotechnology, encapsulating techniques, and bioactive-rich food matrices (Ye et al., 2018).

Rigid clinical trials and evidence-based recommendations are necessary to educate healthcare providers and consumers about the increasing number of functional food items and dietary supplements. To further understand the benefits, risks, and ideal dosage of functional foods for different health outcomes, future studies should aim to be well-designed intervention trials, systematic reviews, or meta-analyses.

Continued innovation in functional food solutions for health promotion, disease prevention, and general well-being can be achieved by attending to these future trends and research directions.

Discussion

Functional foods, which offer health advantages beyond basic nutrition, are receiving considerable interest in the field of preventive medicine. Consuming them has been linked to a decreased risk of many diseases, making them a crucial focus of scientific research. This review focuses on functional foods and their uses to prevent and treat chronic diseases. The data look at the scientific basis of their usefulness and effectiveness (Cenic and Chingwaru, 2010).

Functional foods rich in omega-3 fatty acids (fish oil, fish sources such as salmon, mackerel, and sardines, flaxseeds, and walnuts) have shown cardioprotective benefits of lowering triglyceride levels, reducing inflammation, and improving endothelial function. Fortified foods such as margarine and orange juice containing plant sterols and stanols are good for LDL cholesterol, thus lowering its concentration in the blood stream, atherosclerosis and coronary heart disease risk reduction (Ezzati et al., 2013)..

Different functional foods that have been linked to cancer prevention contain antioxidants which help in inhibiting cancer procedures and also regulate cellular pathways associated with carcinogenesis. Broccoli and cabbage from the family of cruciferous vegetables are contained with sulforaphane and studies has shown it to both suppress the development of cancerous cell growth and induce the apoptosis. The green tea also encompasses catechins, which are highly potent antioxidant and anti-inflammatory agents that have potential to reduce the risk of many kinds of cancers, the examples of which are breast cancer, prostate cancer, and colorectal cancer (Bresson et al., 2009).

Diabetes management is based on specific functional food types that help control blood sugar and insulin sensitivity. Consuming foods with a low glycemic index, that is, beans, oats, and barley, is very important in regulating blood sugar. Cinnamon has been looked into for its power to enhance the insulin action and reduce blood glucose metabolism, hence, cinnamon can be considered as a functional food for the treatment of diabetes (Granato et al., 2020).

The fermented foods which contain probiotics such as yogurt, kefir, and kimchi, assist in the treatement of gastrointestinal health by balancing the gut flora and improving the digestive system. Prebiotic foods such as garlic, onions and bananas are a good source of fibre, and this fibre is used by gut friendly bacteria to fuel their activity, maintaining a healthy gut environment and reducing the occurrence of gastrointestinal conditions like irritable bowel syndrome and inflammatory bowel disease (Aghajanpour et al., 2017).

Healthy foods with neuroprotective features are of great importance in terms of the prevention of neurodegenerative diseases such as Alzheimer’s and Parkinson’s. Consumption of berries rich in polyphenols may improve the situation in the brain (by reducing oxidative stress and neuroinflammation), and intake of fatty fish is linked to the decreased incidence of cognitive decline or dementia as they have high content of omega-3 fatty acids (Alkhatib et al., 2017).

Conclusion

While functional foods represent a great opportunity for disease prevention and management, it's simply important to stress, that the evidence of their health benefits is provided by scientific research. The level of your health can be affected greatly by the presence of some foods in your diet, from the cardiovascular diseases to the cancer, diabetes, gastrointestinal diseases and the neurodegenerative diseases. Now the studies about the working mechanisms behind their therapeutic effects and the optimal dietary strategies are necessary to better exploit the potential of the functional foods in the field of human health improvement.

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Chapter 33

Role of Food Supplements in the Management of Brain Diseases

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ABSTRACT

This chapter examines the complex interaction between food supplements and the treatment of various neurodegenerative diseases. Food supplements, which include vitamins, minerals, herbs, and other dietary components, are a viable option because of their potential neuroprotective and neuro-regenerative effects. This chapter begins by explaining the pathophysiology of common brain diseases like Alzheimer's, Parkinson's, Huntington and Motor neuronal diseases (Amyotrophic lateral sclerosis). It then proceeds to a thorough examination of food supplements, including their molecular features and evidence-based therapeutic benefits on brain health. Key supplements such as omega-3 fatty acids, antioxidants (e.g., vitamins B12, B9, C, D, and E), polyphenols, and Coenzyme Q10 are thoroughly explored to assess safety, efficacy, emphasizing their ability to reduce neuronal damage, improve synaptic plasticity, and alter neurotransmitter activity. Furthermore, the chapter investigates the synergistic effects of supplement combinations and their possible use in personalized treatment approaches. Overall, this chapter presents a comprehensive summary of the current understanding of food supplements in the treatment of brain diseases.

KEYWORDS		
Food Supplements, Brain Diseases, Vitamins, Polyphenols, Coenzyme Q_{10}	Received: 18-May-2024 Revised: 10-July-2024 Accepted: 17-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

The saying "you are what you eat" has profound resonance, especially when it comes to the brain. Everyday our brain is engaged in multiple activities around the clock. All these activities are performed with the help of neurons that form the brain network. Better neuronal connections in the brain allow us to work and perform efficiently. Therefore, the brain should be well nourished with a balanced and healthy diet. Proper intake of vitamins, minerals, fats, and anti-oxidants shields the brain from the progression of neurodegenerative disorders. Such disorders not only impair our cognitive and motor abilities but also disrupt our day-to-day activities (Wolfe, 2010).

Nestled within urbanization and cultural advancements, we find ourselves in the rush of life. This leads to the intake of a high-calorie diet and processed foods without considering their nutritional value (Grajek et al., 2022). Epidemiological studies reveal a close relationship between dietary patterns and mental disorders (Owen and Corfe, 2017). Highly processed foods alter the brain and gut microbiota axis leading to dysbiosis which increases the release of pro-inflammatory cytokines. Moreover, these foods contain trans fatty acids that contribute to neuroinflammation and oxidative stress, which are the ultimate cause of neurodegenerative diseases (KsD). That is why about 17.2 million people worldwide are suffering from neurodegenerative disorders. The symptoms of neurodegenerative disease often manifest at an advanced age, so early prevention is necessary for preserving cognitive vitality and mental health (Dickinson et al., 2015). Food supplements can help to address such nutritional deficiencies and influence brain function. They aid in slowing the progression of brain deterioration but cannot replace a healthy diet. They should be used as add-ons to fulfill the requirements lacking in one's diet (Naureen et al., 2022). One of the well-known examples is caffeine, which acts as a mild stimulant for the brain to enhance mental alertness and performance (Grimm et al., 2016). Similarly, concomitant intake of vitamins like C and E reduces the prevalence of Alzheimer's disease (Alam, 2022). This chapter provides a deep insight into these food supplements and their role in improving neurodegenerative disease.

A Comprehensive Insight to Neurodegenerative Diseases

Parkinson's Disease

Parkinson's disease (PD) is a deteriorative neurologic condition marked by the commencement of motor signs as bradykinesia (slow movements), tremors, muscle rigidity and postural instability (bend posture) (Poewe et al., 2017). Furthermore, there are non-motor symptoms as well, such as mental disorders and complicated behavioral problems, apathy, anhedonia, cognitive dysfunction and hallucinations, sleep disturbances, and so forth. Parkinson's disease (PD) affects around 1% of adults over the age of 60, with 5-10% rise in frequency between the sixth and ninth decades of life (De Lau and Breteler, 2006).

Protein agglomerates like α-synuclein, parkin, and other proteins enter in the cytoplasm of deceased neurons found in various parts of the brain and are known as Lewy bodies. Agglomeration of α-synuclein begins with the formation of oligomers by soluble monomers, which then gradually continue to combine to create massive, insoluble fibrils (Xilouri et al., 2013). In addition to these two key clinical indicators, PD comprises several molecular pathways that are connected to one another and the physiopathology of the illness, creating a vicious cycle that speeds up the onset of neurodegeneration (Fig. 1).

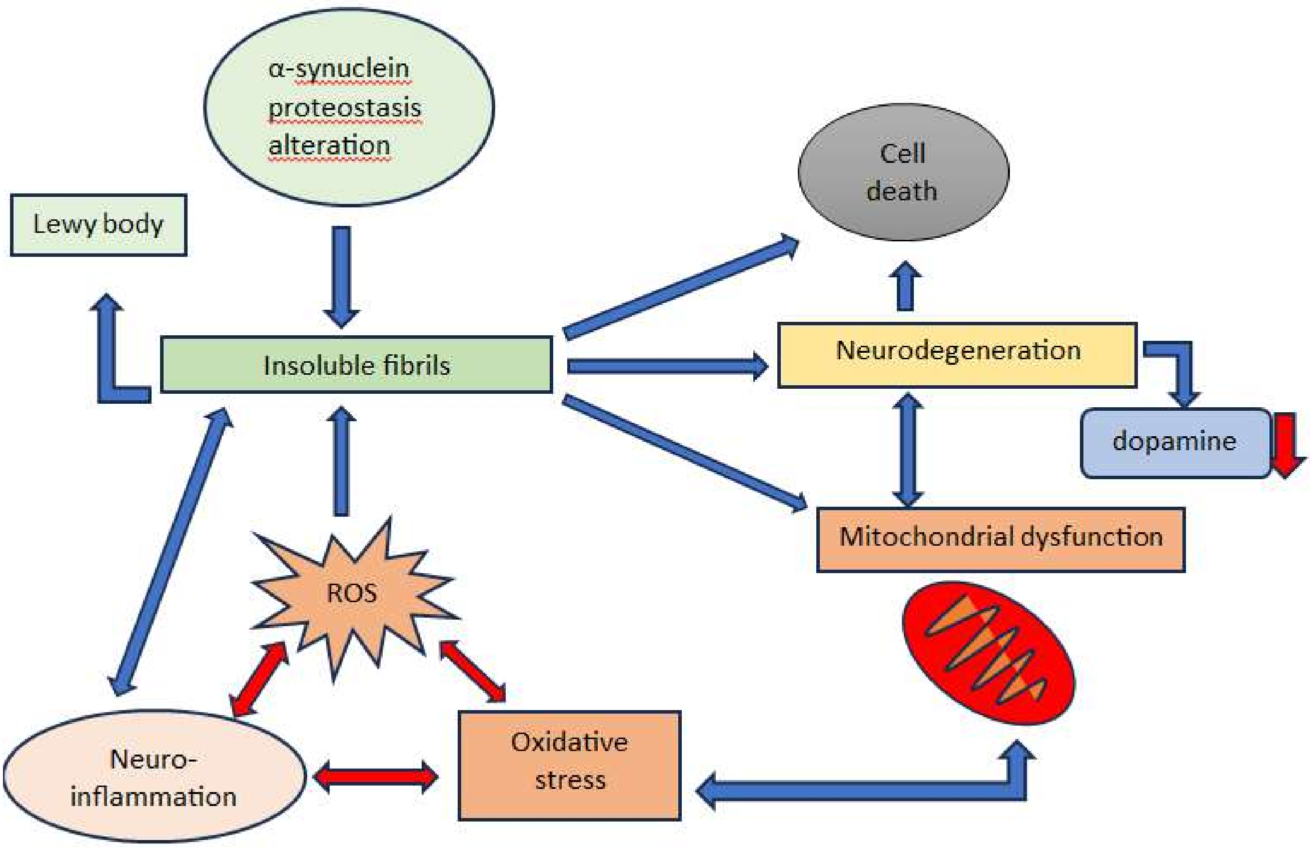

Fig. 1: Interaction among the key molecular processes involved in Parkinson's disease (PD) pathogenesis

Alzheimer's Disease

According to an assessment by the Alzheimer's Association, half of Americans over 85 years old and one in eight over 65 years old experienced this devastating neurological disorder (Kim et al., 2009). Based on this estimate, the number of patients could reach 16M in 2050 (Heo et al., 2004). Alzheimer's disease is characterized by gradual cognitive deterioration, disintegrating plaques (amyloid-β peptide, Aβ), and neurofibrillary tangles. AD symptoms result in dynamic dementia that includes increasing memory loss, impaired ability to learn, and unpleasant speech impacts. Individuals with impaired physical function seem to be more vulnerable to AD and dementia (Wang et al., 2006).

Huntington Disease

This autosomal neurodegenerative disease primarily affects the basal ganglia, causing choreiform development, dystonia, dementia, mental difficulties, and ventricular enlargement. The Huntington disease is linked to the formation of CAG repeats in the Huntington gene, which can be unstable (Gil-Mohapel et al., 2014). Healthy individuals frequently have less than 26 CAG repeats in their HTT gene, which results in appropriate HTT activity in vesicle movement and endocytosis (Beckerman and Beckerman, 2015).

Motor Neuronal Diseases (MNDs)

MNDs are a subset of NDDs that have dysfunctions of the motor neurons. The most common MND, Amyotrophic lateral sclerosis (ALS), causes selective neuronal deprivation in the brainstem and spine. Amyotrophic lateral sclerosis is characterized by deprivation of motor neurons in the front portion of the spinal cord (Taylor et al., 2016). Studies suggest that increased oxidative strain causes mitochondrial malfunction and initiates the typical apoptotic course in individual neurons. Delaying treatment for ALS can result in the loss of respiratory and motor neurons, which can be fatal (Kiernan, 2011).

Food Supplements as Potential Allies in Managing Brain Diseases

Dietary supplements, commonly known as food supplements, are physiologically active enriched substances with nutrients that may be lacking in one's diet. These supplements come in various forms such as tablets, capsules, liquids, etc., and typically include minerals, vitamins, amino acids, and other essential components. (Morani et al.). Food supplements have been proven to be a great way to support brain health and functioning and potentially mitigate the risk of brain diseases (Breitweg-Lehmann et al., 2020). This can be evident through a clinical trial in which 210 Alzheimer's patients received an intervention of 800IU of vitamin D per day. After 12 months of supplementation, they showed enhanced performance in a cognitive assessment than in the control group (Melzer et al., 2021)**.**

Various nutrients, including amino acids like tryptophan, phenylalanine, tyrosine, and taurine, along with glucose, vitamins C, E, and D, and beta-carotene, B-group vitamins such as B12, B6, B4, and B1, and minerals like selenium, zinc, magnesium, sodium, iron, copper, manganese, and iodine, are believed to support and protect the nervous system. The realm of food supplements capable of enhancing brain health and efficacy is not limited to just certain substances, but it extends beyond vitamins and minerals to encompass herbal extracts and other bioactive compounds (Akhondzadeh et al., 2003)**.** This diverse array of nutritional elements unveils a myriad of neuroprotective effects, especially in managing neurodegenerative brain diseases (Table 1).

Phospholipids

Phospholipids are indispensable for membrane structural integrity, neurotransmission, myelination, and synthesis of essential molecules, all of which are vital for optimal brain function and cognition (Schverer et al., 2020)**.** Studies revealed that the production of phospholipids declines with aging due to loss of membrane fluidity, which stems from alterations in the composition and arrangement of membrane phospholipids (Kosicek and Hecimovic, 2013)**.** Molecular studies reveal that phosphatidyl serine is a primary phospholipid in nerve membranes and also plays a vital role in the release of monoamine neurotransmitters (Glade and Smith, 2015)**.** Its oral supplementation to rats promotes the proliferation of the synaptic connections and enhances neurotransmission. Sphingomyelin is a sphingolipid that maintains the myelin sheath integrity and maturation of axons. That is why its deficiency can be the potential trigger for the onset of cognitive impairment (Ozawa et al., 2021).

Coenzyme Q10

Coenzyme Q10 is referred as 1,4 benzoquinone characterized by quinone ring coupled with isoprenyl subunits in its tail. It resides in the mitochondria, where it forms a part of the electron transport chain that plays a vital role in aerobic respiration, ultimately producing ATP. It holds importance not only as an electron carrier but also as a scavenger for free radicals (Glade and Smith, 2015). Its antioxidant properties suggest its significance in the cellular redox system in metabolic reactions. Several in-vitro studies demonstrated the neuroprotective effects of coenzyme Q10. The studies highlighted that the oral supplementation of coenzyme Q10 prevents the deterioration of striatal dopaminergic neuronal fibers in one-year-old mice having MPTP-induced Parkinson's disease (Ciulla et al., 2019).

It works by inhibiting MPTP-induced interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and nuclear factor-κB (NF-κB) expression, thus acting as an anti-inflammatory agent. The deficiency of Coenzyme Q10 diminishes the expression of mitochondrial proteins crucial for oxidative phosphorylation (Sifuentes-Franco et al., 2022)**.** Its dietary supplements are also available in various dosage form like soft gels, powders, suspensions, and tablets to correct its deficiency (Spindler et al., 2009)**.**

Polyphenols

Polyphenols are naturally occurring phytochemicals abundantly present in fruits, vegetables, tea, coffee, red wine, etc. (Williamson, 2017). Chemically, they are characterized as aromatic rings with multiple hydroxyl groups that allow them to act as scavengers to protect our cells from oxidative damage. With their robust antioxidant and anti-inflammatory properties, they can combat the underlying mechanisms leading to neurodegeneration (Vauzour, 2017).

In randomized control trials, polyphenols were reported to be mood enhancers in depressive patients. Polyphenols like blueberries and tea were observed to cause improvement in memory and object recognition in rats. Another example is Quercetin appeared to be neuroprotective in experimental mice. It diminishes the progression of Parkinson's disease by reducing the production of reactive oxygen species and pro-inflammatory cytokines which cause damage to the dopaminergic nerve terminals (Grabska-Kobyłecka et al., 2023).

Table 1: Experimental studies on the impact of supplements in different neurological disorders

Objective	Participants	Description	Main outcomes	Reference
Polyphenols				
To assess the impact of the smoothie of berries on enhancing mood and executive functions	40 healthy individuals were recruited for randomized, single-blinded, placebo-controlled study	Participants were given either a smoothie of mixed berries (blueberries, raspberries, and strawberries) or a placebo. Executive functioning and mood were assessed at the study's outset and after 2,4 and 6 hours.	Enhanced cognition in smoothie takes during day work. Significant results did not appear to enhance mood.	(Whyte et al., 2019)
To assess the neuroprotective effects of caffeic acid	Mice were subjected to permanent occlusion of the middle cerebral artery.	Mice were treated with caffeic acid (2, 20, and 60mg/kg/day) at 0, 24, 48, 72, 96 or 120h after cerebral occlusion. Cerebral infarction, neurological deficit score, locomotor activity, and memory were assessed.	Caffeic acid showed a reduction in the infarcted area and improved the neurological deficit score and memory. Improvements were not observed in locomotor activity.	(Fernandes et al., 2014)
To assess the neuroprotective effects of quercetin in rotenone-induced hemiparkinsonian rats.	Rotenone was administered into the pars compacta of substantia nigra in Inbred Sprague-Dawley rats (250-300g).	Rats were administered with quercetin (20, 50 and 75mg/kg) after the interval of 12 h for four days. Mitochondrial dysfunction, oxidative stress, death of dopaminergic neurons was assessed.	Dose-dependent effects of quercetin were observed. It up-regulated mitochondrial complex-I activity. It reduced oxidative stress by scavenging hydroxal and also reduced the loss of striatal dopamine and nigral glutathione.	(Karuppagounder et al., 2013)
To assess the effect of resveratrol as an anti-depressant and anxiolytic in rat having irritable bowel syndrome.	For 22 days male rats were subjected to chronic acute combined stress (CACS) including food and water deprivation, forced swimming and tail pinching, etc.	Resveratrol was given orally at doses of 10, 20, and 40 mg /kg 50 minutes before the CACS procedure. Behavioral changes, visceral sensitivity, and intestinal motility were assessed by using different tests.	Resveratrol dose-dependent effects were observed in rats. It alleviated IBS-like effects associated with depression, anxiety and visceral hypersensitivity by modulating 5HT-dependent signaling pathways in gut brain axis.	Yu et al., 2019
To assess the safety, efficacy and tolerability of green tea polyphenols in Parkinson's patients.	410 untreated Parkinson's patients were selected, each with a disease duration not exceeding 5 years.	Double-blind, randomized, placebo-controlled assessment was conducted for 12 months. Individuals were randomly assigned to groups having 400, 800 and 1200mg of green tea twice daily.	Conflicting outcomes had emerged. Beneficial effects observed after 6months of intervention were abolished after the period of 12 months.	(Chan et al., 2009)
To assess the effect of pycnogenol on Attention Deficit/ Hyperactivity disorder (ADHD) in children.	61 children allocated for double-blind, randomized, placebo-controlled study.	1mg/kg dose of supplement was given on a daily basis for four weeks. Children were examined at the outset, at the end and one month after the end of the trial.	Reduced hyperreactivity, improved concentration and motor coordination were observed at the end of the trial. Relapse of the symptoms were observed one month after the end of trial.	(Trebatická et al., 2006)
To assess the effect of concord grape juice on the cognitive impairment.	12 older adults including 8 men and 4 women each with declined memory were recruited.	Double blinded, randomized and placebo-controlled 3 months experimental trial were performed with daily supplementation of concord grape juice.	Significant improvements in verbal and spatial recalling abilities.	(Krikorian et al., 2010)
Coenzyme Q10				
To assess the efficacy of coenzyme Q10 in early Parkinson's patients.	80 patients were recruited for double blinded, randomized and placebo-controlled study	Patients are randomly assigned to receive either placebo or coenzyme Q10 at dosages of 300mg, 600mg and 1200mg per day for 16 months.	At 1200mg, Coenzyme Q10 appeared to slow down the advancement of Parkinson's disease.	(Shults et al., 2004)

Omega-3 Fatty Acids

Lipids make up around 70% of the brain's weight when it's dried., with polyunsaturated fatty acids (PUFAs) like DHA and AA being the most abundant, making up about Constituting approximately 20% of the brain's weight, lipids are vital components. About 40% of the fatty acids in the brain are made up of DHA, whereas fewer than 1% are made up of EPA (Dighriri et al., 2022). The fact that, less than 20 years ago, very few individuals were aware of Omega-3 fatty acids in seafood and fish oils is shocking considering the constant attention these chemicals received during the 1980s (Nettleton and Nettleton, 1995). To maintain excellent health and fend against several ailments, one needs include omega-3 fatty acids in their daily diet, which may be obtained from a variety of sources**.**.Omega-3 fatty acids, found in marine (DHA, EPA) and plant (linolenic acid) sources, offer health benefits, contrasting with harmful effects associated with saturated fats (Freeman et al., 2006)**.**

Mammalian brains are known for having large amounts of DHA in brain EPG and phosphatidylserine (PS), which can reach up to 35% of fatty acids in synaptic membranes (Innis, 2008)**.** Significant variations in the levels of DHA are found among women due to the broad variation in omega-3 fatty acid intake throughout pregnancy and breastfeeding babies both at birth and among babies who are breastfed. It can lead to neuropsychiatric illnesses include depression, schizophrenia, and manic-depressive sickness (bipolar disorder) (Meyer et al., 2003)

Over the years, reports of DHA-induced reductions in amyloid, tau, or synaptic neuropathologies in animal models of AD have been made (Kerdiles et al., 2017)**.**The majority of research on the relationship between AD and cognition has come from correlative epidemiological studies, which generally imply that a high intake of foods high in omega-3 polyunsaturated fats (n-3 PUFA) is linked to improved performance and may even help prevent AD or age-related cognitive impairment. The majority of longitudinal or case-control studies indicate a correlation between blood levels or n-3 PUFA consumption and a decreased risk of AD or dementia (Jiang et al., 2020).

Vitamins Essential for Neurodegenerative Diseases

Generally, Vitamins are organic compounds required for the normal functioning of the brain and body and can't be synthesized by the body (Sloan, 2002). Vitamins are significantly advantageous for neurodegenerative diseases. The essential Water-Soluble Vitamins include Vitamin B1 (Thiamine), Vitamin B2 (Riboflavin), Vitamin B3 (Niacin, Nicotinic acid), Vitamin B5 (Pantothenic acid), Vitamin B6 (Pyridoxine derivatives), VitaminB7 (Biotin, Folacin), Vitamin B12 (Cobalamin), and Vitamin C (Ascorbate, Dehydroascorbate) (Key et al., 2019). Essential Fat-soluble vitamins are A, D, E, and K (Kumar et al., 2022). They impact on cognitive function in AD, PD, HD, etc. as well as their influence on other neurodegenerative diseases (Table 2).

Vitamin B12

Vitamin B12 (Cobalt) is an antioxidant and helps to keep nerve cells and red blood cells healthy and produces DNA. Vitamin B12 enhances both motor and cognitive functions. Vitamin B12 may be a potential antidote to leucin-rich repeat kinase 2 (LRRK2) associated Parkinson's disease. (Kumar et al., 2022). Deficiency of vitamin B12 lowers dopamine production. Metabolism of homocysteine is done by folates. Increased level of homocysteine leads to cognitive impairment and dopamine reduction (Mythri et al., 2015).

Vitamin C

Superoxide radicals are neutralized by vitamin C, that are generated in large quantities at some stages in neurodegenerative processes. Moreover, plasma and mobile Vitamin C level decline step by step with age, leading to neurodegenerative diseases (Kocot et al., 2017).

Vitamin E

In the central nervous system, Vitamin E can be stored where it reduces β-amyloid plaque deposition and lipid peroxidation (Icer et al., 2021). In AD patients, there is a correlation between Vitamin E and C level and blood and dementia (Farina et al., 2017). In the Hippocampus, Vitamin E counteracts the molecular substrates underlying synaptic plasticity and cognitive function. It declines the charge of cognitive impairment (Browne et al., 2019).

Vitamin D

It plays a significant role in neurodegenerative processes. Its deficiency is a genetic risk factor for Parkinson's disease, Alzheimer's disease, Multiple sclerosis and Vascular dementia (Gangwar et al., 2015). Vitamin D can minimize the inflammation in the hippocampus and mitigate the deposition of β-amyloid in the process of increased phagocytosis (Sleeman et al., 2017). It can regulate calcium homeostasis and stabilize calcium channels disturbed by the accumulation of β-amyloid (Fig. 2). In addition, it increases the expression of Vitamin D receptors.

Minerals

Minerals obtained from vegetables and fruits; it plays a vital role similar to vitamins their contribution to brain management. It supports various functions including brain metabolism, mood, learning and memory (Shah et al., 2023). It leads a crucial role in supporting cognitive function and brain health. The most significant are magnesium, zinc and iron. Magnesium is vital for neurotransmitters function, which is helpful for learning and memory. It also helps to regulate mood and may have a calming effect on the brain (Maier et al., 2022). Iron plays a significant role in oxygen transportation to the brain. Their deficiencies lead to reduced brain function and cognitive impairments (Mezzaroba et al., 2019). Zinc is involved in variable functions of brain management, including learning and memory formation. It acts as an oxidant and helps to protect brain cells from lethargic abnormalities (Mezzaroba et al., 2019).

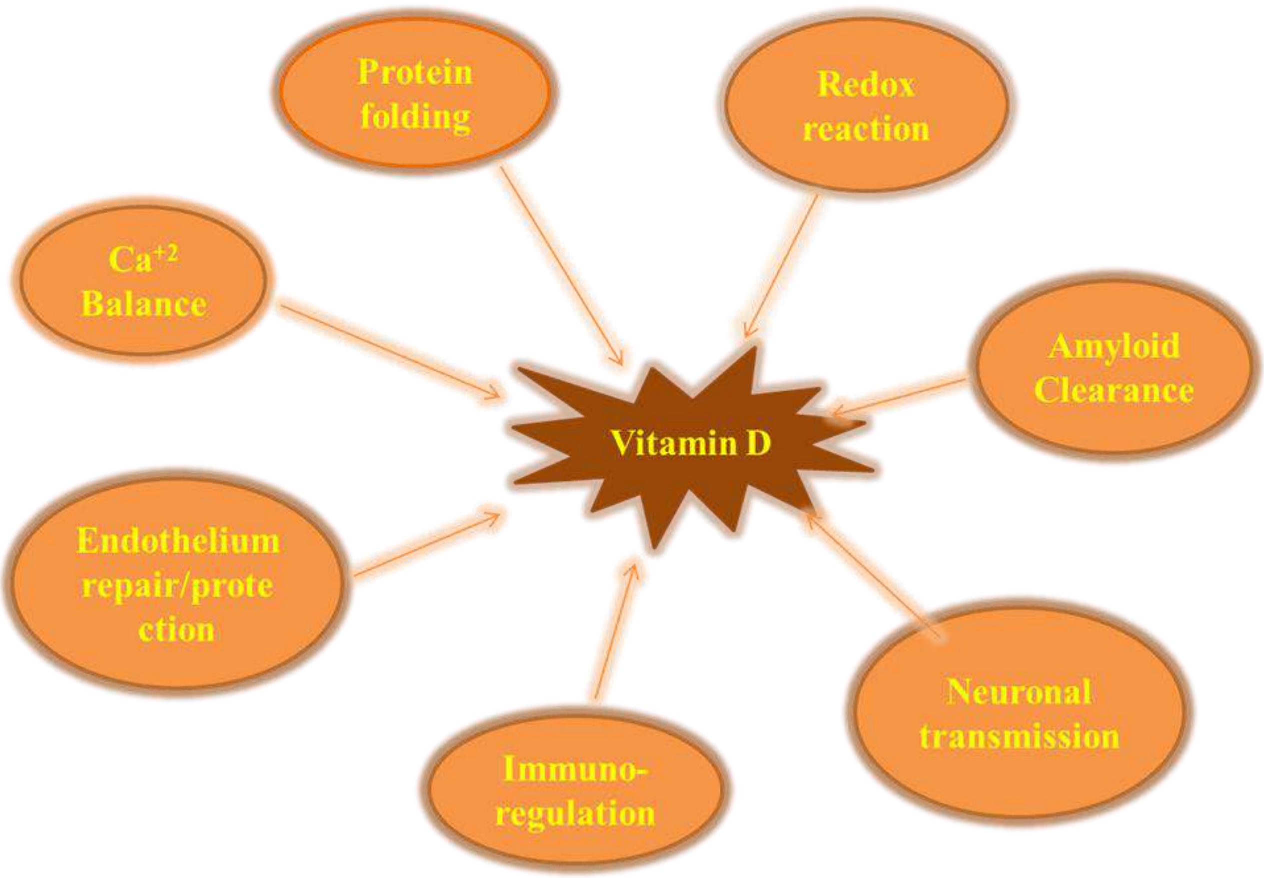

Fig. 2: Role of Vitamin D in Neurodegenerative Processes

Table 2: Role of Vitamins in neurodegenerative diseases

Sr#	Diseases	Affected brain region	Aggregating protein	Vitamins	Site of actions	Sources	References
01	Alzheimer's Disease	Cerebral cortex, hippocampus	β-amyloid	Vitamin C Vitamin B (B12, Folic acid, B9)	Lower the homocysteine concentration in the blood and CSF, the long-term benefit to AD is not known	Red meat, Egg, yeast, leafy Green vegetables	(Monacelli et al., 2017)
02	Parkinson's disease	Spinal cord, motor cortex, brain stem	α-synuclein	Vitamin A, B, C, D, E	Frontal Lobe cortex, Regulate postsynaptic actions of GABA and Glutamate	Citrus fruits, broccoli, white potatoes, Liver of Animals	(Chang et al., 2021)
03	Hungtington's disease	Striatum, cerebral cortex	Huntington protein	Biotin, Thiamin(B1), B6, B12	Regulate Genes in metabolic pathways and modulate protein aggregation	Beef, Poultry, Nuts, Beans	(Lim et al., 2022)

Clinical Evidence and Effectiveness

Over the past four decades, extensive research has highlighted the significant impact of diet on both the developing and mature brain. Various examples illustrate this influence, such as folate deficiency affecting neural tube development in early pregnancy, essential fatty acid deficiency impacting visual function in infants, and the role of amino acids like tryptophan and tyrosine in neurotransmitter production. While the functional consequences of these dietary influences are often apparent, the underlying biochemical mechanisms remain unclear in some cases, like folate and essential fatty acids, while in others, such as tyrosine and tryptophan, the biochemical effects are well-known but their specific impact on brain function remains elusive (Fernstrom, 2000).

B12 and B6 is crucial as the severity of neurological complications may only be reversed with prompt treatment. (Azzini et al., 2021). A case study highlighted a strict vegetarian female with demyelinating polyneuropathy and low serum vitamin B12 levels. After three months of intramuscular hydroxycobalamin therapy, clinical improvement was observed, accompanied by elevated B12 levels. At one- and three-year follow-ups, nerve conduction studies demonstrated early clinical improvement and gradual recovery of polyneuropathy (Azzini et al., 2021). Folic acid's vital role in neuroplasticity and neuronal maintenance is underscored by its involvement in one-carbon metabolism, where it aids in the conversion of homocysteine into methionine, a precursor for S-adenosylmethionine (SAM), the primary methyl donor in essential methylation reactions (Kronenberg et al., 2009).

Turmeric is recognized for its potential neuroprotective properties, with Indian populations, who frequently incorporate turmeric into their diet as part of curry, exhibiting a lower prevalence of Alzheimer's disease (AD). Additionally, epidemiological research suggests a correlation between consuming dietary curry and enhanced cognitive performance among elderly individuals. These beneficial effects are attributed primarily to the presence of curcumin in turmeric. The exploration into the therapeutic potential of resveratrol was sparked by its association with the "French Paradox" in the early 1990s. Studies suggested that regular consumption of red wine might be linked to a reduced risk of developing dementia, including Alzheimer's disease (AD) and vascular dementia. Orgogozo et al. demonstrated a positive relationship between moderate red wine consumption and a lowered incidence of dementia. This protective effect is believed to be primarily attributed to the presence of phenolic compounds, notably resveratrol, in wine. In vitro and in vivo studies have underscored the neuroprotective potential of curcumin and resveratrol, indicating their ability to impede the progression of Alzheimer's disease (AD) through various mechanisms.(Mazzanti and Di Giacomo, 2016)

The impact of PUFAs on the central nervous system (CNS) function can be evaluated through dietary manipulation in animal models. Chronic deficiency in alpha-linolenic acid (ALA) in rodents notably alters the fatty acid composition of cerebral membrane phospholipids. The balance between arachidonic acid (AA) and docosahexaenoic acid (DHA) plays a critical role in brain function maturation. Studies on rodents and nonhuman primates have demonstrated that inadequate n-3 PUFA supplies during the perinatal period led to impaired learning capacity, neurotransmission processes, and visual function. Therefore, ensuring sufficient intake of n-3 PUFAs is essential for optimal brain development, particularly during crucial stages such as neuronal migration, myelination, neurite growth, and synaptogenesis (Balanzá-Martínez et al., 2011).

Ginkgo biloba extract (GBE) is recognized for its potential in enhancing brain function, supported by numerous research studies investigating its efficacy across various conditions. Research reports have demonstrated promising results regarding the use of GBE in addressing cerebrovascular insufficiency, memory impairment in the elderly, Alzheimer's disease, multi-infarct dementia and resistant depression. Ginkgo leaf extract is recognized for its ability to impede the formation of Aβ from β-amyloid precursor protein (APP), a crucial step in Alzheimer's disease development. This process has been indirectly associated with elevated cholesterol levels. It's hypothesized that Ginkgo leaf extract inhibits Aβ formation by competing with free cholesterol for interaction with Aβ, thereby reducing their aggregation. Additionally, Ginkgo leaf extract mitigates reactive oxygen species (ROS) accumulation induced by Aβ, notably through compounds like flavonol quercitin, while also decreasing neuronal apoptosis, a significant contributor to neurodegenerative diseases. (Mullaicharam, 2013)**.**

Conclusion

In the realm of brain diseases management, use of dietary supplements has become a fascinating area of research, with the potential to reduce the risk and symptoms. Through extensive exploration of these supplements, researchers have found a wide range of therapeutic benefits from omega-3 fatty acids found in fish liver to antioxidants like caffeic acid and herbal extracts like gingko biloba in reducing diseases like Parkinson's disease, Alzheimer's disease and cognitive decline. Beyond these, a myriad of compounds, such as curcumin, found in turmeric, and resveratrol, abundant in red grapes and berries, also exhibit promising neuroprotective properties.

In the light of these encouraging results, it is crucial to proceed cautiously and make well-informed decisions when including dietary supplements into the treatment of brain diseases. Supplements offer a non-invasive adjunct to the conventional treatment, but they cannot replace potential medical treatments or expert's advice. It cannot eliminate the need for a balanced diet as well as preventive care. Along with supplements, it is also crucial to adopt dietary interventions, lifestyle modifications and cognitive exercises for better outcomes. More thorough clinical trials and long-term research are required since the best doses, formulations, and long-term benefits of these supplements are still being investigated.

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Chapter 34

Therapeutic Potential of Fermented Foods in Combating Inflammatory Diseases

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ABSTRACT

A persistent inflammation can result in the development of chronic conditions such as arthritis, obesity, inflammatory bowel disease, ulcerative colitis, multiple sclerosis, and diabetes. Anti-inflammatory or immunosuppressive medications are utilized to alleviate symptoms of inflammation; however, their efficacy diminishes over extended durations and they can induce significant adverse reactions. The fermented foods are rich sources of beneficial bacteria and are highly efficient in managing the inflammation naturally. Currently, a wide variety of fermented foods are available globally. These include dairy-based, meat-based, vegetable and fruit-based products with the ability to alleviate inflammation. The fermented foods effectively regulate the composition of gut bacteria, promoting a healthy balance and eliminating harmful microorganisms. They also generate advantageous metabolites that possess anti-inflammatory properties. The fermentation enhances the antioxidant activity of bioactive substances, which is advantageous for the human health. To summarize, the fermented foods have notable health advantages, such as enhanced management of the inflammation, increased antioxidant activity, and improved antioxidant characteristics

KEYWORDS
Inflammation, Chronic inflammatory diseases, Fermentation, Fermented products

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INTRODUCTION

Inflammation is defined as a defensive mechanism initiated by the immune system of the body against harmful agents including pathogens, dead cells, lethal compounds, or radiation, and functions by eliminating the agents, and initiating the recovery process. Therefore, for maintaining good health of the host, inflammation is necessary (Najafi et al., 2018). Basically, a quick and prompt response comprising a cascade of cellular processes and interactions at the molecular level reduce the risk of harm or infection. This prompt and powerful action is then termed as acute inflammation. The mitigating procedure aids in the resolution of the acute inflammation and the return of tissue homeostasis. At the tissue level, inflammation is characterized by redness, heat, pain, swelling, and temporary function loss of the tissue. Major events that happen during the process of inflammation are changes in the vascular permeability, white blood cell activation and accumulation at infection sites, and the release of inflammatory cytokines and chemokines. If the acute inflammation is not resolved, it persists longer and is termed as chronic inflammation (Chen et al., 2018). The chronic inflammation can adversely affect healthy tissues and result in different chronic diseases such as arthritis, obesity, inflammatory bowel disease (IBD), inflammatory bowel syndrome (IBS), ulcerative colitis (UC), multiple sclerosis (MC), and type 1 diabetes (T1D), etc. (Forbes et al., 2016).

To reduce inflammation and improve the associated diseases, seeking treatment becomes compulsory. Anti-inflammatory or immune suppressive drugs are mostly used to relieve the inflammatory symptoms and treat the disease. These drugs, either steroidal or non-steroidal, temporarily relieve the symptoms but are ineffective for longer periods of time and also cause severe adverse effects (Khumalo et al., 2022). Therefore, people are looking for alternative approaches that have long lasting benefits with minimal or no side effects. A growing interest has been observed in utilizing natural remedies for the management of inflammation. These remedies include changing behavioral and dietary habits or using specific natural foods or products (Karati et al., 2022). Different plant-based products have been used for the treatment of various chronic diseases, including IBS, UC, and T1D. Furthermore, fermented foods, a natural reservoir of beneficial microorganisms, ancient culinary inventions, that have been enjoyed for millennia by people from many cultures, are becoming more widely known for their possible medicinal benefits (Karati et al., 2022).

Fermented Foods

Fermentation and its History

Fermentation is an anaerobic process run and controlled by the microorganisms in which they utilize complex constituents of the food and convert them into simpler and digestible compounds (Ross et al., 2002a). The microorganisms playing a major role in the food fermentations are lactic acid bacteria (LAB), some yeasts, and molds. Fermentation is the oldest method of food processing, as its history is as old as human history itself. People were consuming fermented foods when they were not even familiar with the process and benefits of them (Hutkins, 2008). It is believed that fermentation started with brewing of the beers in Egypt in 1300 B.C, but it happened a long time ago. Reports dates the production of wine, cheese, and soy sauce-like products to 600 BC. However, the researchers maintain that food processing predates this era (Prajapati and Nair, 2003). Fermented products are produced when microbes present in the food utilize the proteins, carbohydrates, and fats of the food and convert them into less complex compounds (Ohemeng-Ntiamoah and Datta, 2018). Fermentation has not been carried out intentionally but has naturally happened in response to changes in pH, humidity, and temperature of the foods (Vallee, 1998). There were no resources or appliances available at that time for food preservation, and mild changes in pH and temperature triggered the fermentation. In old times it was considered spoilage but then used to preserve or enhance the nutritional properties of foods (Ross et al., 2002b). If we look at the term "fermentation" it dates back to 1856, when Louis Pasteur firstly used it, and from this, he meant respiration without air, which he linked to the fermentation initiated by yeasts (Yadav et al., 2021). In 1910, Elie Metchnikoff stated that consumption of fermented products can improve the lifespan and health of people. Until this time, fermented products were not considered to be beneficial for health (Ghoshal, 2018). Exploring the health benefits of fermented foods is among the hottest research topics these days.

Types of Fermentation

The LAB divides fermentation into two types based on its activity and the final product it produces. i.e., homo-fermentation and hetero-fermentation (Khumalo et al., 2022).

Homo-fermentation: In this type of fermentation, lactic acid is the only end product produced in response to LAB activity. More specifically, one molecule of glucose is converted into two molecules of lactic acid.

Hetero-fermentation: In this type of fermentation, along with lactic acid, methanol and carbon dioxide are also produced as end products of fermentation.

Fermented Foods from Around the World

The fermentation has been a part of human existence since ancient times. Although our ancestors lacked knowledge of the scientific principles underlying these processes, they relied on trials and errors, as well as occasional spontaneous actions, to develop these rhythmic culinary techniques that have now become integral to cuisines worldwide. Fermentation was initially used because of its ability to improve the food digestibly and taste. Additionally, people used it to prolong the shelf of food. In the present day, we have a wide variety of skills that have originated from many cultures around the world (Galimberti et al., 2021). Each region possesses at least one distinct culinary product that is an integral component of its cultural legacy. This fermented product distinguishes itself from other regional goods based on the specific cultural practices employed, including the choice of food to be fermented, the duration of fermentation, and the specific microbes used in the fermentation process. The foods such as milk, meat, vegetables, fruits and drinks are fermented to make new products (Tamang et al., 2020). The following are some examples of such foods.

Beneficial Microbes Involved in Fermentation

The fermentation of foods involves a heterogeneous assortment of microorganisms, such as bacteria, yeasts, and fungus. Among all the microorganisms, bacteria are the most prevalent, with LAB being particularly abundant in the manufacture of fermented foods. The LAB has been classified as generally regarded as safe (GRAS), which is why most of the probiotics available in the market belong to the LAB group. However, the non-LAB species, like members of *Bacillus, Bifidobacteria, Brachybacteria, Brevibacteria, Micrococca,* and *Propionibacteria*, are also utilized in the food fermentation. They mostly serve as a helper microorganism that assist in facilitating the progression of the fermentation process. The non-LABs are either deemed safe or have no documented detrimental effects on the host. Additionally, there is a current tendency to classify the non-LAB members derived from dietary sources based on their probiotic qualities. Research has documented the potential probiotic properties of strains belonging to the *Bacillus* and *Bidiobacterium* genera (Sulieman, 2022).

Table 1: Some famous fermented foods around the globe

S. No	Fermented food	Origin	Description
Milk based fermented products			
1	Yogurt	Central Asia	It is fermented with specific lactic acid bacteria mostly *Lactobacillus bulgaricus* and *Streptococcus thermophilus*. It is either consumed plain or flavored with other flavor products
2	Kefir	Russia	It is fermented with strains of LAB and yeasts and has a tangy type flavor.
3	Cheese	Middle East	Milk proteins are coagulated, using coagulants and then are fermented with lactaria and yeasts. Based on the type of bacteria, yeasts, milk and procedure used they have variety of types with specific tastes.
4	Buttermilk	Europe	The liquid after churning butter from cultured cream is fermented with LAB. It also has tangy type flavor
5	Lassi	Indo-Pak subcontinent	It is a liquid made from the fermented milk product known as Dahi/curd. The taste of lassi is varied due. It is either used plain or flavored.
Meat based fermented products			
1	Sucuk	Turkey	Different spices are mixed into grounded meat and dried for several weeks. Mostly lactic acid bacteria are involved in the fermentation of the sucuk. The taste of the Sucuk is determined by the spices used and the final cooking method.
2	Pastrami or Pastirma	Middle East	Similar to Sucuk, Pastrami is made from cured meat that is salted, coated in a thick crust of different spices and then air dried. Mostly LAB are involved in the fermentation of Pastrami but other strains can also be used in the fermentation process.
3	Salami	Italy	Salami is fermented meat sausage that is prepared from cured meat mixed and coated with different spices and salts. The product is then left to ferment for several weeks. LAB mostly *Lactobacillus* and *Pediococcus* along with yeasts like *Candida* and *Debaromyces* are used in the fermentation of Salami.
4	Saucisson	France	Similar to Salami, Suacisson is made from cure meat that is hardened, filled into moldings and left to ferment for several weeks. LAB mostly *Lactobacillus* and *Pediococcus* are involved int eh fermentation of Saucisson. Somes species of molds like *Penicillium nalgiovense* or *Penicillium chrysogenum are applied on the exterior of the meat for maturation of the product.*
5	Lạp xưởng	China	It is made from meat that is seasoned with rice wine or soy sauce and then filled in some defined castings. The castings are air dried and allowed to ferment for several weeks. The species of LAB mostly *Lactobacillus* and *Pediococcus* are involved in the fermentation of Lạp xưởng.
Vegetables and Fruits based fermented products			
1	Table olives	Aisia	Olives are with 6-10% salts (w/v) are directly placed in brine and is allowed to ferment for more than 10 months. LAB along with yeast are involved in the fermentation of table olives.
2	Kimchi	Korea	Kimchi is mostly made from cabbages and Radishes but other vegetables can also be used. These vegetables are mixed with paste made from corn flacks, garlic and ginger. The product is then allowed to ferment for several days or weeks. The species of LAB such as *L. kimchi, L. plantarum,* and *L. mesenteroides* are mostly involved int eh fermentation of kimchi.
3	Sauerkruat	Germany	Saurkruat is similar to kimchi but in Sauerkruat mostly shredded cabbages are used and instead of *L. kimchi, L. brevis* is used.
4	Miso	Japan	Miso is made from a paste that is prepared from a mixture of soybeans and rice or barely. The paste is then salted and a starter culture of *Aspergillus oryzae* (koji) is applied on it. The paste is then allowed to ferment for several weeks to years. Based on the desired qualities of the product species of LAB are also used in the fermentation of Miso.
5	Tempeh	Indonesia	For making Tempeh, soybeans are cooked and then inoculated with *Rhizopus oligosporus. The product is then left to ferment for a day or two.*
Fermented drinks			
1	Beer	Iraq and Egypt	For making beer, barley is firstly malted and then mashed. The mashed product is then cooked with hops. Then it is cooled and *Saccharomyces cerevisiae is added to it. The product is then allowed to ferment for one to two weeks.*
2	Sake	Japan	Sake is mainly prepared from rice. The rice is steamed and *Aspergillus oryzae is mixed in it. After that, some water and Saccharomyces cerevisiae are added to it followed by fermentation for several weeks.*

3	Kombucha	China	Kombucha is made from black or green tea that is cooked with sugar and a synbiotics culture of yeast mostly *Saccharomyces cerevisiae* and bacteria mostly *Acetobacter xylinum is added to it. The product is then fermented for weeks.*
4	Cider	UK	It is made from apple juice that is fermented with weeks to months with yeasts. In most of the cases *S. cerevisiae* is used but other strains of yeast can also be used.
5	Pulque	Mexico	Pulque is made from sap of agave like plant. The sap is collected and is then left to ferment naturally.

Among fungi, species from *Aspergillus, Fusarium, Rhizopus,* and *Penicillium* have documented role in the fermentation of foods (Copetti, 2019a). Such as *A. acidus, A. sojae, A. niger, A. sydowii, A. flavus*, and *A. versicolor* are utilized in the manufacturing processes of awamori liquors, miso, sake, soya sauce, and puerh tea production. Within the genus *Fusarium,* there are currently around 200 species that are officially recognized and utilized in the process of cheese fermentations. Species belonging to the *Fusarium* genus are acknowledged as potential sources of various enzymes for commercial use. Additionally, they serve as facilitators in the creation of fragrances and pigments in the final products. The *Fusarium* sp. strains create secondary metabolites, some of which are toxins that can harm the health of both human and animals. However, research has shown that the formation of mycotoxins ceases under industrial circumstances (Copetti, 2019a). The species of *Rhizopus* like *R. arrhizus, R. delemar, R. oryzae*, and *R. stolonifer* play a significant role in the fermentation process of yaoqu, banh men, and tempeh, which are all types of fermented soybean cuisine. The *R. oryzae* is classified among GRAS fungi and is frequently utilized in the preparation of several Asian fermented dishes. There is no published evidence of any negative effects on other species (Copetti, 2019a). The species of genus *Penicillium* including *P. biforme, P. camemberti, P. caseifulvum*, *P. chrysogenum, P. commune, P. expansum, P. fuscoglaucum, P. nalgiovense. P. nordicum, P. palitans,* and *P. solitum* are frequently found in the microbiota of various cheeses, including blue cheeses, Brie, and Camembert as well as fermented half-ripened sausage and raw dried or smoke-cured meat products. These species are reported to have positive impact on the quality of the final fermented products have no negative impact on their host (Copetti, 2019a).

Moreover, yeasts belonging to genera such as *Candida, Clavispora, Cyberlindnea, Debaromyces, Kzachstania, Pichia,* and *Saccharomyces* have a role in fermenting olives, sourdough, wines, beers, milk, and beans, respectively (Copetti, 2019b). Yeasts have a longstanding history of interacting with LAB and exerting a positive influence on the quality of the products. Furthermore, they do not have any detrimental effects on their hosts (Copetti, 2019b).

Anti-Inflammatory Role of Fermented Foods

The fermented foods improve inflammation though various mechanisms including maintaining homeostasis of the gut microbiota, producing metabolites with anti-inflammatory effects, modulating the immune system or enhancing the antioxidant activity. The detail is provided below.

Impact on Gut Microbiota Composition and Function

Studies have shown that the human intestinal tract has a significant number of bacteria, with a range of 600-1000 different species. These bacteria have a far larger number of genes compared to the complete human genome. In recent decades, there has been extensive research on the role of gut microbiota in relation to health and disease. It has been established that a well-balanced gut microbiota is linked to good health, while an imbalanced gut microbiota, also known as gut microbiota dysbiosis, is initially associated with inflammation followed by various diseases. The microbial composition of the human gut is distinct, akin to a fingerprint for each person, and functions as "endocrine" tissue or the "second brain" for every individual. Studies have primarily concentrated on altering the composition of gut microbiota as a means of treating and controlling inflammation and associated diseases (Anwar et al., 2019).

In this regard, the capability of fermented foods to mitigate the gut flora has been extensively demonstrated. A study examined the impact of plant based fermented products on the microbial and metabolomic variations in more than seven thousand individuals. It was found that there was a substantial difference in β diversity between those who consumed fermented food and those who did not (Rettedal et al., 2019). The microbiomes of individuals who consume fermented products were found to be associated with various bacterial species including *Bacteroides, Pseudomonas, Dorea, Lachnospira, Prevotella, Alistipes putredinis, Oscillospira, Enterobacteria, Fusobacterium, Actinomyces, Achromobacter, Clostridium clostridioforme, Faecalibacterium prausnitzii, Bacteroides uniformis, Clostridiales,* and *Delftia* (Rettedal et al., 2019). Additionally, a group of 115 individuals who had eaten fermented foods at different frequencies were studied for a period of 4 weeks. The study revealed that the participants who consumed fermented foods had a combination of microbes that are typically found in fermented foods (such as *L. acidophilus, L. brevis, L. kefiranofaciens, L. parabuchneri, L. helveticus*, and *L. sakei*), as well as bacteria that are not typically linked with these foods such as *Bacteroides paurosaccharolyticus, Enorma massiliensis Enterococcus cecorum, Prevotella melaninogenica, Prevotella multiformis,* and *S. dysgalactiae* (Taylor et al., 2020). Following a similar approach as in the earlier study, the impact of a diet containing a significant number of fermented foods (dairy products, fermented vegetables, and virgin beverages) on physically fit individuals over a seventeen-week period was investigated, comparing it to a high-fiber diet (Spencer et al., 2022). Over the course of the four-week dietary intervention, the daily diet's proportion of fermented foods was raised. A six-week period during which a substantial amount of fermented food was consumed came next. Finally, there was a four-week period where participants could choose their desired level of fermented diet consumption. The consumption of a diet rich in fermented foods led to an augmentation in the α diversity of the gut microbiota, a phenomenon that remained un-observed with the consumption of a fiber-rich diet. Surprisingly, the microbiome diversity continued to develop during the 'choice' period, even though the intake was raised through the 'maintenance' period. There was a clear correlation among time and diversity, as indicated by a strong connection (Spencer et al., 2022).

Production of Beneficial Metabolites with Anti-inflammatory Effects

The microorganisms generate certain metabolites during fermentation that possess anti-inflammatory properties. Below, we will describe instances of fermented food products that contain anti-inflammatory metabolites.

Kombucha, a fermented product contains flavonoids and other polyphenols that hinder oxidative enzymes, resulting in anti-inflammatory benefits. The high antioxidant concentration of oak-derived Kombuchas is mostly attributed to their phenolic composition and its ability to decrease the synthesis of nitric oxide, TNF-α, and IL-6 by lipopolysaccharides, indicating a notable anti-inflammatory effect. Consuming Kombucha also stimulate the proliferation of gut bacteria that produce butyrate, which has anti-inflammatory properties (Villarreal-Soto et al., 2019).

Curcumin, a primary constituent of curcuminoids present in fermented turmeric, is a molecule having antioxidant and anti-inflammatory properties. It has demonstrated efficacy in alleviating symptoms of osteoarthritis, type 2 diabetes, and dyslipidemia. The curcumin has been found to interact with various molecular targets involved in inflammation, such as inhibiting the production of pro-inflammatory cytokines, TNF-α, and IL-1, in LPS-induced human monocytic macrophages and L929 fibroblasts. Additionally, it inhibited the synthesis of nitric oxide and the activation of NF-kB, a transcription factor that regulates inflammation (Ghiamati Yazdi et al., 2019).

Kimchi, another fermented product contains a bioactive compound called 3-(4′-hydroxyl-3′,5′-dimethoxyphenyl) propionic acid (HDMPPA), which has been discovered to reduce the levels of pro-inflammatory mediators and cytokines. More precisely, BV2 microglial cells that were exposed to LPS were protected from the activation of TNF-α, IL-1β, and NF-κB. A newly discovered antimicrobial peptide (YD1) derived from kimchi has been shown to enhance Nrf2 signaling and inhibit NF-κB activation, resulting in a decrease in the production of pro-inflammatory cytokines in both cellular and animal models (Yun et al., 2023).

In a study conducted, where the researchers demonstrated the ability of the soybean peptide QRPR to reduce interleukin levels and inhibit the expression of inflammatory signaling pathways PIK3, AKT, and mTOR in a RAW 264.7 cell inflammation model. Research indicates that the fermentation process of cooked soybean produces free isoflavones, which have been found to help decrease inflammation. A study conducted in a laboratory setting examined the effects of seven indole alkaloids found in fermented Korean soy sauce (kanjang) on BV2 cells that were stimulated with LPS. The results showed that two of these alkaloids were able to decrease the production of nitric oxide synthase, the expression of COX-2, and the activation of the NF-κB pathway. These findings demonstrated the potential of these metabolites to reduce neuroinflammation (Yusof et al., 2019).

Modulation of the Immune System Response

The microorganisms and metabolites included in fermented foods possess the capacity to regulate and enhance the immune system, hence improving inflammation. Here are some examples that are discussed. Sauerkraut is a distinct and exclusive provider of LAB, a group having recognized probiotics. They have a significant role in enhancing both innate and adaptive immunity and reducing inflammation by influencing the composition of the gut microbiota. In a study, the researchers found that giving the LAB strains to BALB/c mice reduced the inflammation in their airways caused by allergens. This was achieved by balancing the Th1/Th2 immune response and increasing the number of Tregs. Analysis of the microbiome showed that administration of LAB increased the frequency of the prominent phyla (*Firmicutes* and *Bacteroidetes*) in the gut microbiota. D-phenyllactic acid, a phenolic molecule synthesized by LAB in sauerkraut, strongly binds to the hydroxycarboxylic acid receptor 3 (HCA3), a constituent of G protein-coupled receptors that bind to hydroxycarboxylic acids. These receptors have a crucial function in controlling immunological activities (Akhtar et al., 2021).

Similarly, studies have unequivocally demonstrated the beneficial health impacts of another fermented food kimchi. The Kimchi and its components have an anti-inflammatory effect by inhibiting the expression of COX-2 and iNOS, as well as the activation of the NF-κB pathway. Animal investigations have shown that the dichloromethane fractions of kimchi exhibit significant free radical scavenging activity and a strong antioxidant impact against LDL oxidation. KIMCHI3-(40-Hydroxyl-30,50-dimethoxyphenyl) propionic acid, a compound found in kimchi, has been shown to reduce inflammation in BV2 microglial cells that were stimulated with LPS. It achieves this by decreasing the secretion of pro-inflammatory cytokines such as TNF-α and IL-1β. Atopic dermatitis is a skin condition that involves inflammation and is characterized by immunological responses dominated by T helper 2 (Th2) cells and an increased level of immunoglobulin E (IgE). The application of *Lactobacillus sakei* WIKIM30, a probiotic strain derived from kimchi, to mice with 2,4-dinitrochlorobenzene-induced atopic dermatitis suppressed the Th2 immune response and the production of Th2 related cytokines (IL-4, IL-5, and IL-13). It also regulated the balance between Th1 and Th2 cells, promoted the differentiation of Tregs, and reduced skin lesions. In addition, the application of both live and heat-inactivated *L. sakei* probio-65, which is also derived from Kimchi, improved cutaneous inflammation and lesions by decreasing serum IgE levels and/or inhibiting Th2-related cytokines. The strain *L. plantarum* K-1, which was obtained from kimchi, has the potential to reduce inflammation and relieve allergy disorders. This is achieved by decreasing the expression of TNF-α and IL-4 and blocking the activation of NF-κB (Shahbazi et al., 2021).

Antioxidant Activity of Bioactive Compounds Enhanced by Fermentation

Nature is abundant with natural antioxidants, and research on antioxidants consistently confirms their positive impact on health, including their anti-inflammatory, anti-aging, anti-bacterial, anti-viral, and anti-cancer properties. The primary rationale for these benefits is from the components' capacity to mitigate issues arising from oxidative damage in the body. So far, about 8000 compounds with antioxidant properties have been discovered. The primary categories include flavonoids, lignans, phenolic acids, and stilbenes (Adebo and Gabriela Medina-Meza, 2020). Foods are the primary suppliers of these chemicals. While a wide range of food products include anti-oxidant chemicals, their ability to be absorbed by the body may be restricted. These chemicals have the potential to be liberated or transformed into more potent forms by fermentation. This phenomenon has been discussed with a limited number of cases as outlined below.

A comparative study was conducted to assess the total phenolic content (TPC), 2,2-Diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging effects, anti-oxidant activity, reducing effects, and chelating capacity of unfermented and fermented pineapple (Rashad et al., 2015). The fermented pineapple exhibited superior outcomes in all relevant domains as associated to the unfermented waste. The PC reached its peak at a level of 8 mg/mL, with a value of 120 mg/100 g dry weight. Above this concentration, the total phenolic content decreased in an inversely proportional manner. The findings also indicated a rise in the antioxidant activity of pineapple towards linoleic acid radicals, with the unfermented sample exhibiting 88% activity and the fermented sample exhibiting 95% activity. In addition, a gas chromatography/mass spectrometry (GC/MS) was performed to determine the chemicals that are thought to be responsible for the observed antioxidant activity. The investigation revealed that hydrazones accounted for 27.93% of the components, while β-stesterol, a type of phytosterol, made up 11%. Additionally, phenolic moieties and chemical classes such as chromenes, furanones, and heterocyclic compounds were identified as the key responsible agents, collectively representing 39% of the composition (Rashad et al., 2015).

The grape pomace underwent fermentation using *A. elegans and U. isabelline* (Dulf et al., 2020). The total phenolic compound (TPC) level of the pomace fermented with *A. elegans* grew by 47.00% from the initial value of 4.80 mg GAE/g dw by day four, and thereafter decreased till the end of the fermentation duration. On the other hand, fermentation with *U. isabelline* resulted in a 27% drop in TPC content. For TFC, *A. elegans* showed a 51% increase till day 4, followed by a reduction. On the other hand, *U. isabelline* exhibited a 48% decrease from its baseline value of almost 1 mg QE/g dw. The rise in *A. elegans* values was linked to the ability of *A. elegans* to release cellulolytic enzymes, which break down β-glycosidic bonds and generate free phenolics. The DPPH radical scavenging assay was employed to measure the antioxidant activity, which revealed contrasting outcomes for the two fungi. The fermentation of *A. elegans* exhibited a 21.42% increase on day 4, which was subsequently followed by a decrease. On day 8, *U. isabelline* initially reduced antioxidant activity by 16%, but later experienced an increase (Dulf et al., 2020).

(Leite et al., 2019) utilized a diverse range of byproducts derived from the wine industries. The article indicated that the outcomes differed depending on the specific extracts and strains employed. The microbe *R. miehei* NRRL 5282 was used to ferment the residues of apple, black grape, and yellow pitahaya using freeze and oven drying individually. The outcomes were assessed and contrasted for PC and DPPH radical scavenging test. PC of the freeze dried residues were 477, 1956, and 495 mg gallic acid equivalents (GAE) per 100 grammes dry weight (dw) for apple, grape, and pitahaya, respectively.

Conclusion

Persistent inflammation can result in the development of chronic conditions such as arthritis, obesity, inflammatory bowel disease, ulcerative colitis, multiple sclerosis, and type 1 diabetes. Anti-inflammatory or immunosuppressive medications are utilized to alleviate symptoms of inflammation; however, their efficacy diminishes over extended durations and they can induce significant adverse reactions. Fermented foods are rich sources of beneficial bacteria and are highly efficient in managing inflammation naturally. Currently, there is a wide variety of fermented foods available globally. These include dairy-based products such as yoghurt, kefir, cheese, buttermilk, lassi, as well as meat-based products like sucuk, pastrami, salami, saucisson, Lạp xưởng. Additionally, there are vegetable and fruit-based fermented products like table olives, kimchi, sauerkraut, miso, tempeh, and cider. Research has demonstrated that fermented meals can effectively regulate the composition of gut bacteria, promoting a healthy balance and eliminating harmful microorganisms. Fermented foods also generate advantageous metabolites that possess anti-inflammatory properties. Compounds including flavonoids, polyphenols, and curcumin inhibit oxidative enzymes, leading to anti-inflammatory effects. Fermented foods possess bacteria and metabolites that have the ability to control and boost the immune system, hence alleviating inflammation. By achieving equilibrium in the Th1/Th2 immune response and augmenting the population of Tregs. Through the suppression of COX-2 and iNOS gene expression and the stimulation of the NF-κB signaling pathway. Fermentation enhances the antioxidant activity of bioactive substances, which is advantageous for human health. Antioxidants, such as phenolic acids, flavonoids, lignans, and stilbenes, have been discovered to possess beneficial effects on human health. These effects include their ability to reduce inflammation, combat bacterial and viral infections, slow down the ageing process, and inhibit the growth of cancer cells. Food is the main source of these substances, and their absorption by the body may be limited. However, due to fermentation, they become more accessible or exhibit increased activity. To summarize, fermented foods have notable health advantages, such as enhanced management of inflammation, increased antioxidant activity, and improved antioxidant characteristics.

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Chapter 35

Supplementation of Various Biotics in Poultry Nutrition for Optimizing Well-Being

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ABSTRACT

Global commercial poultry production has core importance for subsistence and the economy. However, antibiotic use has accelerated its expansion, giving rise to concerns regarding drug-resistant bacteria and residues. The growing number of drug-resistant bacteria and the buildup of antibiotic residues in chicken products complicate the treatment of diseases in both humans and animals. Even, the modest dose of antibiotics administrated in poultry leads to residues, which are hazardous to human health. Antibiotics used in livestock and poultry are often defecated intact, building up in the ecosystem and entering the human food system (meat and egg). Consequently, considerable scholarly attention has been devoted to the exploration of antibiotic substitutes, specifically in the context of the European Union's prohibition on antibiotic usage in poultry and animals. In poultry production, probiotics, prebiotics, postbiotics, synbiotics, phytobiotics, organic acids, and bioactive peptides have acquired enormous attention. These alternatives promote feed intake, metabolism, performance, and growth while decreasing disease by regulating the immune system and gut bacteria, reducing infections, and enhancing gut health and antioxidant status. Additionally, feed additives effectively competing with antimicrobial resistance and leave no residues in poultry products. This chapter aims to provide a thorough description of these innovative feed additives, and their impacts on poultry production.

KEYWORDS
Antioxidant, Feed additives, Growth performance, Gut morphology, Immunity, Poultry

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INTRODUCTION

It is well known that the inappropriate and uncontrolled use of antibiotics is a massive threat to human and animal health. The immediate global steps should need to be taken to redress the adverse effects of the antimicrobial resistance outbreak pandemic (Anderson et al., 2019). The poultry industry, which is expanding as a component of business path of the agricultural and veterinary sectors to cope with the increasing global demand for economical eggs and meat, is reliant on antibiotic growth promoters due to the growth of animal feeds (Rafiq et al., 2022). These antibiotic growth promoters (AGPs) are playing a substantial contribution in international farming or farming technique intensification, since they influence gut health, prevent subclinical infections, and improve feed efficiency. (Cox and Dalloul, 2015). Superbugs or drug-resistant bacteria have spawned as a result of the regular use of sub-therapeutic dosage of antibiotics, genuinely upsetting the natural gut flora and ingenious health hazards while they were transmitted to human receivers through infected chicken products (Castanon, 2007; Ripon et al., 2019). Regulatory organizations like the European Union had begun imposing restrictions on adding AGPs in animal feed as early as 2006 due to this incidence which compelled the sector to germinate for feasible alternatives (Alam and Ferdaushi, 2018). On that note, lots of studies have accomplished some nutritional supports as natural potentialities that can be used in place of it with spirulina, probiotics, prebiotics, phytobiotics, and synbiotics (Abd El-Hady et al., 2022; Rahman et al., 2022; NO and FC, 2023; Rafeeq et al., 2023; Dong et al., 2024). The above alternatives bring the same growth-promoting attributes as AGPs but with the added benefits of innocuity, lack of residuals, and a net positive influence on the gut ecology and animals' general health (Ferdous et al., 2019; Hafeez et al., 2020). Moreover, recent research has indicated how efficient such feed additives as phytogenic are at relieving stress and boosting immunological responses in stress-induced chickens without inflicting the adverse effects of antibiotics (Mehdi et al., 2018). As more data is availed, the method of rearing poultry continues to evolve. The purpose of this chapter was to detail the advantages of the natural feed addition over the AGPs, which can be summarized in significant health promotion and sustainable chicken production. Because of urbanization, growing populations, rising purchasing power of people, the demand for antibiotic free chicken products has been increased, so as a result the production of antibiotic free poultry products is crucial (Erdaw and Beyene, 2022). Challenges persist, especially with conventional poultry farming methods, which are more vulnerable to outbreaks of diseases due to their intensive nature (Graham et al., 2007). These issues are exacerbated by recent US Food and Drug Administration rules that limit the use of certain antibiotics, which have historically been essential to the financial stability of chicken farming. Subtherapeutic antibiotics such as tetracyclines, aminoglycosides, lincosamides, macrolides, penicillin, streptogramins, sulfonamides, and aminoglycosides have been prohibited (Brown et al., 2017; Yang et al., 2019). Organic chicken production prohibits the fertilizers and antibiotics usage, has challenges such as disease outbreaks, slower growth, and higher mortality rates. As a result, organic poultry products are often more expensive and find it challenging to meet the increased demand from customers (Mongeon and Dam, 2021).

In light of the aforementioned challenges, this chapter presents a range of innovative approaches, including the use of several types of feed additives (biotics), which constitute the cutting edge of research in poultry health and nutritional management. These solutions not only address the current issues of antibiotic resistance but also provide a route to improving poultry growth and health in a way that meets customer expectations for safety and sustainability.

Probiotics

The term probiotics was derived from the Greek word's "pro" "in favor" and "biotic which means "life" (Metchnikoff, 1908). Probiotics are live microorganisms which when added to feed at a specific dietary level, stabilize the unbroken microflora of the host and thus stimulate health and well-being of poultry. Yousaf et al. (2022) defined as a live compound that, when taken in sufficient amounts, has a favorable effect on the host's well-being, thereby improving the balance of intestinal microflora. Some of the probiotics used are; *Lactobacillus (L.) acidophilus, L. plantarum, L. bifidus, L. bulgaricus, L. fermentum, L. casei, L. ruminis, L. lactis, L. salivarius, Bifidobacterium bifidum, Bacillus subtilis Enterococcus feacium, Streptococcus feacium, Streptococcus thermophilus, Saccharomyces cerevisiae, Aspergillus oryzae,* and *Candida pintolopesii*. (Sharma et al., 2018; Khomayezi and Adewole, 2022). Probiotics increase the infection resistance. Stimulate the defense system and microbiota balance (Brisbin et al., 2008). Additionally, studies have shown that Lactobacillus strains increase the populations of lactic acid and anaerobic bacteria in the GIT and improve the optimal condition for nutrient absorption by the host (Olnood et al., 2015; Reuben et al., 2021). Probiotics maintain the balance between beneficial and pathogenic bacteria, a critical factor to poultry' gut health and proper development, and inhibit the growth of adverse microorganisms by reducing the intestinal pH due to short chain fatty acid synthesis (Yaqoob et al., 2022). Probiotics also affect the intestines' histomorphology by increasing villus height and villus to crypt ratio, thus increasing the available surface area for nutrient absorption and proper functioning (Huang et al., 2012; Abdel-Rahman et al., 2013; Bai et al., 2013; Afsharmanesh and Sadaghi, 2014). They also contribute to enhancing the intestinal morphology after damage by pollutants, such as deoxynivalenol, especially in laying hen chickens (Awad et al., 2006; Lei et al., 2013). Probiotics play a crucial part in managing enteric pathogens of the likes of *Salmonella spp.* and *E. Coli* O157 through competition for nutrients, the presentation of receptor sites on the intestinal mucosa, and the secretion of antimicrobial compounds (Mehdi et al., 2018; Al-Sagheer et al., 2019; Abd El-Hack et al., 2022). Furthermore, with or without antibiotics, probiotics noticeably improve the immune system of poultry through increasing the formation of antibodies and improving the defense system against diseases such as infectious bursal disease and Newcastle disease virus, which are specifically noticeable in turkeys (Çetin et al., 2005; Haghighi et al., 2006; Khaksefidi and Ghoorchi, 2006; Hussein et al., 2020). *Lactobacillus gallinarum* PL53 lowered the *C.jejuni* and enhanced *Lactobacillus* and *Bifidobacterium* counts in the gut and inreased the weight gain in *C.jejuni* challenged broilers (Khan et al., 2019). In summary, the findings seem to show that probiotics have the potential to significantly boost the immune system, growth performance and health of chickens.

Prebiotic

Prebiotics are indigestible food elements that ferment in the colon, promoting useful bacteria to improve the host's health (Gibson and Roberfroid, 1995). They generally comprise materials like mannan-oligosaccharides, fructooligosaccharides, galacto-oligosaccharides, lactulose, and inulin, which arise naturally from legumes or by various treatments. These compounds are referred as generally recognized as safe (GRAS), as these maintain a microbial equilibrium by providing good bacteria in the gut and inhibiting destructive bacteria (Solis-Cruz et al., 2019). The gut microbiota helps leave out pathogens, digest nutrients, and reinforce the immunological reaction. When used at prescribed dosages, prebiotics for example MOS and FOS have been shown to have a significant impact on GIT health and efficiency by reducing pathogenic bacteria such as *E. coli* and *Clostridium perfringens* and favoring the production of tolerant microorganisms, such as type *Lactobacillus* (Kim et al., 2011; Pourabedin and Zhao, 2015; Slawinska et al., 2019). It has also been reported by Rehman et al., 2020 that the administration of prebiotics or probiotics can lead to better broiler growth performance. Toghyani et al. (2011) reported that the use of prebiotics in a broiler diet improves the characteristics of the carcass. The potential mechanism is similar to the previous one, reduced colonization of the intestinal pathogen, and excretion of more attention to the final utilization of these nutrients. Chen et al. (2005) reported that supplementation of Oligofructose (Raftifeed®OPS) and inulin (Raftifeed®IPE) at the rate of 1% each of the prebiotic in the diet of laying hens increased the egg production and feed efficiency compared to the control group. Prebiotics induce significant changes in the bird's immune system. They increase the synthesis of antibacterial substances – bacteriocins and short-chain fatty acids, which inhibit the intestines' growth and multiplication of bad flora and support improvement of immune cells while stimulating the level of immunoglobulin, which is an essential factor in enhancing the bird's immunological response (Vamanu and Vamanu, 2010; Lopetuso et al., 2019). Prebiotics play a vital role in achieving the ideal gut morphology where it improves the villi length and density resulting in efficient feed utilization and nutrient absorption. According to evidence, "Consistent FOS administration has improved crypt depth as well as lengthened villi; this resulted in nutrient ingestion and overall intestinal health being optimised" (Hanning et al., 2012; Rehman et al., 2007). The obtained results indicate a wide range of prebiotic advantages in poultry nutrition, as shown by intestinal health and the digestive system to the sub-set immune system, and gut morphology. Therefore, the nutrient uptake and bird performance is improved.

Postbiotics and Parabiotics

The concept of metabolic compounds poised through probiotics is postbiotics, and poses a beneficial effect on the host either direct or indirect ways, as initially defined by Tsilingiri et al. (2012). According to the International Scientific Association of Probiotics and Prebiotics (ISAPP) postbiotics are inanimate microbes or their constituents that deliver health advantages (Shelar et al., 2022). Postbiotics cannot multiply or create toxins and are most likely to assure consumers about protection concerns, while hazard of genetic stability or infectivity is substantially decreased than living probiotics. However, it might require further safety evidence such as potential hazardous metabolite release (Sousa et al., 2008; Sanders et al., 2010; Cotter et al., 2013). To maintain an adequate viable count of probiotics at the situation in the present product that varies with storage conditions postbiotics, the postbiotics semen large-scale processing and storage is critical aspect intriguing. Following processing and storage of probiotics, the postbiotics maintains its shelf life by supplying a steady product dose (Nataraj et al., 2020; Salminen et al., 2021). Postbiotics or parabiotics are cell-free supernatants, metabiotics, or cultured and other biological compounds or inactive microbial products with bioactive properties. However, the names are used interchangeably. These are liquid factors from microorganisms such as peptides, short-chain-fatty acids, and enzymes that increase host bioactivity (Patel and Denning, 2013; Aguilar-Toalá et al., 2018). Postbiotics have a complicated composition and soluble factors. The soluble factors and complexes produced by the many microbial strains include biomolecules, vitamins, and acidic and alkaline organic elements with several useful nutritional qualities for livestock (Rai et al., 2019; Rad et al., 2020; Homayouni Rad et al., 2021). The potential of such soluble factors in animal nutrition becomes increasingly attractive, as these products boost immunological responses, promote growth, and facilitates the absorption of diet nutrients (Kareem et al., 2016; Haileselassie et al., 2016; Tiptiri-Kourpeti et al., 2016; Compare et al. 2017). Postbiotics are also recognized utilized to have antibacterial, antioxidant, anti-inflammatory, immunomodulatory, hypocholesterolemic, antitumor, hepatoprotective and growth-stimulant effect (Aguilar-Toalá et al., 2018). Abd El-Ghany et al. (2022), reported that postbiotic lyates applied to hens provided significantly more advantages over controls in relation to the disease profile, growth performance, immunological status, bursa-to-body weight ratio, and reduced coliform population. Humam et al. (2019) revealed that postbiotic from *L. plantarum* group improved gut health, growth performance and overall health. Of the broiler chickens. The above results show that postbiotics in poultry feeding possess benefits advantages. Specifically, they act on the build-up of intestinal structure and enhance nutrient absorption, which consequently positively affects the bird growth performance. Moreover, these promote immunological and gastrointestinal health of the poultry birds.

Synbiotics

A novel approach combining probiotics and prebiotics is known as synbiotics and is being explored with the goal to enhance their beneficial effects in the host. This combination aids in the survival and colonization of microbiological supplements in the gastrointestinal tract by boosting the development and metabolic activity of specific health-promoting bacteria. Referred regarded as "synbiotics," these combinations include of probiotics as well as prebiotics (Gibson and Roberfroid, 1995; Collins and Gibson, 1999). Some of the examples of synbiotics include; *Bifidobacteria*-fructooligosaccharide (FOS), *Lactobacilli*- lactitol, *Lactobacilli*-FOS, *Saccharomyces cerevisiae* -boulardii, *Pediococcus acidilactici*- mannan olidosaccaride (MOS), *Bifidobacteria*-inulin, *Enteroccoccus faecium*-FOS and *Lactobacilli*- inulin (Markowiak and Śliżewska, 2018; Sharma et al., 2018). In the chicken industry, antibiotics are widely used to boost production. However, this has resulted in problems such drug residues in poultry, alteration of the microbial flora, and antibiotic-resistant bacteria. By promoting the growth and activity of beneficial bacteria in the gastrointestinal system, synbiotics—a combination of probiotics and prebiotics—are used to address these issues and boost the efficacy of dietary microbial supplements (Sørum and Sunde, 2001; Gibson and Roberfroid, 1995). Synbiotics appear to significantly enhance chicken performance, according to several research. The growth performance, feed conversion ratio (FCR), and carcass output of broilers were found to dramatically improve when they were given nutritional supplements including synbiotics rather than just probiotics or controls (Awad et al., 2009). Song et al. (2022) discovered that synbiotics containing FOS and L. plantarum improved the digestibility of calcium and phosphorus and increased growth, immunological, and antioxidant indices. These results may point to a potential replacement for antibiotics in the diets of meat-eating birds. A synbiotic of *Enterococcus faecium*-FOS and *Clostridium butyricum*-FOS with marine algae improved the efficiency of yield, mass and shell of egg, egg quality, amino acid digestibility, jejunal structure, and physiological response in layers chickens (Radu-Rusu et al., 2010; Liu et al., 2019; Obianwuna et al., 2023). Studies have shown that synbiotics can enhance the productivity and well-being of chickens, suggesting that they can replace conventional antibiotics used in chicken feeds. Fig. 1 summarizes the beneficial effect of the biotics in poultry birds.

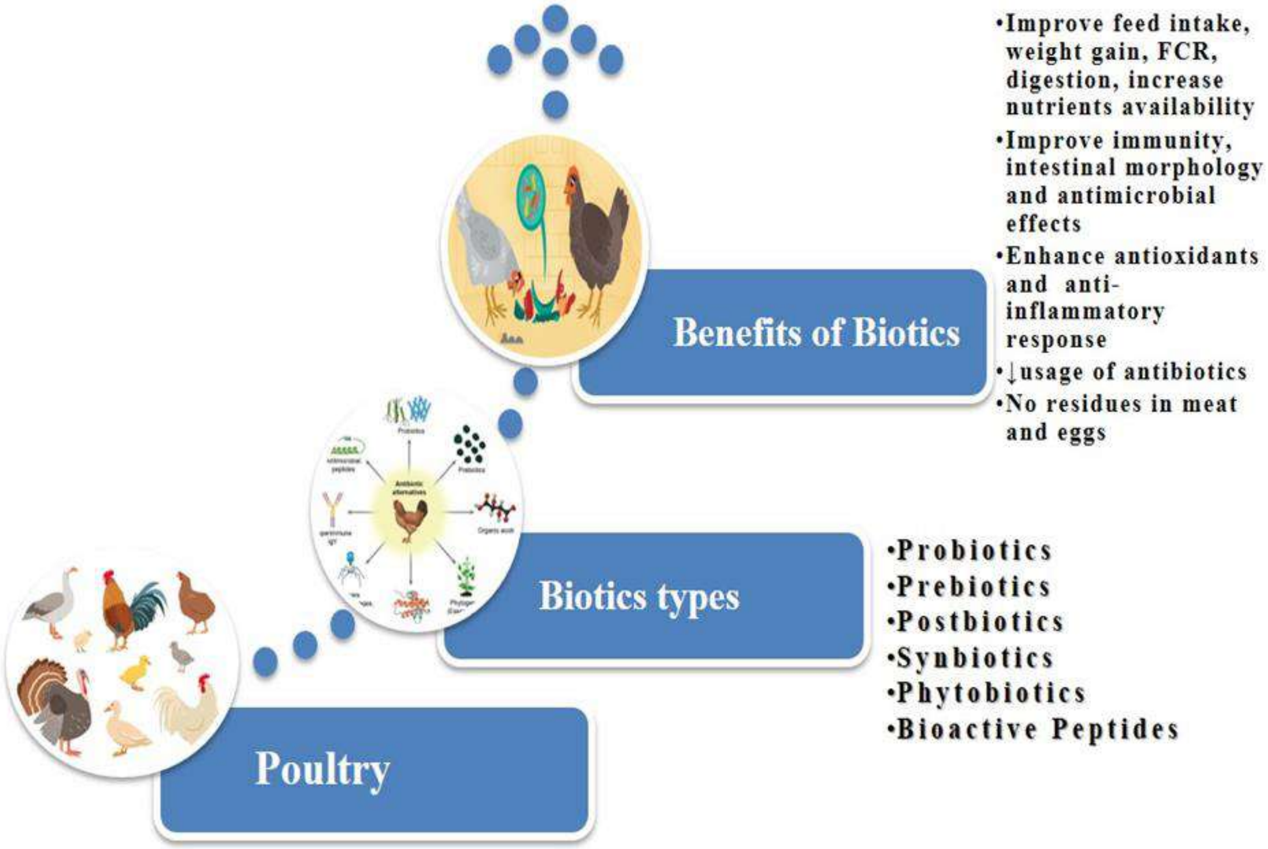

Fig. 1: The beneficial impacts of various biotics in poultry

Phytobiotics

Phytobiotics, also known as phytogenics or botanicals, are natural plant-derived products that are gaining popularity as environmental friendly and nontoxic alternatives to traditional antibiotics in the poultry sector. Phytobiotics, which may confer health benefits on the host include bioactive chemical substances such as phenolics, glycosides, terpenoids, and alkaloids and are derived from one or more sections of plants. The action of these chemicals on poultry as anti-bacterial, anti-coccidial, anti-parasitic, and immunostimulant has been extensively studied (Wang et al., 2008; Shad et al., 2014; Jin et al., 2023). Research on the potential of phytobiotics, prebiotics and probiotics, to improve poultry health and growth has been ongoing since the European Union banned the use of antibiotics as growth promoters in 2006 (Yasodha et al., 2019; Özbudak, 2019; El-Ghany, 2020). Due to the same reasons, these chemicals have been also investigated in several other animal species includingmonogastric species, comprising fish and rabbits, so on (Naiel et al., 2019; Mohammadi Gheisar and Kim, 2018; Alagawany et al., 2018).

Because of their antioxidant properties, phytobiotics may be used when there is heat stress (Chung et al. 2020b). Due to their high concentrations of thymol, carvacrol, and monoterpenes, oregano and thyme have been shown to have beneficial effects on antioxidant enzymes such as glutathione peroxidase and superoxide dismutase, which help regulate lipid metabolism in animals. However, plants such as mint, sage, and rosemary have an indirect antioxidant effect. The content of phenolic compounds, which include hydrolysable tannins, phenolic terpenes, proanthocyanidins, flavonoids, and phenolic acids, as well as the presence of certain vitamins, such as A, C, and E, is considered to provide these antioxidant qualities (Suganya et al., 2016; Filazi and Yurdakok-Dikmen, 2019). Aljumaah et al. (2020) reported that that the use of avilamycin with phytobiotics feed additive can help preserve growth performance of broiler chickens and improve meat quality in broilers challenged with *S. Typhimurium*. The use of phytobiotics together with cinnamon oil has been shown to positively affect growth performance of chickens, which is due to an improved immunological, antioxidant metabolic response and morphometry of the small intestine and an increase in the activity of the beneficial microbiota in the gut.

When chickens have the diet containing the plant with high flavonoids such as Chinese herb and green tea, lipid oxidation is arrested (Suganya et al., 2016). Introducing spices in the diet, such as garlic and onion, results in improving serum lipid profile and increasing liver antioxidant capacity (Khan, 2014; Suganya et al., 2016). Applying of phytobiotics in poultry diet to curb lipid oxidation not only have antioxidants qualities but also boost the host immune system, which makes them more beneficial than those of synthetic antioxidants. It is observed that components such as powdered Ganoderma lucidum mushroom and black cumin seed have been found to increase immune ability against specific pathogens and respond to vaccines at large, particularly at the time of vaccinating (Wang et al., 2002; Ogbe et al., 2008; Al-

Mufarrej, 2014). Moreover, plant extracts have also been reported to increase T cell activity with stimulating immunoglobulin synthesis, increasing humoral immunity and effectiveness antigen presenting cell (Kong et al., 2006; Khaligh et al., 2011; Chung et al., 2020a). The results show that how promisingly the use of phytobiotics is likely to improve the immune system of chickens, antioxidant activity, grow performance and health.

Bioactive Peptides

Bioactive peptides are peptides of short chain and of variable amino acid chain lengths that vary between 2 to 50 which have antihypertensive, antimicrobial and antioxidant properties (Sharma et al., 2011; Sánchez and Vázquez, 2017). The Biopep database contains 1500 bioactive peptides and details their diversity and importance (Singh et al., 2014). These are obtained through enzymatic hydrolysis of proteins from different available sources, which include fish, meat, milk, plant proteins, soybeans, wheat, corn, and many others. Through enzymatic hydrolysis, peptides of different psychoactivities such as biogenic, opioid, immunomodulatory, and others are generated (Barati et al., 2020; Tadesse and Emire, 2020). It is, therefore, possible that the BPs, which are gotten from natural products like sesame, canola and soya beans are added to poultry feeds which makes the intestinal health be enhanced and hence the antibiotics can be replaced (Abdollahi et al., 2017; Osho et al., 2019; Salavati et al., 2020). A subclass of bioactive peptides is the antibacterial peptides (AMPs), which have a spectrum of activity against bacteria. AMPs always kill bacteria by facilitating cell membrane disruption and inflammation. Conventional antibiotics and AMPs function in opposite ways, as the latter build dry envelopes as a method of extinguishing. This BPs attack through barrel stave and toroid pores processes (Trabulo et al., 2010; Li et al., 2021). According to the results of modern research, BPs significantly surpass traditional feed additives, such as mannan-oligosaccharides and antibiotics, in terms of the effectiveness of influence on chicken performance. Thus, the therapeutic potential of these peptides is displayed in the reduction of pathogenic bacteria and the multiplication of needed gut flora (Nakano et al., 2006; Liu et al., 2015; Salavati et al., 2020). The use of BPs as poultry performance enhancers has shown that some peptides can drastically decrease the content of gram-negative bacteria, which has a beneficial effect on nutrient absorption and the health of the intestines in general (Wen and He, 2012).

Moreover, antioxidant peptides reduce the adverse effect of reactive oxygen species. The mechanism of action on amino acids depends on their composition and structure (Stadnik and Kęska, 2015; Esfandi et al., 2019). Peptides produced from rice and soybean proteins boost the body's defenses by acting on hormones and immune system function (Ngo et al., 2012; Kang et al., 2015). Similarly, peptides have robust anti-inflammatory properties and can both reduce inflammation and increase immune function at the same time. Certain peptides produced from fermented milk yielded outcomes like that of anti-inflammatory medicines (Ialenti et al., 2001; Zhao et al., 2016; Aguilar-Toalá et al., 2017). Cottonseed bioactive peptides added to the broiler diets at a rate of 6 g/kg improved immune responses, growth performance, and serum total antioxidant activity in the absence of antibiotics (Landy et al., 2020). Supplementation of small peptides derived from soybean at the rate of 4.5kg/kg in the laying hens' diet, enhanced the growth performance, immune system efficiency and antioxidant activity. Moreover, the addition of short peptides improved the intestinal microbiota, barrier integrity, intestinal morphology and overall health of the chickens (Zhao et al., 2022). The findings indicate that bioactive peptides can be used in poultry diet as useful additives and as a therapeutic agent but further research is needed to fully understand their mechanism of action and their benefits for application.

Conclusion

Based on the above findings, it is concluded that different biotics have a positive impact on the growth performance, immune system and antioxidant efficiency, and the gastrointestinal health of chicken birds. Future researchers can use the biotics in all the poultry birds in different proportions and combinations.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Chapter 36

Alternative Source of Micro Minerals for Enhanced Production of Animals

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ABSTRACT

Microminerals are essential for different physiological processes in animals' such as enzymatic activity, immune functions and reproduction. Conventional sources of microminerals included in animal diets are restrained due to cost, bioavailability and sustainability. This chapter intends to unfold the alternative sources of microminerals for animal growth. These microminerals include marine-driven substances, microminerals, bio fortified crops and substrates rich in microminerals. These alternative sources offer benefits such as economic feasibility, environmental feasibility and nutrient density. Explored that alternative sources are highly bioavailable and diverse. Enriched substrates and bio fortified crops also enhance animal productivity and health. Research requires exploring regulatory approval and quality assurance to efficiency and bioavailability of these nutrients. Collaborative efforts are therefore needed to implement and standardize the innovative solutions, ensuring nutritionally adequate and sustainable animal feed.

KEYWORDS
Microminerals, Alternative sources, Marine supplements, Plant-based nutrients, Enriched substrates, Bioavailability, Sustainability

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INTRODUCTION

This chapter intends to examine the micro minerals for the enhancement of the productivity of the animals. The micro-minerals required for the efficient growth of animals are substantially present in substrates such as bio fortified crops, marine minerals, insects and plants. This chapter will uncover the pros and cons of consequences on animals' nutrition (Alagawany et al., 2021). The chapter also examines case studies where alternative sources of animal nutrition are assessed to explore their use and absorption mechanisms. This exploration will clear the path animal of nutrition.

Importance of Micronutrients for Enhanced Animal Production

The term to describe micro-minerals is the elements that are essential to maintain the physiological processes, especially those raised for food. Trace elements are required in very small amounts as compared to micro but they are essential for adequate operations of metabolism, enzymatic systems, hormone control and immune function. Furthermore, micro minerals have several biological operations as they cofactors in enzymatic reactions. For example, zinc is a cofactor for over 300 enzymes that lead to the production of proteins and assist in wound healing and cell division (Bature, et al., 2022). Likewise, copper is another micro mineral acts as an enzymatic cofactor in mechanisms, antioxidant stimulation, iron metabolism and production of connective tissues. Additionally, microminerals have other roles in neurotransmitters and hormones that regulate the overall hormone level in animals' bodies. For example, iodine is another factor for growth, metabolism and development. Selenium, on the other hand, does cell protection by activating the antioxidants during oxidation (Moore, et al., 2023). It also works in activating thyroid glands. Moreover, other microminerals also maintain an immune ability to avoid infections and illness among animals. Microminerals are crucial for preserving, antibodies and immunological homeostasis. Likewise, microminerals further guarantee the effective and safe reproduction cycle of animals. In this regard, decreased fetal development, embryonic death are reproductive issues caused by micronutrient deficiency (Hunt, 2003). An optimum lifestyle and diet for animal growth are thus encouraged by a nutritionally balanced diet, as the discussion above confirms that microminerals are distinct from other minerals.

Exploring the Limitations in Fulfilling the Mineral Requirements in Animals' Diet

A diet rich in microminerals is a challenge in ensuring efficient animal growth. There are severe complications and restrictions in this regard. These complications vary from the financial limits of providing a nutrient-rich diet to environmental aspects. Hence, this section lists the limitations in sufficient microminerals in animals' diets (Alagawany et al., 2021).

Technology Obstacles

The traditional mineral supplementation technique comprises the applicability, palatability and bioavailability of mineral salts and chelated minerals. The types of minerals may not be readily absorbed or may have unpleasant tastes that reduce overall preference (Byrne and Murphy, 2022). The component of research and development in feed consumption implies supplementing techniques that prioritize the effectiveness and bioavailability of microminerals while lowering logistics restrictions and costs. They are indeed costly, Because of animals' diets, particularly in subsistence farming or small-scale production. The resources at such farms are also restricted (Madeira et al., 2017). Moreover, the alterations in accessibility may further complicate the requirements of animal husbandry to a satisfactory level.

Environmental Considerations

Environmental aspects further affect the availability of in animals' diets to a great extent. Factors such as farming techniques, climate and soil quality are environmental factors. The soils deficient in nutrients produce feed and forage crops. It is because of imbalanced fertilization, poor soil health and environmental contamination. Consequently, plants grown on poor soils or soils with restricted supplements (Zhang and Schroder, 2014).

Absorption of Nutrients

The absorption of high concentration of dietary macro-minerals such as phosphorus and calcium. Therefore, it can be stated that the bioavailability of microminerals is influenced by the interactions among elements present in the animals’ feed, the antagonistic interactions among microminerals further limit the absorption of these microminerals while worsening their accessibility. Hence, developing a balanced diet according to the animals’ requirements with adequate concentration of microminerals and understanding the nutrient interaction ensures maximum nutrient absorption (Moore et al., 2023).

Nutrient Levels

Certain foods may not contain enough of certain important minerals to meet a person's complete nutrient needs. This is because micro minerals in their diet are inadequate and not support physiological needs of lactation, metabolic and reproductive and development. In addition to this, the difference in mineral composition of forages and feed crops is due to variations in cropping techniques and soil quality that result in different availability of nutrients in distinct areas at different times of the year (Uniyal et al., 2018).

The provision of microminerals for animal growth in the modern production system has several restrictions and difficulties. To overcome the challenges in feed formulation (Pajarillo et al., 2021), immense advancements in soil management techniques, technology advancements, and supplementing strategies are further needed to address the issue.

Alternative Sources of Micro-minerals

Standard supplementing techniques may fail because of the limitations in providing microminerals to animals. Therefore, there is a need to investigate alternative sources to ensure availability of these essential minerals to animals. Such an exploration problems of nutrients in animals' diets but also updates the traditional methods of diet provision and offers new opportunities to raise the standard of productivity, sustainability and animal nutrition (Moore et al., 2023).

Nutritional Quality Leading to Animal Health

Alternative sources of microminerals lead to improved animal health and enhanced nutritional value of their feed. The isolated components of microminerals are available in traditional supplements, whereas alternative sources include a broader range of bioactive substances and nutrients that improve their bioavailability and biological activity. For example, plants high in mineral content, seaweeds, and herbaceous plants with high minerals are specifically beneficial in an enriched diet. These alternate sources are crucial as they facilitating the absorption and use of these nutrients (Zhang and Schroder, 2014). Likewise, insect-based diets such as larvae of black army flies and mealworms are rich in readily available essential proteins, amino acids and lipids in addition to microminerals. Hence, they support providing a balanced diet for animals. Therefore, a sustainable solution to the problem of deficient diet in animals is the enhanced intake of biofortified crops and nutrient-rich meals obtained from insects or plants.

Sustainability and Environmental Impact

Sustainable farming practices and reduction in environmental impact are the key advantages of using alternative sources of in animal diets. Environmental contamination is highly controlled when substitutes for biofortified crops, insect-driven products and plant-based minerals are in use. Moreover, ecosystem resilience and biodiversity have greatly improved soil health by incorporating alternate sources of agricultural systems that long-term and sustainable food production. Mineral sources from sustainable means such as agro ecological production and waste streams further advance and strengthen the circular economy and environmental sustainability (Alagawany et al., 2021).

Diversifying Resources of Feed

Expanding the types of feed supplies in animal husbandry through alternative sources of microminerals is important. Traditional mineral supplements are expensive as well as rare. Therefore, reducing the dependence on supplements in animal diets may be an option. Moreover, diversification also helps risks related to reliance on supplements from a single source. Hence, animal production is enhanced economy or environment. Farmers should also try to increase the production and health of their animals by promoting an optimized consumption of nutrients and a balanced diet by including feed obtained from alternative sources (Byrne and Murphy, 2022). Moreover, exploring the micro mineral from alternate sources the challenges of sustainable animal production, environmental stewardship and animal wellbeing. Likewise, producers can enhance to create an environment of sustainable farming. Embracing innovation and diversification of feed options further improve the process (Uniyal et al., 2018).

Animal Growth as Affected by Microminerals

Each micromineral in diet plays a significant and unique role animals’ health and productivity. As stated earlier, microminerals are vital for carrying out normal physiological functions such as enzymatic reactions, hormone regulations, immunological operations and reproduction. Thus, lack of essential minerals in animals’ diet may lead to severe health issues (Byrne, et al., 2021). Furthermore, ensuring the addition of sufficient microminerals as supplements in their diets is also crucial to wellness, development and optimal production of both livestock and companion animals. An overview of the role of different microminerals in animal physiology has been presented in Table 1.

Table 1: Role of essential microminerals and the effect of their deficiency on animal growth

Microminerals	Role in Animal Physiology	Effects of Deficiency
Zinc	Cofactor for enzymatic reactions, protein synthesis, cell division, wound healing, immunological function, hormone balance, and reproductive performance.	Anemia, stunted growth, skeletal deformities.
Copper	Necessary for iron metabolism, connective tissue development, antioxidant systems, hemoglobin synthesis, cellular respiration, and collagen creation.	Anemia, stunted growth, skeletal deformities.
Iron	Components of and myoglobin, essential for cellular respiration, energy metabolism, and immune system function.	Anemia, poor activity performance, weakened immune system.
Manganese	Activates enzymes related to carbohydrate, lipid, and amino acid metabolism, and contributes to bone formation, cartilage development, and reproductive function.	Skeletal deformities, poor development, reproductive problems.
Selenium	A powerful antioxidant, essential for thyroid hormone metabolism, and critical for immunological function, reproductive success, and muscle health.	Muscular dystrophy, decreased immunity, reproductive failure.
Cobalt	Part of vitamin B12 is required for red blood cell formation, neurological function, DNA synthesis, energy metabolism, neuron function, and myelin synthesis.	Anemia, neurological problems, stunted growth.
Iodine	Essential for thyroid hormones controlling metabolism, growth, and development, reproductive activity, brain development, and temperature regulation.	Goiter, reproductive disorders, developmental abnormalities.

Microminerals from Conventional Sources

Microminerals obtained from traditional sources have been used for animal production for ages. They are added to the animal's diet to in animals' diets, but they also have issues and limitations that are crucial to address.

Premixes and Fortified Feeds

Other popular sources of in animal nutrition are premixes and fortified feeds. These alternate feeds are formed by mixing different ingredients in specific concentrations of microminerals into animal diets (Madeira et al., 2017). The unique aspect of this type of diet is that it contains a specific concentration of nutrient levels. Likewise, fortified feeds offer a complete feed with all essential nutrients, i.e. microminerals. However, premixes are defined as blends of additives and microminerals mixed into base feeds with other feed components usually served on farms. Both premixes and fortified feeds are efficient and practical approaches to providing a balanced nutritional diet to animals while ensuring enough levels of critical microminerals in animals' diets (Ani and Ajith, 2021).

Mineral Supplements Available Commercially

The commercially available and used mineral. Mineral concentrates, loose minerals and mineral blocks are a few forms of supplement intake. The variety of designs of these supplements depends on the specific amount of micro-minerals which are formed according to the nutritional needs of the animal species (Hunt, 2003). It also depends on the growth stage of the animal which requires a specific concentration of certain types of micromi neral. Commercial mineral supplements have been designated as easy-to-use widely available and accessible products. Hence, it is stated that commercial mineral supplements are used to ensure a sufficient amount of particular micromineral in an anticipated deficit diet.

Limitations of Conventional Sources of Microminerals

Despite their widespread usage throughout the world, they have certain limitations. One of these challenges is the cost of utilizing and obtaining commercial mineral supplements, premixes and enriched diets. These items are highly costly even if purchased in bulk. Also, they are prepared in high concentrations of bioavailable minerals. Financial afford nutrient-rich feeds daily (Hassan, Hassan and Rehman, 2020). Moreover, the microminerals obtained from traditional sources have bioavailability based on nutrient interaction, particle size and mineral type, the minerals have different absorption rates animals. Hence, in addition to this, another challenge is over-dependence on traditional supplementation by runoff and mineral excretion from animal feces. Furth ermore, the microminerals obtained from sources may not always provide sufficient concentration of required microminerals to overcome the specific requirement of an animal's developmental state. This happens typically during reproduction, lactation and growth. It causes increased chances of illness, restriction of metabolic problems, decreased reproductive capability and poor (Ani and Ajith, 2021).

Microminerals from Alternative Sources

The microminerals from alternative sources are listed as of microminerals (Table 2).

Table 2: Description of the microminerals obtained from alternative sources

Alternative sources of micro-minerals	Description
Plant-based sources	Natural sources such as seaweed. Legumes, forages, and herbs rich in such as iodine, iron, magnesium and calcium
Insects	and macro-minerals such as calcium, phosphorus, iron, zinc, fats and proteins.
Marine-derived micro-minerals	Marine and seaweed mineral supplements provide essential micro-minerals such as potassium, magnesium, calcium, iron and iodine.
Biofortified crops	Staple crops genetically bred or engineered to contain higher levels of microminerals like iron or zinc, addressing nutrient deficiencies in animal diets.
Micro-mineral enriched substrates	Using agricultural byproducts and soil amendments to increase micromineral content in animal feed, improving soil fertility and health

Marine Life as a Source of Microminerals

Micro-nutrients have been proven to be highly promising and innovative sources of nutrients for animals' diets. Likewise, marine minerals and seaweed-based supplements offer bioactive micromineral components that animal performance and health (Hassan et al., 2020). Moreover, are more frequently and readily available supplements animal diets. It plays a crucial role in increasing animal productivity as well as health. Micronutrients derived from seaweed have multiple benefits such as enhanced antioxidant activity and activated immune function. These supplements a rich source of minerals from sea sediments or algae as they have various trace elements including calcium, selenium, magnesium and calcium (Arthington and Ranches, 2021). These supplements are easily digestible and well-concentrated with vital minerals, helping animals overcome their deficiencies and promote maximal performance and health.

Insects as a Source of Microminerals

After plants, insects are considered as animals' diets. However, an insect-based diet provides more nutritional and sustainable alternatives. Research demonstrates that insects are rich in vital nutrients such as minerals, vitamins, fats and proteins. Hence, they are for animal diets (Pointke and Pawelzik, 2022). The larvae of the black soldier fly have excellent nutritional value and are used as a sustainable. Furthermore, the larvae of the black soldier fly are rich in zinc, iron, phosphorus and calcium. Hence, adding the larvae of the black soldier fly to animal's diet may be action to address micronutrient shortage because it has decreased the dependency on traditional (Mateos et al., 2020). In mealworms are insects are studied to have high nutrient levels for macro and micro minerals. Table 2 their nutrient availability. Mealworms are also rich in many micro-and-macronutrients. Such as protein, lipids, and calcium. Magnesium, and selenium. They are easy to raise on organic wastes. Another increasingly popular source of nutrient-rich compounds in animal feed is Cricket flour, extracted from cricket powder. It is to that crickets are rich in protein, fats, and vitamins and minerals, such as copper, zinc and iron (Pajarillo et al., 2021).

Plants as a Source of Microminerals

Based on the challenges and limitations of using traditional sources of micro minerals, research on using alternative sources from nature has been carried out. The alternative sources of microminerals include novel and innovative techniques to supplement nutrients in animals' diets. In addition to supplementing diets, alternative sources also address the concerns of environmental sustainability, bioavailability and cost of alternatives. Micro-minerals obtained from plants are considered the most sustainable and environmentally friendly (Hassan, Hassan and Rehman, 2020). Legumes, forages, botanicals and herbs are all natural sources of bioactive chemicals and microminerals required essentially for better performance and health of animals. Many botanicals and herbs have large concentrations of micro-minerals in their composition, making them highly beneficial to animal diets. Seaweeds, alfalfa, dandelion, and nettle are some of the most commonly used herbs that provide. Plant-based supplements are not only a source of micronutrients but also have anti-inflammatory and antioxidant qualities that are a bonus to animals consuming those (Pointke and Pawelzik, 2022). Moreover, legumes and forages such as soybean, alfalfa, and clover are other items in animal feed that provide important micronutrients. These plants have deep-rooted plant orientation deep in the soil. Hence, they become zinc, copper, magnesium, and selenium sources. Furthermore, as Khillare, et al., (2007) mentioned, forages and legumes in animal feeds also significantly improves the nutritional quality without animal health and production.

Substrates Enriched with Microminerals

Substrates enriched with microminerals are a sustainable and innovative way to supplement essential nutrients in animal feed. Soil amendments and agricultural byproducts like pomace husk and crop residues are identified as significant substrates that can be sourced to add microminerals in livestock feed. These agricultural by-products an opportunity to solve the problem of agricultural waste through recycling. These substrates are recycled to make livestock feed formulas. Certain minerals like copper, magnesium, and zinc are constantly obtained through feed formulas made through such agricultural products. These substrates usually contain gypsum, lime, and organic compost that affect the concentration of microminerals in animal feeds. However, the bioavailability of essential microminerals in animal feeds can be enhanced soil pH, microbial activity, and nutrient availability in the substrates. Moreover, substrates with higher concentrations of microminerals prove advantageous for agricultural production systems, in their 2022 study. Further research has revealed that such substrates with higher ratios of microminerals are sustainable sources of supplements for animal feeds.

Microminerals Obtained from Bio fortified Crops

The nutrient content of the plants can be altered. Farmers nowadays, innovative, such as genetic engineering to enhance the nutrient content of the crops used for animal feed. Iron and zinc can be easily increased by that boost the in the crops used as forages. For example, beans, wheat, rice and maize. Moreover, artificial selection and accumulation capacity have been to improve the bioavailable microminerals in these crops. Therefore, research verifies that bio fortified crops are highly cost-effective and sustainable. Although bio fortified crops potentially improve the nutritional content of animal feed, there might be possibilities and problems that need attention from researchers (Mateos et al., 2020). instability of bio fortified characters and the efficacy of these crops in different climatic and environmental conditions, genetic alteration and unintended consequences, barriers to consumer acceptance and regulatory obstacles are limitations to using this technique with success.

Mechanism of Absorption and Utilization of Microminerals in Animals

Various factors affect the absorption of microminerals and their use in the digestive system throughout the digestive tract to regulate mineral metabolism. There are multiple processes through which microminerals are dissolved in the digestive tract of animals including assisted diffusion, active transport and passive diffusion. Microminerals travel across intestinal membranes according to the concentration gradient, passive diffusion occurs. Active transport requires energy and carrier proteins to take microminerals against the concentration gradient. On the other hand, facilitated diffusion carries microminerals through carrier proteins along the concentration gradient (Durge, et al., 2022). On the absorption in the body, Such as shape of the minerals, dietary consumption, and pH of the digestive tract. Likewise, mineral type also effects the absorption efficiency and bioavailability of microminerals. Fiber content, phytate levels and interaction among minerals in the digestive tract effect on the overall absorption mechanism. However, these minerals have certain of interactions, i.e., based on their concentration in the digestive tract. Additive interactions are defined as those where have individual effects but have a common effect when combined. Antagonistic interaction happens for both. In this case, the effectiveness of both minerals is lowered in terms of absorption. Synergistic interactions happen when more microminerals combine and improve the overall absorption and biological activity (Švarc et al., 2022). The synergistic interaction of microminerals produces positive effects and advantages for the animal by improving the absorption. Moreover, genetic variables have a significant role in mineral metabolism that affects the excretion, use and absorption of minerals in animals. The requirement of mineral absorption with its variances affects the genetic variants that in response dietary treatments and regimens.

Challenges and Future Directions

All these factors have unique challenges and opportunities to adapt to strategies and sustainable practices for improving animal nutrition. Negotiations and approvals of regulatory procedures the primary challenge (Byrne, et al., 2021). It requires the application of comprehensive safety for approval of new food such as alternate sources. It is a time-consuming and costly procedure. Nevertheless, regulatory procedures and regional standardizations further assist in expediting the usage and establishment of standardized animal feed. Therefore, the production process requires validation from research to standardize the formulations and quality assurance. In this regard, stakeholders and regulatory agencies are required to collaborate and prepare quality assurance. In addition, the integration of alternate sources in animal husbandry has critical challenges and acceptability of the feed by animals. The producers assess the compatibility of alternate sources for their animals and rectify the production processes, management approaches et al., 2022).

The opposition against using alternative sources of micro mineral availability can be ignored based on its health, environmental and economic benefits. Nevertheless, future research. It should be based on the key objective of increasing bioavailability and efficacy of alternate sources. It further uses the mechanism of action and bioavailability to determine the suitability of the source for animals. Additionally, nanotechnology, genetic engineering, project additionally the innovation gaps in new technology and alternative of microminerals for animal growth.

Conclusion

By physiological processes, it means reproductive efficiency, immunological functions, hormone regulation and enzyme activity. Nevertheless, nutritional imbalances, limitations of conventional systems, budgetary restrictions, and environmental aspects are the challenges that obstruct the availability of microminerals. This chapter explains the importance of microminerals in animals' diets. Accurate requirements have been met, and alternatives for other sources have been investigated to reduce the associated problems. The primary implications of the research conducted in this chapter emphasize the need for microminerals for production, growth and health of animals. There is also a high need traditional supplementing method. alternative sources of microminerals, such as substrates rich in microminerals, biofortified crops, marine derivatives is the most promising solution to overcome the limitations of conventional systems. Moreover, the alternative sources of microminerals identified in this chapter are highly sustainable, cost-effective and nutritionally balanced compared to traditional supplements.

Further research is required to bridge the gaps in improving and using alternative microminerals in animal husbandry. The research on safety, efficacy and environmental sustainability. Likewise, collaboration between regulatory bodies, industry stakeholders and research is crucial for streamlining regulatory procedures and encouraging farmers to use alternative micromineral sources.

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Chapter 37

Innovations in Animal Nutrition: The Role of Natural Feed Additives in Veterinary Practice

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ABSTRACT

Animal feed additives, or FAs, are used worldwide in the livestock industry for many purposes, including the provision of vital nutrients, enhancing feed palatability and growth rate, and optimizing feed consumption. High-producing animals must retain a high level of health, and using the right supplements is an ongoing debate in these situations. There is more pressure on the industry to find more organic alternatives to the FAs due to the desire for healthful food products with animal origins, as well as rising customer awareness. The important alternatives to animal FAs are determined mostly by human and animal welfare issues. Probiotics as well as prebiotics, herbs, and enzymes are a few substitutes that are being considered for usage as animal FAs. The scientific and empirical evidence regarding these alternatives supports the selection of FAs, as plants and their extracts have been shown a broad spectrum of activity that includes stimulating endogenous secretions, feed intake, and having other properties like anti-inflammatory, antibacterial, etc. Herbal FAs are becoming more important in the production of sustainable livestock due to the ban on the use of antibiotics as growth promoters in response to their detrimental residual effects. Therefore, further research is needed in this field to optimize animal productivity and profitability.

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INTRODUCTION

Feed additives (FAs) have been around since farmer's added salt to animal feed in the past to make it more palatable. The application of FAs expanded in the early 1900s as researchers started to focus on the dietary requirements of animals (Nolinda et al. 2024). Since then, they are becoming a vital part of animal nutrition. They are utilized to raise growth, enhance feed efficiency, and improve the health and welfare of animals (Whittemore, 2001). Government organizations control the use of FAs to guarantee their effectiveness and safety. We may anticipate more advancements in the discipline of FAs as research moves forward, which will enhance animal nutrition, welfare, and health even more. A healthy diet is a must for any livestock business to be successful and effective (Wani et al., 2023; Kiczorowska et al., 2017).

FAs are compounds that are introduced to the diet for various reasons other than satisfying dietary requirements. In short, FAs are substances or mixtures of substances that are incorporated into the standard feed mix, or portions of it, to meet a particular need (Kumar et al., 2014). They must be handled and mixed carefully because they are typically used in small amounts. They are used to increase feed efficiency, minimize and control infections, and protect against environmental factors in addition to increasing weight gain (Hossain et al., 2024). Examples of these additives include various vitamins, amino acids, enzymes, prebiotics and probiotics (Iegorov et al., 2023). Furthermore, FAs have the potential to improve the nutritional value of animal products. They can also increase feed conversion ratios and decrease the likelihood of diseases. The use of FAs must be legal and ethical to protect customers' and animals' safety. FAs are currently widely used in the cattle industry to improve animal health, growth, and productivity (Al-Jaf et al., 2019). The world market for FAs is expected to continue growing as a result of the increasing demand for animal protein and the need to improve the efficiency of animal production (Anadón et al., 2019). It is alarming that certain chemicals may have negative effects on the environment, the health of humans and animals, or both. The food additives sector must continue to research and produce safe and effective FAs (Badshah et al., 2023)

Factors to be Considered for the Selection of Feed Additive

Several factors must be taken into account while deciding the procurement and utilization of various feed ingredient

Ingredient Composition and Quality

Common nutrient values for the majority of crude materials can be found in ingredient composition tables or scientific literature. Nevertheless, for ingredients formed in limited amounts at local levels, it is prudent to inspect individual market suppliers and validate nutritional profiles as well as quality through certain scientific ways like various laboratory analyses (Ilias et al., 2023).

A typical proximate analysis ought to have all information regarding the level of ash, protein, fat, and moisture. Furthermore, assessing the quantity of micro and macro minerals along with amino acids can deliver additional indicators of end-formulated product quality. So, it is important to validate the nutritional profiles and quality of alternative FAs through laboratory investigation (Pandey et al., 2019).

Nutrient Variability

The significant obstacle to incorporating more alternative ingredients into feed formulations often lies in their nutrient variability. Understanding the source and supplier is crucial, as is having accurate nutrient profiles collected over an extended period. When variability is high, it is important to consider lower inclusion levels as a precautionary measure (Okey, 2023).

Nutrient Utilization and its Digestibility

Nutrient digestibility and utilization refer to the ability of animals to effectively absorb and utilize the nutrients present in feed ingredients. While some ingredients may contain abundant nutrients, not all may be readily accessible to animals for growth or productivity. For example, a feather meal may boast high protein content but could lack sufficient essential amino acids (Wani et al., 2023).

It is essential to carefully scrutinize ingredients derived from processing industries, especially those that undergo drying. Employing digestibility studies, laboratory analyses, literature reviews, and consulting ingredient catalogs (such as those maintained by amino acid commercial suppliers) are valuable methods for gathering information. Additionally, the application of FAs such as enzymes and phytogenic chemicals may be taken into consideration to improve the digestion of particular nutrients in substitute raw materials (Pandey et al., 2019).

Material type /Suitability

Although some materials or feedstuffs might be easily found in the market, the type of material could pose limitations on transportation, storage, or processing. This scenario may arise with by-products existing in a liquid state or ingredients inadequately dried. Adapting or redesigning feeding systems might be necessary to facilitate the efficient utilization of such ingredients. Moreover, substantial moisture content can dilute the nutritional values of feed, which must be considered while formulating feed (Iegorov et al., 2023).

Relative Value

Relative value (RA) of feed ingredients allows for evaluating its nutrient content to standard levels of protein, lysine, phosphorus, and particularly energy content based on the availability of other FAs in the market. Most frequently, soybean and cornmeal are commonly used as benchmarks for other ingredient measurements. The comparative RA does not include inclusion levels; instead, it indicates the price per unit of nutrition at a given time (Nolinda et al. 2024).

Anti-Nutritional Factors

Some raw materials naturally contain components that can impede animal digestion, metabolism, or overall health. Trypsin inhibitors, lectins, mycotoxins, tannins, and glucosinolates are a few examples of these. When possible, it is critical to employ analysis to discover these anti-nutritional aspects and modify inclusion or use decisions appropriately. In some circumstances, using FAs such as mycotoxin deactivators may be necessary to protect animals against their detrimental effects (Markowiak and Śliżewska, 2018).

Palatability

Palatability refers to the ease with which animals consume the material under consideration. Some ingredients, like rapeseed meal, may contain bitter components or have off-flavors and aromas, which can reduce consumption when added to diets. Phytogenic FAs can improve the palatability of feed and possibly cover up offensive odors., thus improving overall consumption (Kumar et al., 2014).

Hazard-Free

The safety of feedstuff depends on its source and processing method, with some alternative ingredients potentially containing foreign materials unsafe for animal consumption. For instance, bakery waste might inadvertently contain plastic or other packaging materials. Additionally, hazards like chemical carcinogens or heavy metals may be present in certain ingredients (e.g., minerals), and should be considered carefully (Silveira et al., 2021).

Handling and Storage

For a raw material to be an inexpensive and useful ingredient in formulations, it must flow smoothly within the feed milling process. Considerations include bin space, warehousing capacity, and storage options, all of which should be evaluated before purchasing a new ingredient (Vandenberghe et al., 2021).

Inclusion Rates

The right amount of a component to add to a feed formula depends on several factors and interpretations. Setting boundaries for non-traditional ingredients requires experience because different nutritionists or companies have different approaches or ideologies when it comes to using non-traditional raw materials (Vijayaram et al., 2022). To optimize cost-saving potential, it is crucial to challenge initial inclusion levels that are provided by publications, industry standards, or scientific literature. The developmental and research program of all feed formulating companies should have a primary focus on determining the inclusion levels of alternative ingredients (Al-Jaf and Del, 2019).

Stability

Ingredients must have the ability to be stored without losing quality. High moisture content ingredients (15–25%) are more prone to deterioration, rapid fermentation, fungus growth, and a gradual loss of nutritional value (Alem, 2024).

Availability of FAs and Consistency of Supply

Before assessing the cost and nutritional value of the raw material under consideration, it is essential to ensure an ample supply. Factors such as the types and number of animals to be fed, their diets, inclusion criteria, and the quantity of feed produced must be determined to calculate the potential amount required over a specified period (Mantovani et al., 2022).

Effect on Quality of Pellet and Final Formulated Feed

The particle size and moisture levels of different feed ingredients can influence the feed formulation and production process. The feedstuffs to be chosen must have the least effect on the quality of the pellet and final output of the formulated feed (Ivanova et al., 2024).

Effect on Milk, Meat and Egg Quality

Similar to the pellet quality and feed, the feedstuff must not introduce any adverse effects on the quality of the final animal food products (Asrar et al, 2023). For instance, excessive volumes of fishmeal can impart undesirable flavors to milk, egg, and meat products, necessitating limitations in feed formulations (Kiczorowska et al., 2017).

Cost-effectiveness

The potential for feed cost savings is often the primary consideration when deciding to use alternative-based ingredients. Feed formulation software, precise nutrient content characterization, and careful consideration of the aforementioned aspects can all help to establish the most economical feed prices and formulations. Production expenses are usually lower when a more cost-effective formula is developed without compromising the health and growth of the animals. Additionally, it is important to consider other cost factors beyond ingredient price, such as the requirements for special storage, processing, or transport (Karásková et al., 2015).

Types of Feed Additives

There are many types of FAs, each having its own advantages and specific functions. The first category is the nutritional FAs which are used in animal feed with valuable nutrients, for example, enzymes, minerals, and amino acids (Ayalew et al., 2022). The use of nutritional FAs is very essential for increasing production performance, health, and growth of animals. Technological additives are another type of FAs that are employed to enhance the quality of feed in terms of its durability, stability, texture, and shelf life (Pandey et al., 2019). They may also help in the absorption and digestion of certain nutrients in the body of animals. Zootechnical is the third type of FAs, which is used to boost immune response, feed efficiency, conversion ratio, and growth rate as well. Sensory FAs are used as coloring and flavoring agents in feed formulations, which are most commonly used in aquaculture feed formulation (Velázquez-De Lucio et al., 2021). A few more compounds from anti-parasitic drugs are also used to control the growth and damage caused by gut parasites. Here are a few examples of commonly used FAs as follows.

Binders

Binders are a very important element in the production of feed formulations because of their property to keep feed particles together and prevent them from disintegration. Binders can be derived from a variety of sources such as animal and plant-based compounds and synthetic material as well. Plant-based feed binders are easily available, and cheap in terms of production cost thereby seeking more attention among people dealing with animal FAs (Kumar and Srivastava, 2023). However, they possess less binding strength as compared to animal-based products. Collagen and gelatin are examples of animal-derived binders having strong binding capacity. There is only one drawback that they may not be equally effective against all types of animal species as some species can have allergic reactions towards these binders. Synthetic binders are the most popular and effective forms of binder posing greater binding strength as compared to all other types, but they are not cost-effective and also have availability issues. However, the selection of binders depends upon various factors such as production cost, availability, suitability, and specific requirements of particular FAs (Okey, 2023).

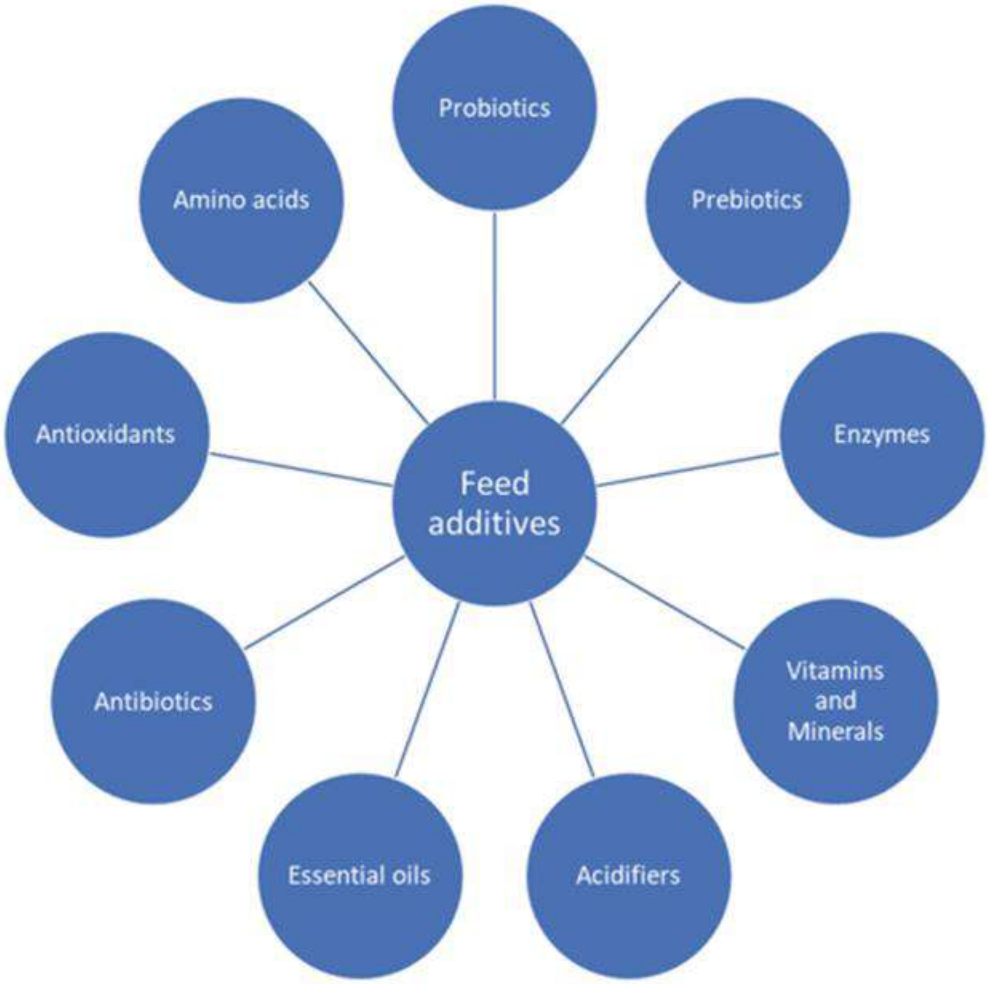

Fig. 1: Type of feed additives

Preservatives

These are the compounds that are used in feed formulations during the manufacturing process, to enhance their shelf life by inhibiting spoilage and decomposition. They are also of various kinds like artificial and natural. The main purpose of adding them in FAs is that feed remains fresh and full of nutrients when fed to the animals (Wani et al., 2023).

Probiotics

Live strains of certain microbes are selected based on certain criteria, and when added in sufficient amounts in diets pose beneficial health effects to hosts. These are called probiotics as it is originated from a Greek word meaning "for life" (Savvidou et al., 2023). Probiotics are predominantly used in the animal feed industry particularly poultry, because of their known beneficial effects of growth stimulation. This kind of feedstuff generally contains one or two selected microbial strains and is supplemented in feed in various forms such as powder, pellets, suspension, or gel form based on the host's immune response and age. Various species of *Bifidobacterium, Enterococcus,* and *Lactobacillus* are used as FAs (Iegorov et al., 2023).

Prebiotics

Prebiotics are the elements that are added to feed to enhance the growth, proliferation, and specific activities of beneficial microbial organisms. The gastrointestinal tract (GIT) is the ideal place where maximum beneficial microbes are available thereby prebiotics can change and enhance the fermenting ability of all these organisms including bacteria and fungi (Markowiak and Śliżewska, 2018). Nowadays, there is extensive use of prebiotics in the livestock industry with the purpose of increasing growth performance. All the species vary from one another in various factors such as their nutritional requirements, gut flora, and habitat, physiology of body, and anatomy also. So, the overall effect on health and growth also varies through the application of prebiotics in the same way (Kiczorowska et al., 2017)

Protein, lipids, and non-absorbable carbohydrates are commonly used as prebiotics nowadays.

However, organic sources of prebiotics include various fruits, cereals, and legumes as well as many other compounds that can be used based on their enzymatic and chemical properties. There are generally five basic rules or assumptions of food items regarding their use in the form of prebiotics (Anadón et al., 2019).

1- They may not absorb and digest in the upper GIT so that they can reach the lower portion of the large intestine.

2- Prebiotics must be fermented by the gut microbiota present in the intestine.

3- The immune system should be boosted after fermenting gut microbes, executing a positive effect on the overall growth and health of the host

4- The most important factor is that they must pose a beneficial effect on probiotic bacteria by enhancing their growth.

5- Each prebiotic is unique in its function based on its formation and rate of metabolism of the bacterial population present in GIT (Wani et al., 2023).

Synbiotics

The word symbiotic is used as a combination of both prebiotics and probiotics. This combination exerts superlative effects on host immune response and growth by stimulating the proliferation of beneficial bacteria and their metabolism as well. Synbiotics work on the formula of synergism based on the growth and survival of gut microflora as a prominent feature of probiotics and prebiotics (Al-Jaf and Del, 2019).

The GIT of animals performs a dual function, first providing a conducive environment for a large number of microbes and secondly also providing protection against harmful effects caused by their toxins. Although, synbiotics have shown superior effects using key features of both prebiotics and probiotics, the data regarding their use in animal science is not much available thereby, indicating the need for further research to be done in this area (Vijayaram et al., 2022).

Enzymes

Enzymes are important biological molecules and combinations of various chemical ingredients that are supplemented in feed to improve digestion and mark the effects caused by anti-nutritional substances present in feed. They generally improve the feed conversion ratio and its efficiency by reducing the production cost of animal products like eggs and meat which is a key feature of enzymes (Badshah et al., 2023). Improvement in the gut environment, health, and digestion process is also helpful to reduce the growth of harmful pathogens. All enzymes work by breaking down the substrate into a useful product such as phytase enzymes remove the phosphate group by acting on the phytate substrate. Similarly, protein is broken down by proteases which is helpful in its digestion. Nowadays, the use of enzymes is so extensive that every industry is incorporating them including paper, leather, medical, and food industry (Velázquez-De Lucio et al., 2021).

Amino Acids and Minerals

Amino acids are the essential component of feed formulations in the form of FAs nowadays.

They may work as a substitute for natural proteins, by limiting excretion of nitrogen and waste of extra proteins. The use of amino acids has a bright future in animal feed in the sense that important feed reserves will not be wasted needed by both human and animal populations (Biswas et al., 2023).

Similarly, minerals are important chemical substances that are required in a definite amount for the basic functioning of the body. Every cell of the body has to have a specific amount of minerals to complete its metabolic functioning. Both macro and microminerals are increasingly used in the feed industry in the form of FAs based on the requirements of each species. Ruminants mostly has huge sources of minerals from forages. The body requirements of each species are variable so the same forage cannot fulfill all the needs of them. The use of FAs is important in this scenario so that each mineral is supplemented in a balanced ratio (Savvidou et al., 2023).

Antioxidants

The use of vegetable and animal fats has increased nowadays, thereby increasing the demand for the production of more FAs comprised of antioxidants. Oxidative process leads to the breakdown of amino acids, and various energy products in feed and food stuffs which is the main reason for the use of anti-oxidants in feed industry (Ayalew et al., 2022). Both synthetic and natural antioxidants are employed in the animal feed industry to enhance the feed quality and upgrade the shelf life of the ingredients used in it. Termination of free radicals' production and prevention of damage caused by reactive oxygen species (ROS) is the major beneficial aspect of using antioxidants as FAs. It is worth noting that, the use of antioxidants should not be irrational, as certain species can pose deleterious effects against them (Wani et al., 2023).

Antibiotic as Growth Promoters

Antibiotics as growth promoters (AGPs) are chemical compounds that are added to feed at a low concentration with the aim to improve performance and health by destroying or inhibiting the growth of certain pathogenic bacteria. The use of fermentation byproducts generated through tetracycline incorporated in feed led to the discovery of the use of antibiotics as a growth-promoting agent in the 1900s. Afterward, the use of AGPs has expanded throughout the world (Silveira et al., 2021). With the advancement in livestock farming as a result of increasing demand for organic sources of proteins, the usage of AGPs has also increased with beneficial effects on health and performance (Okey, 2023).

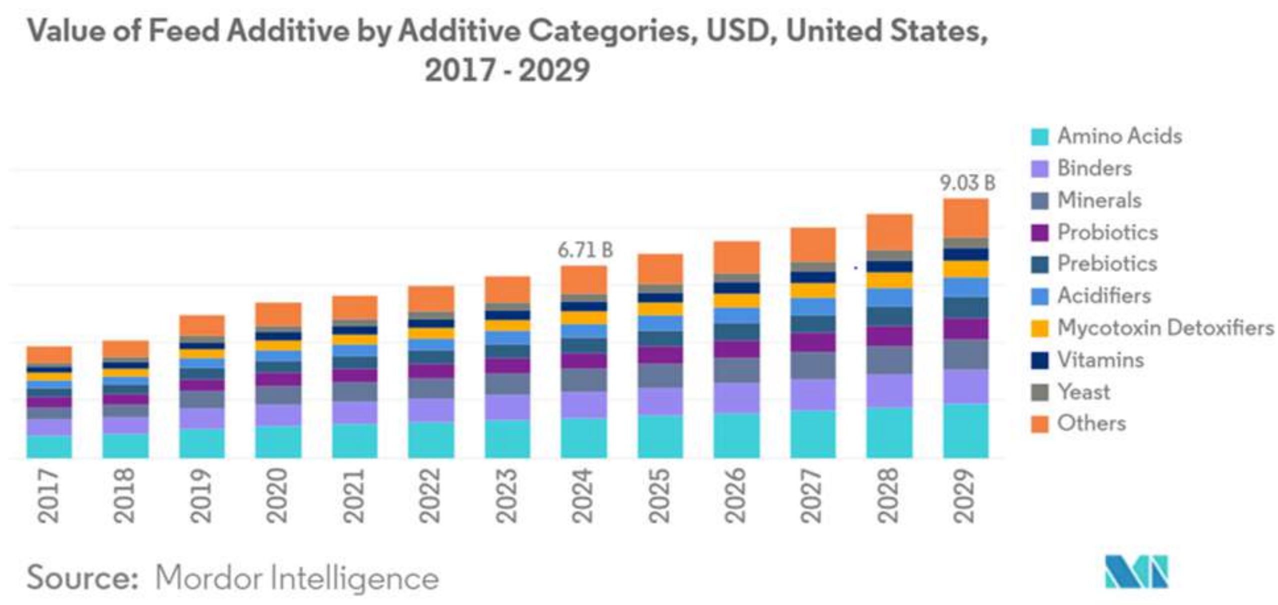

Fig. 2: Increasing trend of use of FAs in animal nutrition

Table 1: Various types of FAs available in market

Category	Product	Company	Ingredients/Composition	Uses
Binders	BETAFIX	Profarm	Bentonite, Cell Wall (S. cervesiae), Algae (Lithothamnium Calcareum)	Binds aflatoxins with provision of yeast (yeast based binder)
	STARFIX	Profarm	Bentonite, non-GMO Hydrolyzed yeast (S. cervesiae)	
	TOXO	LCI	Smectile clay minerals Yeast cell wall fractions	
	TOXO-MX	LCI	Smectile clay minerals	Binds aflatoxins without yeast (clay based binder)
Pre-biotics	Hilyses	Profarm	Saccharomyces cerevisiae, B-Glucans, Vitamins (B1,B2,B12, folic acid, Biotin and choline, Nucleotides, Mannan Oligosaccharides (MOS)	Enhance Immunity, Intestinal Integrity, higher growth and better feed conversion
	Immunowall	Profarm	Saccharomyces cerevisiae, B-Glucans, MOS	Enhance Immunity, higher growth
Pro-biotics	Rumen-Yeast	Profarm	Yeast Metabolites, MOS, B-Glucans	Prevents acidosis, SCC reduction, Increases Milk production
Minerals	Pro Premix	Profarm	Vitamin A, D3, E, B1, B2, B6, Niacin, Biotin, FeSO4, KI, Granulated Cobalt, CuSO4, MgO, ZnO, Sodium Selenite	Improves milk yield, fertility, enhance bone growth, control of lameness, control of mastitis, improves skin shine, immunity booster, SCC reduction
	ProVita Plus	Profarm	Vitamin A, D3, E, B1, B2, B6, Niacin, Biotin, Iron, Copper, Organic Copper, Cobalt, Selenium, Organic Selenium, Zinc, Organic Zinc, Manganese, Organic Manganese, Iodine, Potassium	
	ProVita	Profarm	Vitamin A, D3, E, Niacin, Biotin, Iron, Copper, Cobalt, Selenium, Zinc, Manganese, Iodine, Potassium	
Preservatives	Citric Acid	Profarm	Citric Acid	As a preservative for ingredients
Amino Acids	LipoAktiv Amino	LCI	DL-Methionine, L-Methionine, L-Lysine HCL, L-Histidine	Improve milk yield and fertility

A wide variety of antibiotics are used as FAs to reduce disease incidence and improve growth in the livestock industry. The irrational use of AGAs is prohibited in many countries due to their residual effects on animal byproducts. Their use can be made more beneficial after certain scientific testing regarding afterward effects on both human and animal health (Ayalew et al., 2022).

Herbs as Phytogenic FAs

Medicinal plants have been used a long time ago, in ancient times based on the availability of multiple biologically active metabolites present within the herbs posing a wide range of positive effects on animal health (Anadón et al., 2019).

This concept has been gaining more attention among the livestock industry and stakeholders because of the deleterious effects caused by certain antibiotics such as FAs. A lot of research has been done on the use of herbs and their extract as FAs, showing the promising effect of phytogenic compounds on the health and production of animals. Production quality and quality in terms of milk, meat, and eggs improves through the use of phytobiotic substances. The concept of phytobiotics as FAs will expand more in the future due to their increasing demand as a natural source of growth-promoting agents (Ivanova et al., 2024).

One Health Concept and FAs

One health (OH) concept has gained worldwide attention, primarily dealing with zoonoses. Nowadays this concept also includes the human, animal, and environmental interaction related to hazards originating from food sources. With this perspective, every feed and food ingredient must be tested for benefits, hazards, and toxicity to ensure the safety of animals, humans, and the environment as well (Lavilla et al., 2023).

For example, people working in feed mills and factories can get infected through inhalation or ingestion of certain chemical substances. Moreover, during the manufacturing of FAs, certain amino acids that are broken down by bacteria through fermentation can also be a source of danger for workers, although they are not detrimental to various animal species. Similarly, after using this kind of FAs, the excreta of animals released into water and soil may pose toxicological effects on the ecosystem. Therefore, it is very imperative to develop some risk-benefit assessment tools for food items in this respect. Implementation of these kinds of tools paved the way for assessing the contamination of nutrients present in food and feedstuffs. These approaches could be very fruitful in creating a strong backup on various grounds of food safety and environmental protection (Mantovani et al., 2022).

Conclusion

Conclusively, the FAs are commonly used in animal nutrition due to their crucial role in enhancing animal health, productivity and growth. The supplementation of essential nutrients is helpful in improving feed efficiency, and digestion, thereby significantly contribute in overall well-being and production performance of livestock. As the demand for sustainable and healthier animal production systems continue to increase, the tactical use of FAs will remain as an integral element of modern animal nutrition. The investment must be continued in research and development to discover and refine more new FAs including novel elements such as next generation probiotics. A harmonized regulatory framework must be ensured globally which can facilitates the innovation and development of FAs and by providing education and training for the nutritionists, farmers and field workers on the benefits and accurate use of FAs will increase their future demand. Covering all these aspects, animal nutrition industry will continue to grow and a resilient livestock production system will be established.

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Chapter 38

Tannins as a Dietary Additive in Animal Feed

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ABSTRACT

Tannins are polyphenols in nature. Tannins are secondary chemicals found in plants and also available in feeds, meals, and beverages. Tannins are a major component of wood, bark, leaves and fruits; however, acacia species belonging to the Leguminosae family of the plant kingdom are considered to be the most common source of tannins. Plant tannins are divided into two categories: condensed tannin (CT) and hydrolyzable tannins (HT), which include tannin derivatives such as gallic and ellagic acids. Tanning agents help lessen the symptoms of foamy bloat, a frequent gastrointestinal ailment in ruminants that is brought on by gas buildup in the reticulum and rumen. Tannins are a useful substitute for medications in the treatment of parasites. Condensed tannins have been shown to have antiparasitic properties through two mechanisms: they attach to proteins in the rumen and stop microbes from degrading them, which inhibits the larval development of digestive system parasites. The hydroxyl groups, degree of polymerization, and redox activity of tannins enable them to scavenge free radicals, hence exhibiting a potent antioxidant action. Tannins consumption leads to an increase in milk production. The utilization of forages containing both CT and HT has a significant role in improving nutrient utilization for meat and dairy farming as a natural and environmentally acceptable strategy. Although tannins have long been recognized as advantageous bioactive substances in ruminants, they have also been linked to antinutritional effects in poultry diets therefore its usage and toxicities should be considered when it is added to the animal feed.

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INTRODUCTION

Tannins, known for their polyphenolic nature that causes protein precipitation, exist in diverse forms and molecular weights (Haslam, 1989; Sahakyan et al., 2020). Within plant sources, tannins are categorized into condensed tannins (CT) and hydrolyzable tannins (HT), encompassing derivatives like gallic and ellagic acids (Haung et al., 2018). Furthermore, a third family of tannins exclusive to brown algae is phlorotannins (PT). The ellagitannins and gallotannins were both included in the hydrolyzed tannins. As polyphenolic waste and polyols have different C–C interactions, ellagitannins may not hydrolyze yet are nevertheless categorized as HT for particular uses. Together with hexahydroxydiphenoyl (HHDP), the C-glycosidic catechin units were first identified in tannins in 1985 (Ruddock and Facey, 2024). The isomeric HT's structural and functional components. Tannin can be added to food as an extract or as a supplement from plants that contain it (Kelln et al., 2021). In a large-scale, commercialized ruminant production system, such a feedlot, tannin extract is usually preferred over plants that contain tannins. The widely utilized tannin extract sources are mimosa, acacia, quebracho, and chestnut. The uneven and extremely varied effects of tannin extract from diverse sources and dietary supplementation in varying doses on ruminant production parameters, including nutrient intake, digestibility, production performance, methane emissions, and product quality, may result (Hassan et al., 2020).

Sources of Tannins in Animal Diets

Tannins, which are phenolic secondary compounds, can be found in a variety of feeds, meals, and beverages. They occur in approximately 15% of annual and herbaceous perennial dicotyledon species as well as 80% of woody perennial dicotyledon species (Butkutė et al., 2018; Mueller, 1999). These compounds are distributed throughout different parts of plants such as seeds, fruit, leaves, wood, bark, and roots, serving primarily to provide protection against microorganisms, herbivores, insects, diseases, and pests (Dixon et al., 2013). Tannic acid content of the majority of plant tissues, typically ranges from 2 to 5% of the fresh weight, such as fruit and leaves, but in pathological circumstances, Tannins may build up quickly (Guo et al., 2021; Haslam, 2007; War et al., 2012).

Species	Plant part	Reference
Arbutus unedo	Foliage	Ammar et al. (2005)
Ceratonia siliqua	Leaves	Silanikove et al. (1996)
Hedysarum coronarium L. (sulla)	Fresh plant	Priolo et al. (2005)
Quercus calliprinos	Foliage	Silanikove et al. (1996)
Astragalus cicer	Whole plant	Williams et al. (2011)
Bituminaria bituminosa	Stems, leaves	Sumbele et al. (2012), Ventura et al. (2012)
Lotus corniculatus var. japonicas	Stems, petioles, flowers	Morris et al. (1993)
L. corniculatus	Whole plant, roots, leaves, stems	Acuna~ et al. (2008), Marshall et al. (2008)
Lotus pedunculatus	Whole plant	H€aring et al. (2008)
Lotus tenuis	Shoots	Acuna~ et al. (2008)
Medicago sativa	Seed coat	Koupai et al. (1993)
Trifolium repens	Flowers	Burggraaf et al. (2003)
Trifolium pretense	Flowers	Barry,1985
Vicia amphicarpa	Seeds	Berger et al. (2003)
Vicia faba	Seed hulls, seed coat	Vilarino~ et al. (2009)
Genista florida	Shoots	Frutos et al. (2002)
Genista occidentalis	Shoots	Frutos et al. (2002)
Mimosa hostilis	Leaves	Guim et al. (2006)

Chemical Structures and Properties of Tannins

Tannic acids, also known as tannins, are polyphenolic compounds found in plants. Tannis exist as light yellow-brown powder, flakes, or spongy masses. These phenol-containing solids dissolve in water and are commonly found in plant fruits, barks, roots, and wood (Erb and Kliebenstein, 2020; Lara et al., 2020). The solubility of tannins in water is a factor of central focus in its biological activity and till now about 500 tannins have been described and characteristics are explained (Villalba et al., 2019). The solubility of tannins in aqueous organic solvents depends on the degree of polymerization and chemical structure of proanthocyanidins. Proanthocyanidins, when heated in acidic alcohol solutions, undergo an oxidation reaction catalyzed by an acid, producing red anthocyanidins. Two well-known anthocyanidins that are generated are delphinidin and cyanidin. Tannins that are catechins, which are not broken down by diluted acids or enzymes are the condensation product of catechin and undergo dry distillation to become pyrocatechol (Akiyama et al., 2001). The number of phenolic compounds that bind numerous locations with carbonyl peptide groups determines the high affinity of protein tannins (Karonen et al., 2019, Haung et al., 2017). The degree of affinity between the participating molecules and the protein in question, which is determined by the chemical properties of each tannin, determines how these complexes develop (Prasetiyono et al., 2018, Buitimea et al., 2018, Bunglavan et al,. 2013). Tannins' comparatively large molecular weight and flexible chemical structure are among the elements that promote the formation of complexes (Engström et al., 2019). Furthermore, it was discovered that ruminant animals' reduction in CH_4 emission can be facilitated by supplementing their diet with condensed tannin (CT) extract (Aboagye et al., 2019).

Mode of Action and Functions of Tannins

Tannins are a wide range of polyphenolic chemicals that have been found in many different types of plants. Due to their greater molecular weight proanthocyanidins, these molecules have astringent and browning properties (Czochanska et al., 1986). The molecular weight of tannins usually ranges from 500 to 5000 Da, according to Hagerman and A.E. (1992). Leguminosae species of acacia are known to be a major source of tannins, however they can be found in a variety of plant parts such as wood, bark, leaves, and fruits (Isam et al., 2014).

Because tannins can precipitate proteins, obstruct digestive enzymes, and reduce the absorption of vitamins and minerals, they were once thought to be harmful (Amarowicz and R, 2017). Furthermore, their high molecular weight and tendency to combine with dietary ingredients such proteins to create insoluble complexes point to a limited capacity for absorption (Hagerman et al., 1991). Notably, variations in weight have been associated with modified consumption of dry matter due to the presence of tannins in poultry feed (Hagerman et al., 1991). CT are more common than hydrolyzable tannins, which are found in smaller amounts. Plant genetics, tissue development, and environmental conditions all affect the amount of tannins present.

Tannins Impact on Nutrient Utilization

The source of the tannins determines how much protein digestion is impacted. For instance, the tannins in Lotus pedunculatus Cav. decreased the in vitro breakdown of green plants' primary protein (Rubisco) far greater than the tannins in L. corniculatus (Aerts et al., 1999, Min et al., 2005; Gazzar et al., 2022). The strength of the interaction between tannin and protein complexes is probably a key component in the digestion of ruminal proteins (Hagerman et al 1998, Osborne et al., 2001, Lowry Mueller-Harvey I et al., 2019). Moreover, the proteolytic bacteria in the rumen were directly impacted by the tannins from L. corniculatus (Min et al., 2004). Nevertheless, rumen bacteria pre-incubation of L. corniculatus tannins led to greater Rubisco breakdown than pre-incubation containing tannins from L. pedunculatus (Molan et al., 2010). Tannins from L. pedunculatus are not beneficial for ruminant nutrients as a result of their inhibition of ruminal degradation. The impact of tannins on animal performance may fluctuate based on their type and concentration. HT, on the other hand, effectively increases bypass protein in ruminants, leading to great milk supply and yield performance (Orzuna et al., 2021). Furthermore, tannin can be managed by intestinal parasites and bloat issues in grazing ruminants (Kumar et al., 2020).

Role of Tannins in Animal Health

1. **Tannins and Gastrointestinal Health**

Tanning agents help lessen the symptoms of foamy bloat, a frequent gastrointestinal ailment in ruminants that is caused by gas buildup in the reticulum and rumen. This condition damages the function of the respiratory and gastrointestinal tract (Nawab et al., 2020;Wang et al., 2012).Bloat in alfalfa pastures can be prevented by mixing condensed feed containing tannins, like sainfoin, into the crop. Additionally, it has been shown that tannins assist ruminants in managing parasites within their digestive systems (Harju et al., 2014). In animal models, plant tannins have demonstrated antidiarrheal properties. According to a study by Bonelli et al. (2018) giving tannins to calves that have diarrhea may reduce the length of the episode of diarrhea (DDE). Certain plant tannins contain anti-diarrhea properties, according to study Galla Chinensis oral solution (GOS) and oil have shown notable antidiarrheal action, indicating the potential utility of GOS in supplementing other treatments since it's a reliable and efficient remedy for diarrhea(Yang et al.,2017).

Anti-parasitic Properties of Tannins

A significant pathological danger to the production of cattle and poultry is parasitic diseases. Tannins are a useful substitute for medications in the treatment of parasites. Viral bioassays assessed the impacts of Lotus pedunculatus is the source of condensed tannins (CTs). (DP), Dorycnium pentaphyllum (DP), Lotus corniculatus (LC), Rumex obtusifolius (RO) and Dorycnium rectum (DR) on an egg hatching, growth of larvae, and Teladorsagia viability the Ostertagia circumcinctaand the Trichostrongylus colubriformis L3 larvae (Molan et al., 2000; Pineda et al., 2020). These investigations demonstrated that CTs could prevent egg hatching, impede the growth of larvae, eliminate immature larvae, and interrupt the nematode life cycle (Thitz et al., 2020; Minho et al., 2010; Molan et al., 2010; Molan 2014). Generally speaking, anthelmintic medications are used to manage parasites in the digestive tract. Customers are prompted to consider when they see these medication residues in animal products (Arsenopoulos et al., 2020; Jackson and F, 1993). As a result, the need of these medications is decreased when plant species that lessen the quantity and impact of parasites are included in the diet. For example, lantana camara, or sage tea, is well-known for its significant role in controlling nematodes and parasites in the digestive tract. Goats are said to benefit from the antihelmintic properties of eucalyptus species (Bennet et al., 1996). According to reports, condensed tannins have two ways of acting against parasites: directly by blocking the growth of digestive system parasites into larvae, and indirectly by attaching to rumen proteins and obstructing microbial breakdown. Consequently, it is believed that they facilitate the transport of amino acids, which strengthen the host animal's immunity boosting the breakdown of proteins in the duodenum by acids. The rations' consumption of tannin enhanced the live weight gain of parasite-infected lambs and sheep. This resulted in a drop in the quantity of parasite eggs laid on manure (Min et al., 2005; Barry et al., 2003; Hoste et al., 2015).

Immune System Modulation (Antioxidant and anti-inflammatory effects)

The hydroxyl groups, degree of polymerization, and redox activity of tannins enable them to scavenge free radicals, hence exhibiting a potent antioxidant action (Ricci et al., 2016, Nawab et al., 2020). Indeed, ruminant antioxidant levels are enhanced by supplementing with tannins (Maggiolino et al., 2019, Barreira et al., 2008, Huang et al., 2015, Peng et al., 2016). When it comes to chemical properties, HT are thought to be the strongest antioxidants (Chambi et al., 2013). CT have been shown to have antiparasitic properties through two mechanisms: they attach to proteins in the rumen and stop microbes from degrading them, which inhibits the larval development of digestive system parasites. Therefore, it is believed that they allow amino acids to flow through, enhancing the host animal's immunity acids into the duodenum and improving the breakdown of proteins. The eating of rations containing tannin enhanced the live weight gain in lambs and sheep with parasite infections. This resulted in fewer parasite eggs being deposited with manure (Torres et al., 2022; Min et al., 2003).In the food and medicinal industries, tannins' antioxidant qualities are widely used. Currently, it has been demonstrated in several animals that plant tannins possess antioxidant qualities. According to a mutton study, the longissimus dorsi muscle's (LM) color stability was prolonged with fewer alterations when supplemented with tannin compared to the control group in the color angle of the treatment groups (Luciano et al., 2011).

Tannins and Animal Production

A. Effect on feed efficiency and growth performance.

The majority of CT's effects on an animal's performance are related to its feed value. Nutritive value (NV) × intake is the definition of feeding value (Waghorn and Clark, 2004; Orzuna et al., 2021).

The idea represents the quality of forages even if it isn't a direct indicator of achievable animal performance (Martens and Barnes, 1988). Understanding the possible nutritional value (the kind and quantity of nutrients that can be absorbed and the effectiveness of their usage), the degree to which anti-nutritive elements are present, and the possibility of voluntarily consuming dry matter (connected to feedstuffs' chemical and physical properties, as well as how they combine with other feeds, as by elements unique to each species).The majority of CT's effects on an animal's performance are related to its feed value. The value of feeding is referred to as intake × nutritive value (NV) (Waghorn and Clark, 2004; Peng et al., 2021).

High CT concentrations in this situation, and generally speaking, will limit the total amount consumed since they will make less of the theoretically digestible dry matter and overall palatability. Nevertheless, over the past 20 years, a mix of field tests, gut physiology, and chemical studies has shown unequivocal advantages for fertility, intestinal parasite resistance, lamb growth, and wool production (Waghorn, 2008; Patra and Saxena, 2011).

In comparison to the control group, incorporating forages containing CTs has shown significant benefits, potentially leading to improvements ranging from 8% to 38% in daily gain or 10% to 21% in milk production (Waghorn, 2008). This enhanced productivity can be attributed to the increased availability of essential amino acids, including branched-chain amino acids, methionine, and lysine, which play crucial roles in lactose synthesis (through neoglucogenesis) and the production of milk proteins, ultimately contributing to overall output growth (Wang et al., 1996). When feeds containing tannin are consumed, the tannin produces a combination with the salivary glycoprotein. A significant tannin content lowers the feed's consumption and flavor. Consequently, it results in a drop in the production in creatures. Certain animals can adjust to diets high in tannin by raising the amount of proline-rich proteins in saliva to reduce tannin levels. It stops saliva from combining with proteins (Butter, 1999).

B. Tannins and Reproductive Performance

Nutrition is one of the key elements influencing sheep reproduction. Sheep feeding L. corniculatus were shown to have, on average, 22% greater ovulation rates than sheep grazing meadow grass and clover. Most likely, the condensed tannin content of The PEG-determined ability of L. corniculatus to raise the lambing rate is because of the higher percentage of oocytes fertilized (Min et al., 2003). The rate of ovulation (OR) in sheep is impacted by nutritional levels, as noted by Downing and Scaramuzzi. However, the specific mechanism(s) through which nutrition affects OR remain(s) unclear. The OR is dependent on animal feeding, which is most likely connected to the hormonal and metabolic regulation of the ovary (Downing et al., 1991). Variations in the energy and protein balance, as well as changes in muscle protein synthesis brought on by nutrition, are compatible with variations in the plasma concentrations of growth hormone, insulin, and insulin-like substances. These variables may alter ovarian function directly or via influencing the function of ovarian gonadotropin (Downing et al., 1995). Further research has demonstrated a correlation between elevated levels of essential amino acids (EAA) and branched-chain plasma amino acids (BCAA) and ovulation rate (Wang et al., 1996).

Effect of Tannins on Ruminal Microbiome and Fermentation

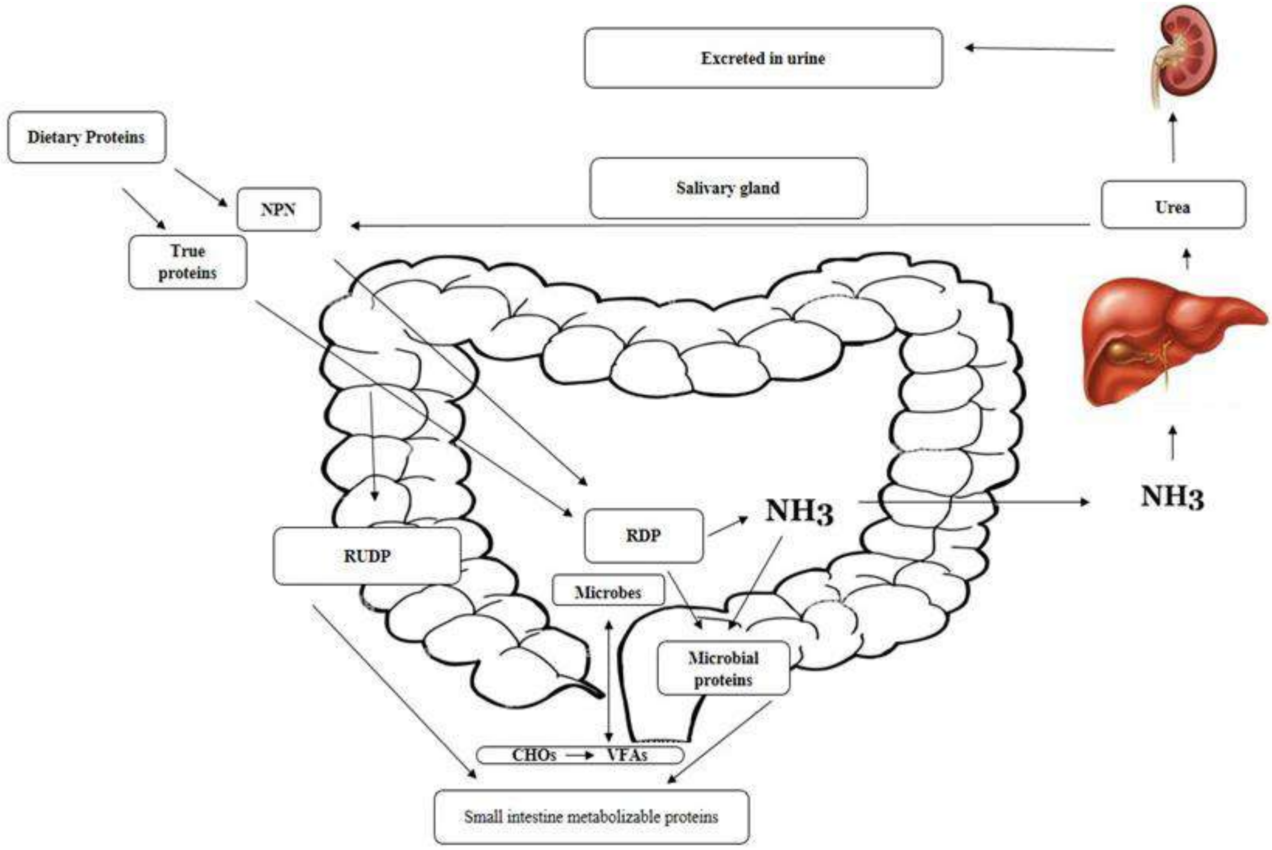
Rumen microbiota is very essential in converting fibrous and non-fibrous plant material into valuable products such as meat and milk (Millen et al., 2016). Gut environment hosts a diverse range of microbes, including bacteria, protozoa, fungi, archaea, and bacteriophages (Sweeney et al., 2005). The symbiotic relationship exist between the rumen microbiome and the host and each producing substances that benefit the other. For instance, in chewing and rumination process food's surface area is increased for microbe attachment and promoting fermentation and the production of volatile fatty acid compounds (VFAs). In addition, rumen helps remove harmful substances, maintaining optimal conditions for microbial growth and life while recycling urea, which is then used for microbial development (Millen et al., 2016).

Effect of Tannins on Milk Production and Composition

Dairy cows fed L. corniculatus with a tannin content of 27 g/kg DM showed a daily milk yield of 16.5 kg, while those given L. corniculatus and polyethylene glycol (PEG) produced 13.8 kg per day (Harris et al., 1998). Dschaak et al. (2011) found that cows on a diet supplemented with concentrated tannin extract (CTE) had lower milk urea and rumen ammonia nitrogen concentrations without affecting milk protein production. Comparatively, cows fed L. corniculatus produced 60 percent more milk than those on perennial rye grass, with a 10 percent increase in milk protein. Results from PEG experiments suggested that condensed tannin could explain half of the observed lotus effect (Min et al., 2003). In lactating ewes, condensed L. corniculatus tannin had minimal impact on early lactation milk production but significantly improved whole milk, lactose, and protein secretion by 21 percent, 12 percent, and 14 percent, respectively, during mid and late lactation (Wang et al., 1996).

C. Tannins in the Context of Sustainable Animal Farming

The exact processes via which tannins affect the health and performance of animals remain unclear despite much investigation. Additionally, it is frequently impossible to compare the results of different tannin determination methods due to the use of disparate standards (Koopmann et al., 2020). Potential interactions are thought to be between other main and secondary compounds and tannins. Plant-based substances might be crucial for palatability as well as biological operation As a result, when feeding ruminants, it's critical to use the right species or types of plants that contain tannins. The possible application of HT as a feed supplement needs more research to strengthen the foundation for comprehension of the potential function of HT in feeding animals. Additional investigation is essential to ascertain the function of rumen microbes in people, to more effectively use diets high in tannins and to stop animals who aren't acclimated to the usage of HT. The utilization of forages containing both CT and HT has a significant role in improving nutrient utilization for meat and dairy farming as a natural and environmentally acceptable strategy (Distel et al., 2020). More investigation is required, with an emphasis on defining suitable tactics to more effectively use plant species that contain tannins and/or significant variations in the diet of ruminants, so enhancing raising animals and promoting environmental durability.



Practical Applications

When given the freedom to choose, an animal expresses preference by consuming a certain amount of one plant more than another (Frost and Ruyle, 1993). The emotional and cognitive systems are two connected systems that help animals learn to avoid plants or plant parts. The postingestive feedback and feed flavor are integrated by the affective system. This method adjusts feed item intake based on whether the Positive or negative feedback can be posted. It is well known that the degree of aversion to harmful sources depends according to du Toit et al. (1991) on the potency of postestive physiological effects. Over the last ten years, the understanding of tannins' antinutritional effects in animals—particularly ruminants—has evolved Singh and Bhat (2001). It has been shown that consuming tannins, especially condensed tannins, at low to moderate levels (2-4% of dry matter) in animal feed might improve ruminant protein metabolism, lessen bloat, and have an anthelmintic effect on parasites in the stomach(Muir ,2011, Patra and Saxena (2011), Rochfort et al., 2008). In animal feeding trials, a variety of feed and fodder with varying tannin contents have been employed, with varying positive impacts on the nutrition and health of the People have seen animals. These were Acacia leaves Salix caprea, A. nilotica, A. tortillis, A. brevispica, and S. sheep, goats, and cattle are fed viminalis Onobrychis viciifolia, C. calothyrsus carob fed to lambs, goats, and cattle (Silatonia Ceratonia), Goats are given Lespedeza cuneata, Prosopis cineraria, and Quercus semecarpifolia Dorycnium rectum, Desmodium ovalifolium, and Hedysarum fed to coronarium, L. pedunculatus, and Lotus corniculatus sheep as well as Leucaena leucocephala supplied to cattle. The fruits—Dichrostachys cinerea, Acacia tortillis, and honey locust (Gleditsia triacanthos), which goats are fed(Peng et al.,2016), are eagerly consumed by sheep and Quercus rotundifolia acorns, which were discovered to be superior for ruminants and pigs in the Mediterranean.

Dosage Considerations and Safety Concerns

Although tannins have long been recognized as advantageous bioactive substances in ruminants, they have also been linked to antinutritional effects in poultry diets (Redondo et al., 2014). Under rumen pH conditions (5.5–7.0), tannins in ruminants' gastrointestinal tracts (GIT) bind proteins, preventing microbes from breaking down food proteins. The non-covalent bonds between proteins and tannins are broken in the abomasum (pH 2.5–3.5), allowing free protein to be absorbed by the host in the distal small intestine (pH 7.5) (Barry et al., 1986]. Thus, tannins have been shown to improve ruminant protein consumption and reduce gas production (Berard et al., 2011, Goel et al., 2012). Nonetheless, tannins were mostly regarded as phytotoxins in chickens because of their ability to bind to proteins, which hinders the digestion of food proteins and lowers the activity of digestive enzymes (Medugu et al., 2012). Furthermore, tannins bind chicken salivary proteins that are hydrophobic and high in proline, creating complexes that give the feed an astringent flavor, which makes the meal less palatable and causes the hens to eat less (Butler et al., 1984). Furthermore, broiler hens exposed to a high dose of tannic acid (25 g/kg) displayed liver proteolytic activity, indicating harm to chickens (Marzo et al., 2002). Because tannic acid can form complexes with iron, Lee et al. (Lee et al., 2002) observed that tannic acid impacted the growth performance, hematological indices, and plasma iron status in weaned pigs. Still, these poisonous characteristics of tannins were demonstrated when diets containing more than 7.5 g/kg of tannins (based on Tannic acid, which is regarded as the gold standard of HT), and numerous recent investigations have demonstrated that suitable Tannic acid, the standard for tannins, is used to determine the quantities of tannins, which range from 0.5 g/kg to 5 g/kg in Poultry's potential antibacterial, antioxidant and digestive properties could help enhance growth rate and gut health actions that reduce inflammation.

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Chapter 39

The Use of Phytogenic Feed Additives in Animal Nutrition Pakistan Scenario

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ABSTRACT

Phytogenic feed additives (PFAs) are crucial to enhance the product quality, health, and production of animals. Especially in the scenario of Pakistan, these are achieving more attraction due to their high capacity and decreasing dependency on antibiotics. PFAs provide a natural alternative to AGPs (antibiotic growth promoters), enhanced nutrient digestibility, a healthy immune system, and overall health and performance in many livestock species. The present chapter showcases the importance of PFAs in animal feeding and emphasizes advantages, challenges, mechanisms of action, and future prospects. PFAs influence many biological activities in animals, such as antioxidant and antimicrobial properties that enhance disease resistance, growth rates, and feed efficiency. Their use in animal nutrition faces many challenges including bioavailability, different effects, and potential toxicity. Animal health and performance are improving in Pakistan through the usage of garlic, green tea, cinnamon, black cumin, and peppermint as the efficacy of PFAs is highlighted through several studies. Overall, PFAs fulfill consumer demand, increase production, and improve animal welfare by providing a sustainable and natural approach. Therefore, the use of PFAs in livestock production requires further research and critical challenges must be addressed.

KEYWORDS		
Phytogenic feed additives, Antibiotic growth promoters, Animal nutrition, Livestock production	Received: 15-May-2024 Revised: 11-July-2024 Accepted: 05-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Maintaining optimal health and productivity of all animals requires a balanced diet that typically comprises cereal grains and protein sources. Feed additives play an important role in determining the nutritional value of feed, which is affected by several factors such as the presence of anti-nutritional components, microbial contamination, digestibility, palatability, and its effect on intestinal health. Animal diet contains a minor portion of feed additives but aid in enhancing food and feed quality, as well as animal health and performance. These feed additives help increase the digestibility of feed materials, promoting nutrient ingestion and absorption, assimilation, growth, and overall health. These additives influence physiological processes including stress resistance and immune function. Feed additives are immunostimulants, pro- and prebiotics, essential oils, enzymes, coloring agents, and some others including acidifiers, antioxidants, and antibiotic growth promoters. Additionally, feed additives are considered to enhance nutrient digestibility and availability, improve digestion, enhance food quality, and contribute to environmental sustainability. Recently, alternative feed additives obtained from spices or aromatic plants are known as phytogenic feed additives or phyto-additives. These additives are classified on their botanical origin, processing methods, and composition. It includes medicinal herbs and non-woody plants, aromatic spices, essential oils obtained from various plant components, and oleoresins extracted through solvent extraction (Babinszky et al., 2021).

The growing demand for meat has led to selective breeding of farm animals for improved efficiency. However, animal production is influenced by genetics, nutrition and other factors. In recent years, phytogenic feed additives (PFAs) have emerged as a promising alternative to antibiotics in animal feed. PFAs are diverse substances like essential oils, spices, and herbs. They can be classified based on their function in animal feed. Sensory additives, for example, enhance the taste and smell of animal products, like adding pigment-rich plants to chicken feed to create a more vibrant orange yolk color. Technological additives improve feed quality and animal health (Pandey et al., 2019).

The most studied category is zootechnical additives, which directly impact animal performance and health. Some PFAs, like beta-glucans, act as immunomodulators, boosting the animal's immune system. Others, like essential oils, possess antimicrobial properties. By incorporating these additives into feed, farmers can potentially improve animal nutrient digestion, leading to better growth and overall health. Research suggests that PFAs offer a range of benefits. For instance, PFAs can improve nutrient digestion and the immune function of broilers. Laying hens fed diets with PFAs may increase egg production and enhance the quality of meat (Al-Jaf and Del, 2019).

Over the previous many decades, global meat production has been increasing due to continuous enlargement in the human population (Leser, 2013). Efficient production techniques are responsible for supplying a lump of safe meat and quality animal product meat that should focus on the producer's profitability. On the one hand, animal protein is in demand. On the other, strict instructions to focus on animal welfare and protect the environment led to more changes in present production techniques, which is necessary. In the upcoming decades, keeping an eye on live weight gain due to feed or calculating it in feed conversion will be mandatory. Overall, feed contributes 60-70% of production. Thus, a sustainable and profitable product is key to optimizing feed utilization. A certain level of nutrients is provided to animals to meet their suitable needs for meat, eggs, or other products associated with metabolic processes. Feed ingredients, including protein, energy, and phosphorus, are costly in many countries. Therefore, proper utilization should be focused on high production and lower cost. Many countries have been using and some are still using Antibiotic Growth Promoters (APGs) to enhance feed conversion and promote growth to reduce the occurrence of the microbiota in the gut (Dibner and Richards 2005). As a result, several antibiotics are affected by bacterial resistance due to the regular utilization of AGPs in animal diets (Marshall and Levy 2011).

The effect of broad consumption of AGPs causes microbial resistance in humans that are used in animal feed, and it creates awareness among consumers about the negative impacts of the "superbugs" (bacteria heavily resistant towards antibiotics). In 2006, Europe implemented a full ban on AGPs due to public concern. For instance, a worldwide urged trend was to restrict or ban the AGPs used in the feed of animals from outside the European Union countries. Korea and some other countries also banned the utilization of AGPs in animal diets. There was only one solution to reduce the overall use of veterinary antibiotics in animal agriculture, instead of replacing them suddenly. Hence, the research aim is to obtain good health and high production with their growth potential. The indication of photogenic feed additives (PFAs) in animal nutrition turned the focus on the improvement of zootechnical and animal health parameters, which is confirmed by many reports, to increase in number day by day. Overall, phytogenic feed additives hold promise for the future of animal nutrition. These natural additives have the potential to enhance animal health, production, and product quality, all while reducing reliance on antibiotics in animal agriculture (Barug et al., 2006).

Composition and Types of Phytogenic Feed

The economic efficiency of animal production is increasing due to continuous selection in applied farm selection (Svitáková et al., 2014). Various internal and external factors, including nutrition, significantly influence animal production. Phytogenic additives enhance many essential functions in the animal body by emerging as a valuable source.

The Table 1 highlights the plants that are utilized as feed additives in animal production. Feed additives have a role in improving feed quality, animal health, and product quality through their beneficial substances and are categorized into sensory, technological, zootechnical, and nutritional groups. Sensory additives mostly contain compounds influencing food odor, palatability, and coloration. In egg-laying hens, phytogenic additives are commonly used as colorants to affect egg yolk color, which is a key indicator of egg quality and consumer demand (Englmaierová et al., 2014).

Fig. 1 mentions the various types of phytogenic feed additives. Egg yolk pigments, known as xanthophylls depend upon fat-soluble pigments that feed contains. Natural and synthetic sources provide such pigments with natural carotenoids that are pricey and unstable. It has been demonstrated that egg yolk carotenoid deposition and color characteristics can be increased through supplementation with Chlorella biomass which plays a significant role. Notably, adding a well-known carotenoid, astaxanthin, enhances meat color and imparts antioxidant properties to fish feed. Furthermore, Studies have also explored its benefits against reactive oxygen species (ROS) and neuro-protective effects (Gomez et al., 2014).

Mechanisms of Action

Integrated substances in animal feed pose a significant challenge to understanding the mechanism of action of phytogenic feed additives. To enhance animal performance and health in recent years, their concerted effort in research and development has been observed to unravel their role (Windisch et al., 2008; Hippenstiel et al., 2011). Furthermore, the composition of phytogenic compounds utilized across studies makes it challenging to formulate a universal mode of action that applies to all phytogenic feed additives. In recent years, it's observed that phytogenic feed additives primarily exhibit antimicrobial properties that are supported by scientific evidence to demonstrate the antimicrobial activity of plant ingredients, particularly due to underestimations and misconceptions of their effectiveness (Helander et al., 1998; Ultee et al., 2002; Burt, 2004; Nikaido, 2003; Preuss et al., 2005; Ouwehand et al., 2010).

Table 1: Commonly Utilized Plants as Feed Additives in Animal Healthcare and Livestock Production.

Botanical Name	Parts Used	Important Active Constituents	Common Uses	Reference
Asparagus racemosus	Root	Shatavarins I–IV, asparagamine	Galactogogue, antistress, immunostimulant	(Dahouda et al. 2009)
Acacia catechu	Stem wood extract, fruit	Catechin, quercetin, epicatechin	Antidiarrheal, anti-inflammatory, antioxidant	(Mehrotra et al., 2005)
Allium sativum	Bulb	Allicin, allin, methyl allyl disulfide	Hypolipidemic, carminative, antiprotozoal, anti-inflammatory	(Sharma et al., 2005)
Aloe barbadensis	Leaf	Aloin, barbaloin, emodin	Emmenagogue, anti-inflammatory, antibacterial	(Rastogi et al., 2005)
Balanites roxburghii	Fruit, seed, seed oil	Balanitisins A-E, marmesin, bergapten	Purgative, spasmolytic, anti-colic, anthelmintic	(Hussain and Murthy 1992)
Cissus quadrangularis	Stem, root, leaves	Quadrangularins, piceatannol, pallidol	Fracture healing, useful in dyspepsia	(Rastogi et al., 2005)
Curcuma longa	Rhizome	Curcumin, turmerone, desmethoxycurcumin	Anti-inflammatory, carminative, spasmolytic, antioxidant, hepatoprotective	(Blumenthal et al. 1998
Eucalyptus globulus	Leaves, oils	Cineole, pinene, limonene, eucaglobulin	Anti-inflammatory, carminative, digestive, expectorant, antibacterial	(Rastogi et al., 2005), (Blumenthal et al. 1998), (Hussain and Murthy 1992)
Glycyrrhiza glabra	Root	Glycyrrhizin, liquiritin, glabranins	Antihistaminic, expectorant, anti-inflammatory	(Blumenthal et al. 1998)
Leptadenia reticulata	Root	Hentriacontanol, stigmasterol, rutin	Galactogogue, stimulant, uterine cleanser	(Hussain and Murthy 1992)
Ocimum sanctum	Whole plant, leaves, oil	Eugenol, ursolic acid, carvacrol, luteolin, methylchavicol	Immunomodulator, anti-inflammatory, antitussive, antiprotozoal	(Rastogi et al., 2005)
Phyllanthus emblica	Fruit, leaves	Ascorbic acid, gallic acid, emblicanins A and B	Antioxidant, hepatoprotective, immunomodulator	(Rastogi et al., 2005)
Solanum nigrum	Whole plant	Solasodine, solasonine, solanine, solamargine	Hepatoprotective, antioxidant, mycotoxin inhibitor, diuretic	(Hussain and Murthy 1992)
Swertia chirata	Whole plant	Swertiamarin, swerchirin, gentianine	Hepatoprotective, anti-inflammatory, anthelmintic	(Hussain and Murthy 1992)
Withania somnifera	Root	Withaferin-A, withanine, somniferin	Immunomodulator, antistress, antioxidant, adaptogenic	(Brown et al., 1996)

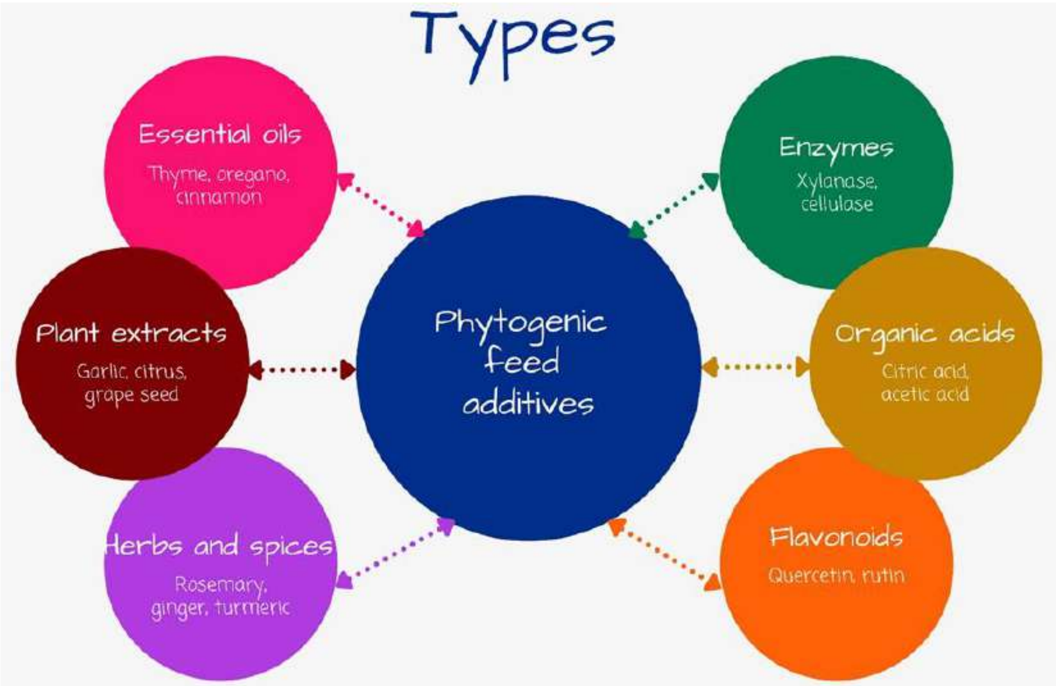

Fig. 1: Types of PFAs

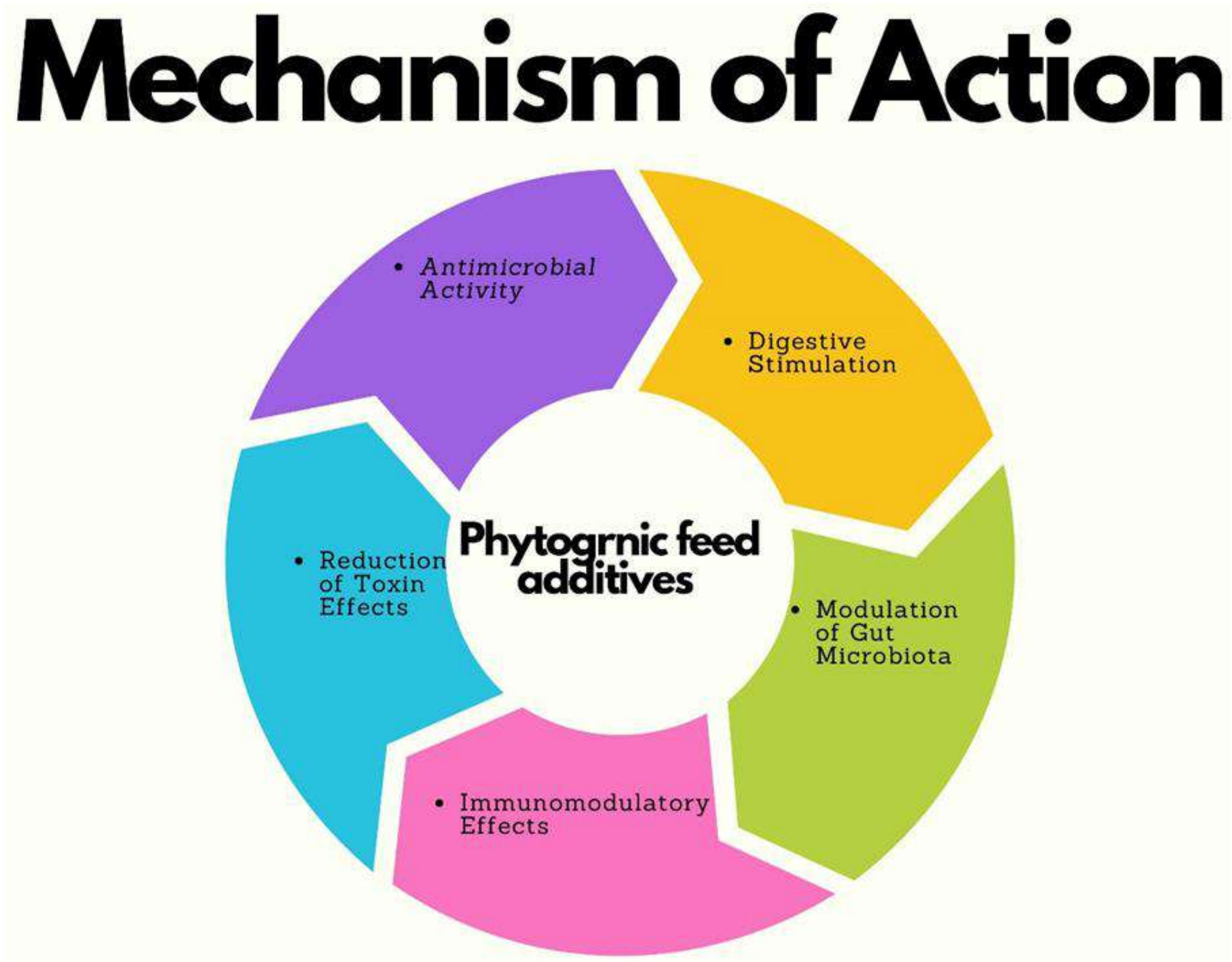

Fig. 2: Mechanism of action of phytogenic feed additives

The effects of the mechanism of action of PFAs are highlighted in Fig. 2. However, the antimicrobial effects would be unjustified if phytogenic substances in animal nutrition have limiting value. The multifaceted effects of phytogenic feed additives on animals are delighted due to recent scientific advancements (Ahuja et al., 2012). These effects enhance feed conversion, usually through improving digestibility that is attributed to various factors including the regulation of digestive juices and enzymes, modulation of the immune system, variation in intestinal morphology, increased nutrient absorption, and subsequent improvements in overall performance. Furthermore, these effects are directly related to positive changes in intestinal tissue morphology hypothesized to improve nutrient digestibility and stabilize intestinal microbiota to decrease microbial metabolite levels thus boosting the immune system and providing energy availability for muscle growth. These substances are utilized as additives in animal feed by confounding a phenomenon that exhibits a mode of action, although, recent scientific findings have more comprehensive yield and insights into the effects of PFAs on animals that encompass many factors through enhancing digestibility emerging as a primary benefit (Singh, and Gaikwad, 2020).

Benefits in Animal Nutrition

The health and well-being of ruminants significantly depend upon the selection of roughages. However, keep in mind the ability of ruminants to choose herbs that are conducive to promoting ruminal processes, which are primarily guided by taste and intricately connected with secondary plant metabolites. Especially, in cases of parasitic infection, condensed tennis is holding evidence, particularly over ruminant feed preference due to its taste. Furthermore, the duration and quantity of feed intake are influenced by the sequence in which feeds with different functional components are offered (Jayanegara et al., 2011).

Beyond taste, avian species have a well-documented phenomenon in which the feed color may also play a significant role in stimulating intake. Carotenoids due to their lipophilic nature, enhance stability during food processing and potentially intensify the appetite of visually-oriented animals and poultry. However, plant-derived colorants don't uniformly enhance intake through their worth which is noted in the mere inclusion. For instance, it is demonstrated that there is no increase in broiler feed intake following the addition of flavonoid phytogenics (Kraemer et al., 2011). Conversely, it was observed that increased feed intake and improved growth rates in weaning animals fed elder pomace, were influenced by its polyphenol content through improving feed palatability (Luehring et al., 2011).

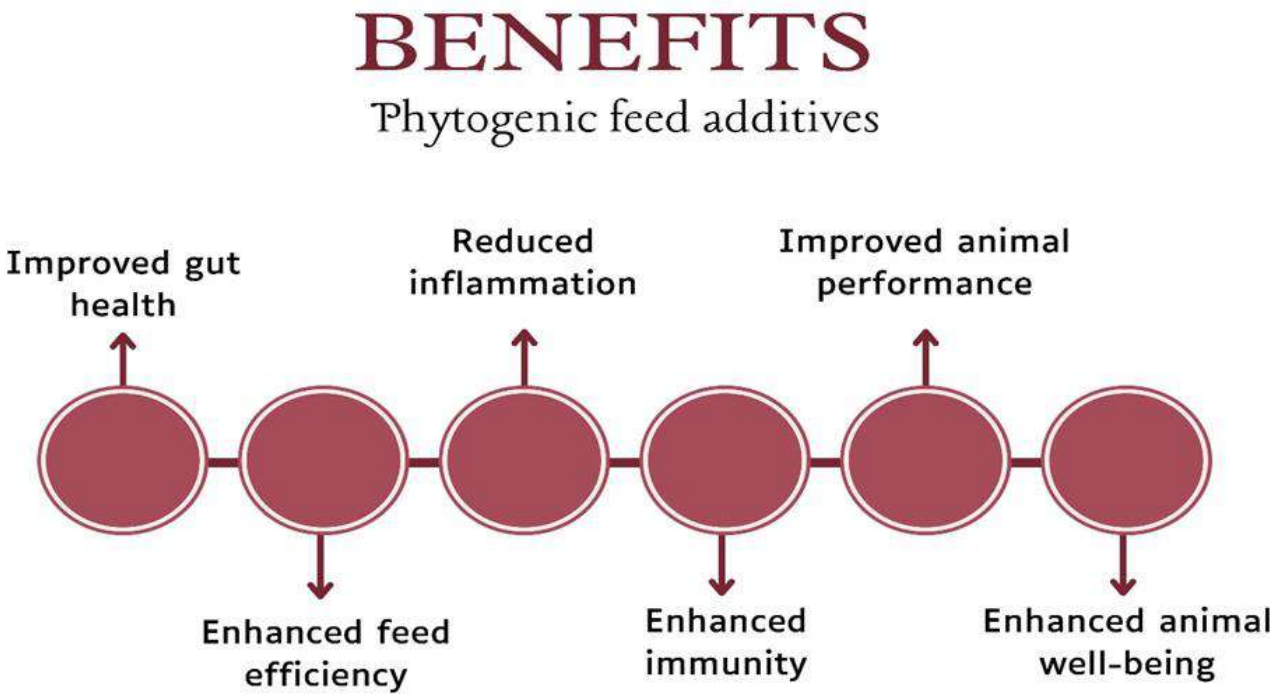

Fig. 3: Benefits of PFAs

As we know, PFAs contain benefits which are noted in Fig. 3. Polyphenols, including flavonoids and condensed tannins exhibit cross-reactivity with enzymes and impact both taste perception and digestive processes. While appetite stimulated by polyphenols may impart a bitter taste and interact with gastric enzymes, potentially reducing nutrient uptake rates. The saliva proteins form indigestible complexes with polyphenols by somewhat mitigating its effects. Many herbs and spices utilized in animal nutrition are biologically active compounds with antioxidant properties. Various spices containing antioxidants and highlight their role in preventing oxidative stress-related diseases including coronary heart disease and tumor development (Hashemi and Davoodi, 2011).

There is evidence about preventive effects against metabolic disorders like fatty liver disease and ketosis in early-lactating cows through antioxidants that help in stabilizing animal health. For instance, improving cow health and reducing the effects of mastitis through supplementation with flavonoid-rich mixtures. Carotenoids and other plant pigments influence the color and oxidative stability of meat and animal fat through their effects on animal products and enhancing their shelf life and nutritional value. Additionally, condensed tannins and flavonoid-like compounds can protect unsaturated fatty acids from bio-hydrogenation leading to higher transfer rates of these beneficial fatty acids into animal products including milk or tissues. Therefore, it's important to note that due to the negative impact on protein digestibility, condensed tannins are generally considered antinutritive in monogastric livestock and they may have positive impacts when applied in small amounts (Wang et al., 2021).

Phyto Additives Help in the Digestion of Nutrients

The use of various phytogenic feed additives (PFAs) shows beneficial effects on nutrient digestibility in animals. The improvement in nutrient absorption may be influenced at least in part by the regulation of saliva and bile secretions, along with enhancing enzyme activity. The overall health status of the animals subsequently depends upon this improved digestibility. So, the diet of broiler chickens can be improved through changes in villus surface area, height, height-to-crypt depth ratio, and muscular layer thickness in the jejunum and ileum by the addition of 100 and 200 mg/kg of thymol and carvacrol. Consequently, increase in villus height compared to control birds through Euphorbia hirta at 7.5 g/kg in supplementation. Furthermore, broiler diets significantly increased the length of the duodenum and total intestine by adding 2.0 and 2.5% Boswellia serrata resin (Gavris et al., 2019).

Crude protein digestibility increased to feed 2.0 and 2.5% Boswellia serrata resin. While dietary metabolizable energy (ME) is not affected by phytogenics, they notably enhanced dietary energy absorption that does not always correspond to growth performance. Additionally, providing the diet with menthol and anethole at 150 mg/kg did not affect performance or apparent ileal phosphorus absorption, while encapsulated essential oils of carvacrol, thymol, and limonene at 100 mg/kg increased performance and nutrient digestibility in broilers, due to enhanced secretion of digestive enzymes and its observed that broiler chickens absorbing gedi leaf juice in their drinking water that exhibits significantly lower apparent metabolizable energy (AME) values at 20 and 30 ml/L as compared to the control diet at 10 ml/L. Furthermore, supplementation with fenugreek seeds (1, 2, and 3%) significantly enhanced the feed conversion ratio in broilers, and adding 1 or 2 g of anise seed to broiler diets, not affecting feed intake, and increased body weight, daily weight gain, and feed conversion ratio. Similarly, improve egg productivity, vitality, and health conditions in treated chicks are also improved with herbal mixture supplements.

Dietary supplementation can enhance the immunological responses of broiler chicks with thyme oil extract, particularly at 100 ppm. Moreover, extracts of Curcuma and Scutelleria effectively reduced gut inflammation and boosted chicken activity by supplementing chicken diets. Furthermore, the recommendation to include it in a quail diet by adding 2.5% wood vinegar improves weight gain, decreases feed conversion ratio, and improves the production efficiency factor. Similarly, it is found that in broiler diets significantly improved dressing percentages by incorporating a mixture of hot red pepper and black pepper at levels of 0.75 and 1%. Additionally, feeding thyme essential oil at 100 mg/kg led to increased dressing yields and dissected sections of the waste involving breast and thigh yields (Mandey and Sompie, 2021).

Challenges and Limitations in the Pakistani Context

Several challenges are present in the livestock industry due to the application of phytogenic feed additives that can be classified into the following categories challenges associated with bioavailability, inconsistency in effectiveness, potential adulteration and the presence of toxic compounds, manufacturing obstacles, and issues related to public acceptance (Bhattaram et al., 2002).

Bioavailability is noted as challenging when the pharmacological properties of phytogenic plants are understood. Many medicinal components exhibit higher efficacy in vitro compared to in vivo studies. Furthermore, it indicates that only a low amount of certain phytobiotic compounds can be utilized in the small intestine resulting in reduced effectiveness. Poor absorption and assimilation, extensive bioconversion in the liver and intestine, and rapid metabolism are factors that contribute to this challenge. Additionally, the bioavailability study makes additional measures to enhance absorption due to synergistic effects between active and consistent compliance. Strict control over the quality and origin of plants along with extraction methods is crucial to balancing the stability and stoichiometry of phytogenic substances particularly given their sensitivity to light, temperature, and air during storage (Stevanović et al., 2018; Trucillo et al., 2018; Bianchi et al., 2021; Kikusato, 2021).

Bioactive substances within a product containing inconsistency in biological activities is another significant challenge and such inconsistency can arise from changes in plant biochemical characteristics, harvesting duration, address, the method of extraction, and extraction methods. The inconsistent effectiveness is the result of variations that lack standardization exacerbates. Feed intake is also decreased through some phytogenic substances due to palatability issues that lead to diminished animal performance. Biological activity is significantly induced by controlling the dosage of phytogenic substances in challenging both low and high. Furthermore, the hygienic status of farms and the stress levels of the animals also involved that influence the efficacy of phytogenic substances (Demir et al., 2003; Hafeez et al., 2020; Sugiharto, 2021; Shehata et al., 2022).

Contamination with toxic substances along with Concerns regarding adulteration also exist. Various traditional herbal products have been found to have harmful effects including hepatotoxicity and impairment of intestinal epithelium with gut motility. Various factors such as the integrity of the bioactive component, contamination possibility, bioavailability, reported side effects, and synergistic effects between compounds in mixtures require considerations to evaluate the toxicity of phytogenic products. (Fennell et al., 2004; Khaligh et al., 2011). However, phytogenic substances in animal production have the full potential to address these challenges. The efficacy and safety of phytogenic feed additives (PFAs) are evaluated by conducting systematic and comprehensive studies that remain challenging due to their complex composition. Furthermore, inconsistencies in results can influence various factors and the substantial variability inherent in PFAs, such as their source, bioactive compounds, botanical origin, growing areas, production, methods, and storage requirements along with the recommended dosage. Environmental factors, management practices, and rearing conditions are the challenges faced by the animals, and variations in microbial challenges, age, and genetics, also contribute to these variations (Al-Mufarrej et al., 2019).

Research and Case Studies in Pakistan

Recently, developing countries having primary indicators of economic growth such as food safety and quality have gained significant attention, (Ronquillo and Hernandez, 2017). However, due to the intensification of antimicrobial use in the food industry, drug-resistant bacteria have reservoirs as food animals that contribute to global antibiotic tolerance challenges.

The increase in antibiotic resistance is due to antibiotic-resistant bacteria in infected patients leading to a rise in remedial failures. Moreover, the spread and emergence of antibiotic resistance are influenced by the continuous addition of AGPs in animal feed. Consequently, the interference of antibiotic resistance in the food chain leads to significant human health risks and necessitates a global ban on antibiotic use in food production industries. However, this ban positively impacts animal performance and reduces disease occurrence (Toghyani et al., 2010).

Therefore, to maintain profitability and productivity in the livestock industry, there is an urgent need to explore promising. Phytogenic feed additives (PFAs) can enhance performance by maintaining a healthy gut environment and have garnered considerable attention as potential alternatives (Stevanović et al., 2018). PFAs contain various secondary compounds such as botanical extracts, essential oils, and spices, that possess bioactive properties including digestion activation, antioxidant effects, and antimicrobial properties (Christaki et al., 2012). PFAs are considered ideal alternatives because they can enhance animal productivity, improve feed efficacy, and sustain immunology (Attia et al., 2017).

Garlic (Allium sativum) contains active alkaloids, proteins, catalysts, and micronutrients, and it is a renowned herb in traditional medicine. These constituents exhibit the antibacterial, anti-inflammatory, and antiparasitic effects (Karangiya et al., 2016). Peppermint (Mentha piperita) belonging to the Labiatae family contains immunity-enhancing properties and protection against many infections and has wide use in herbal medicine. Cinnamon (Cinnamomum verum) contains active components including cinnamaldehyde, eugenol, carvacrol, and others that have beneficial effects on gut health. Black cumin (Nigella sativa L.) an important bioactive plant in Asia has antioxidant, antimicrobial, and anti-cholesterol features with active elements such as thymol, thymohydroquinone, thymquinone, and others.

Green tea (Camilla sinensis L.) is mostly used worldwide and has numerous health advantages due to its antioxidant properties and polyphenolic compounds that improve feed quality, and body weight and affects antimicrobial activities against the microbes in broilers. These plants have significant medicinal attributes and growth-promoting traits that hold promise as alternative growth promoters in the poultry industry. Hence, the performance of garlic, cinnamon, black cumin, peppermint, and green tea has been evaluated through considerable effects on animal performance and broilers depending on the composition of cecal and ileal microflora (Khan et al., 2014).

Future Prospects and Recommendations

According to current literature, phytogenic feed additives (PFAs) are composed of singular components or combinations and act as valuable alternatives to antibiotic growth promoters (AGPs). Feed additive compounds exhibit potential, further, detailed investigation and standardization with controlled conditions are imperative. The entire use of AGPs and antimicrobials in animal feed can be decreased or limited through the movements of PFAs (Windisch et al., 2008). On the other hand, several critical issues that are essential for sustainable livestock production due to the incorporation of PFAs need to be researched. PFAs provide several benefits including production efficiency that maintains profitability, animal health and welfare through minimizing the necessity for therapeutic antibiotics, consumer safety through bolstering consumer confidence by mitigating the risk of bacterial resistance, public acceptance, sustainability, and environmental protection through increasing feed conversion to reduce environmental pollution while currently enhancing performance (Ahuja et al., 2012).

Conclusion

In conclusion, many green non-woody, and flowering plants offers phytogenic feed additives (PFAs) that are alternatives of AGPs (anti-growth promoters) are using in animal feeding in Pakistan livestock industry. These offer many benefits to animals including proper health maintenance, boosted immune function, and overall health. PFAs adoption not only reduces dependency upon antibiotics but also contributes to achieving high livestock production and advocating consumer safety. Evaluating the efficacy of PFAs compounds and their combinations requires comprehensive research under a controlled environment to prevent the PFAs from challenges that these are facing. Similarly, the implementation of these additives helps to achieve sustainable livestock production, animal welfare and safety of consumer with environmental protection. These approaches can improve animal diets and can provide a healthier and more resilient future for Pakistan's livestock industry. Overall, the aim is to explore animal nutrition practices that are sustainable and holistic in Pakistan beyond through using these additives.

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Chapter 40

Nutrition and Feed Additives: A Comprehensive Review of Types, Functions and Regulations

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ABSTRACT

Feed additives improve animal health, performance, and product quality. It covers a wide range of additives, from vitamins and minerals to innovative and sustainable substitutes. Every type of feed additive is examined for its advantages and legal limitations, highlighting the need to use sustainability, effectiveness, and safety as top priorities. Maintaining moral and responsible feed additive practices will be essential as the worldwide demand for animal products grows. This collaboration among industry stakeholders will be aided by scientific research and technological advancements. By following strict regulations and promoting innovation, the agriculture sector can meet the evolving demands of a growing population while overcoming obstacles and protecting the environment, animal welfare, and public health. In order to improve the future for coming generations, feed additives and nutrition have revolutionary potential, as demonstrated by the establishment of a robust and sustainable food system.

KEYWORDS
Feed additives, Animal husbandry, Regulations, Sustainability, ethical utilization

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INTRODUCTION

In order to maintain the wellbeing, development, and production of livestock, nutrition and feed additives are essential components of contemporary animal husbandry (Bocquier et al., 2010). These additives are a wide variety of compounds that added to animal feeds in order to improve their performance, quality, and nutritional content. Every feed addition, including vitamins, minerals, enzymes, probiotics, and antioxidants, has a distinct purpose that is all directed towards maximizing the health and wellbeing of animals (Stevanović et al., 2021).

It is impossible to exaggerate the importance of feed additives and nutrition in animal husbandry (Cheng et al., 2014). Producers are under increasing pressure to maximize efficiency while upholding strict standards of animal welfare and product quality, as the demand for animal products grows worldwide (Stevanović et al., 2021). By increasing feed efficiency, promoting development, enhancing immunological function, and lowering the risk of illnesses and digestive issues, nutrition and feed additives provide workable answers to these problems (Bocquier et al., 2010; Pluske, 2013). In this chapter, many kinds of feed additives will be analyzed, their purposes, and the laws controlling their usage in animal husbandry (Boyko et al., 2021). Every feed additive category from organic acids to antibiotics, flavor enhancers to sustainable substitutes will be thoroughly explored, offering insightful information on each one's functions, advantages, and legal implications.

Types of Feed Additives

Feed additives can be divided into multiple categories according to their makeup and purpose. Among them are: Minerals and vitamins, Proteins and amino acids, Enzymes, Acidifiers, Toxin binders, Probiotics and prebiotics, Antibiotics, Antioxidants, Emulsifiers and surfactants. Additional ingredients include fiber, protein sources, carbs, fats, oils, flavors, sweeteners, humectants, preservatives, growth promoters, binders, pellet binders, flavor enhancers, essential oils, colorants, and nanoparticles (Pandey et al., 2019; Okey et al., 2023). Some of the examples have been mentioned in Table 1.

A. Functions and Regulations of Commonly Used Feed Additives

1. Antibiotics

Animal bacterial infections are prevented and treated with antibiotics (Stevanović et al., 2021). They raise general animal health, boost feed efficiency, and accelerate growth rates (Iegorov et al., 2021). Antibiotic resistance in humans, however, can result from the overuse of antibiotics in animal feed (Liu et al., 2021).

Table 1: Feed additives, types and their functions

Types of feed additives	Functions	Examples
Probiotics	Improve gut health, aid digestion	*Lactobacillus, Bifidobacterium*
Prebiotics	Stimulate growth of beneficial bacteria	Inulin, Fructooligosaccharides (FOS)
Antibiotics	Promote growth, prevent diseases	Penicillin, Tetracycline
Vitamins	Essential for growth, reproduction, and health	Vitamin A, Vitamin D
Minerals	Essential for various bodily functions	Calcium, Phosphorus
Amino acids	Building blocks of proteins, aid growth	Methionine, Lysine
Emulsifiers	Improve feed texture and stability	Lecithin, Mono- and diglycerides
Acidifiers	Lower pH in the gastrointestinal tract	Citric acid, Lactic acid
Mycotoxin binders	Bind and neutralize mycotoxins in feed	Bentonite, Activated charcoal
Antioxidants	Prevent oxidation, improve shelf life	Vitamin E, Selenium
Enzymes	Aid in digestion of specific nutrients	Amylase, Protease

Regulation

In some nations, the use of some antibiotics is forbidden. To maintain the safety of food, regulations also apply to antibiotic residues in animal products.

2. Vitamins

Vitamins are vital micronutrients that are important for metabolism, development, and general health (Pluske, 2013). To fulfil the unique vitamin needs of various animal species, they are added to animal feed.

Rules

Regulations govern the use of vitamins in animal feed to guarantee that the nutrients are safe for animals to eat and do not surpass upper limits established by regulatory bodies (Pandey et al., 2019).

3. Minerals

Minerals are necessary minerals that animals need in trace amounts required for the stale metabolism and overall health (Alagawany et al., 2020). To provide the required minerals to the animal's diet, they are added to animal feed (Zampiga et al., 2021).

Regulations

To assure that minerals do not surpass the upper limits and are safe for animal consumption, the use of minerals in animal feed is regulated.

4. Amino Acids

The building blocks of proteins, amino acids are vital nutrients needed for the development and upkeep of animal tissues (Phujumpa et al., 2022). To provide the animal's diet with the extra amino acids it needs, they are added to animal feed (Hossain et al., 2023).

Rules

In order to ensure that amino acids are safe for animals to eat and do not surpass the upper limits established by regulatory bodies, their usage in animal feed is regulated.

5. Enzymes

Proteins called enzymes aid in the body's metabolic reactions (Pandey et al., 2019). They are put to animal feed in order to lower feed costs, increase digestion, and optimize nutrient utilization (Phujumpa et al., 2022).

Rules

Enzymes are used in animal feed under strict regulations to guarantee that they are safe for animal consumption and do not endanger the health of either people or animals.

6. Prebiotics and Probiotics

Dietary supplements called prebiotics and probiotics encourage the development of healthy bacteria in an animal's stomach (Iegorov et al., 2021). They lower the risk of digestive diseases, strengthen the immune system, and promote nutritional absorption (Iegorov et al., 2021).

Regulations

To guarantee that prebiotics and probiotics are safe for animal consumption and do not endanger the health of either people or animals, their usage in animal feed is controlled.

7. Antioxidants

Antioxidants increase the duration and well-being of animals by shielding their cells from oxidative stress (Stevanović et al., 2021). To stop lipids and other nutrients in animal feed from oxidizing, they are added (Kang et al., 2023).

Regulations

To guarantee that antioxidants are safe for animal consumption and do not endanger the health of either humans or animals, their usage in animal feed is controlled.

8. Organic Acids

In order to reduce the pH of the animal's stomach and stop the growth of dangerous germs, feed additives containing organic acids are utilized (Alli et al., 2023). They lower the risk of digestive diseases, increase animal health, and improve feed conversion (Pitino et al., 2021).

Regulations

To guarantee that organic acids are safe for animal consumption and do not endanger the health of either humans or animals, their use in animal feed is controlled.

9. Essential Oils

Natural plant extracts called essential oils are added to animal feed to enhance the health and performance of the animals (Pitino et al., 2021). They can improve digestion, lessen stress, and encourage growth since they have antibacterial qualities (Righi et al., 2021).

Regulations

To guarantee that essential oils are safe for animal ingestion and do not surpass upper limits established by regulatory bodies, their use in animal feed is controlled.

10. Acidifiers

Feed additives known as acidifiers reduce the pH of the animal's stomach and stop hazardous bacteria from growing there (Dos Santos et al., 2021). They lower the risk of digestive diseases, strengthen the immune system, and optimize nutrient utilization (Iegorov et al., 2021).

Regulations

In order to guarantee that acidifiers are safe for animal consumption and do not endanger the health of either humans or animals, their usage in animal feed is controlled.

11. Emulsifiers

Emulsifiers are feed additives that improve the mixing and stability of feed ingredients (Mujica-Álvarez et al., 2020). They enhance nutrient absorption, reduce dustiness, and improve palatability (Siyal et al., 2017).

Regulations

The use of emulsifiers in animal feed is regulated to ensure that they are safe for animal consumption and do not pose any health risks to animals or humans.

12. Flavors and Sweeteners

Flavors and sweeteners are added to animal feed to improve palatability and encourage feed intake (Craig, 2021). They can also mask unpleasant tastes or odors in the feed (Du et al., 2021).

Regulations

The use of flavors and sweeteners in animal feed is regulated to ensure that they are safe for animal consumption and do not exceed the maximum limits set by regulatory agencies (Doeschate and Raine, 2006).

13. Feed Preservatives

Feed preservatives are used to stop feed from deteriorating and spoiling while it's being transported or stored (Du et al., 2021). They lessen the possibility of mycotoxin contamination and aid in preserving the feed's nutritional content (Sobanbua et al., 2020).

Rules

In order to guarantee that feed preservatives are safe for animals to eat and do not surpass the uppermost limits established by regulatory bodies, their usage in animal feed is regulated.

14. Growth Promoters

Feed additives known as growth promoters help animals grow and develop more efficiently, which raises production efficiency (Lin et al., 2020). They can shorten the time it takes for animals to achieve market weight and increase feed conversion rates (Pandey et al., 2019).

Rules

In order to guarantee that growth promoters are safe for animal consumption and do not endanger the health of either humans or animals, their usage in animal feed is controlled. Because of worries about the growth boosters' effects on the environment and human health, some nations have outlawed their use.

15. Binders

In order to decrease feed waste and enhance pellet quality, binders are added to feed. They can also lower the risk of digestive issues and improve the absorption of nutrients (El-Medany et al., 2021).

Regulations

In order to guarantee that binders are safe for animal consumption and do not endanger the health of either humans or animals, their usage in animal feed is controlled.

16. Toxin Binders

Toxin binders are added to animal feed as feed additives to stop mycotoxin contamination (Mehany et al., 2019). They have the ability to bind with poisons found in food, stopping the animal from absorbing them (Tavangar et al., 2021).

Regulations

In order to guarantee that toxin binders are safe for animal consumption and do not surpass the upper limits established by regulatory bodies, their usage in animal feed is controlled.

17. Colorants

Animal feed is given colorants to improve its appearance or cover up discolorations from storage or processing (Saleh et al., 2021). Although they are nutritionally worthless, they can increase palatability (Coultate et al., 2018).

Regulations

The use of colorants in animal feed is controlled to make sure that the maximum amounts established by regulatory bodies are not exceeded and that the colorants are safe for animal consumption.

18. Flavor Enhancers

Animal feed is made more palatable by adding flavor enhancers, which also improve the feed's taste or aroma (Craig, 2021). Although they are nutritionally worthless, they may urge animals to eat more (Al-Teinaz, 2020).

Regulations

In order to guarantee that flavor enhancers are safe for animals to eat and do not surpass upper limits established by regulatory bodies, their usage in animal feed is controlled.

19. Humectants

In order to stop dry feeds like grains or pellets from losing moisture while being stored or transported, humectants are added as feed additives (Ryczaj et al., 2020). They lessen spoiling and aid in preserving product quality (Tafadzwa et al., 2023).

Rules

Humectants are used in animal feed under strict regulations to guarantee that they are safe for animal consumption and do not endanger the health of either people or animals.

20. Pellet Binders

During the pellet creation process, pellet binders are employed as a binding agent to improve pellet durability, which lowers waste and ensures uniform nutrient distribution across all pellets (El-Medany et al., 2021).

Regulation

In order to ensure the safety of the animals that consume pellet binders and the people who handle them during production, their use must adhere to the regulations set forth by the local government authorities.

21. Probiotic Enhancers

Probiotics, which are live bacteria, probiotic enhancers support the health of an organism's gut flora system by improving growth, lowering stress levels, improving digestion, and other processes (Pandey et al., 2019).

Regulation

Local government agencies have set requirements that must be followed while using probiotic enhancers. These guidelines are designed to ensure both the safety of production procedures and the health of livestock animals that ingest them.

22. Yeast Cultures

Beneficial microorganisms found in yeast cultures have several advantages, including improved development, improved digestion, and increased immunity (Valletta et al., 2023).

Regulation

In order to ensure safety standards throughout production processes and ensure healthy outcomes when ingested by livestock animals, the use of yeast cultures must abide by restrictions set forth by local government agencies (Elghandour et al., 2020).

23. Fiber

For animals, fiber is a vital food because it facilitates digestion and supports gut health (Hayhoe et al., 2022). It can be included in animal feed in cellulose, hay, or straw, among other forms (Sallam et al., 2019).

Rules

Regulations govern the amount of fiber used in animal feed to guarantee that it is safe for animals to eat and does not beyond the upper bounds established by regulatory bodies (Pluske, 2013).

24. Protein Sources

To address the varied protein needs of various animal species, protein sources like fishmeal, soybean meal, and meat and bone meal are added to animal feed (Phujumpa et al., 2022). They are necessary for the development and upkeep of animal tissues (Hossain, 2024).

Rules

In order to guarantee that protein sources are safe for animals to eat and do not surpass the upper bounds established by regulatory bodies, their usage in animal feed is regulated.

25. Carbohydrates

Animals need carbohydrates like corn, wheat, and barley for energy, and these make up a large portion of their diet. They can also be used to pelleted feeds as a binder (Saleh et al., 2020).

Regulations

To guarantee that carbohydrates are safe for animals to eat and do not surpass upper bounds established by regulatory bodies, their usage in animal feed is regulated.

26. Fats and Oils

Animal feed is supplemented with fats and oils to provide energy and vital fatty acids needed for development, reproduction, and general health. They can help make animal feed more palatable.

Regulations

To guarantee that fats and oils are safe for animal consumption and do not surpass the upper bounds established by regulatory bodies, their usage in animal feed is regulated.

27. Feed Additive Combinations

In some circumstances, feed additive combinations can be utilized to produce desired results—such as increased growth rates or better gut health in animals—while lowering the risk of digestive disorders or other health problems associated with the abuse of individual chemicals (Bennett et al., 2021).

Regulations

Pertaining to these mixtures must adhere to established protocols developed by local government bodies with the goal of guaranteeing livestock animals' health and safety during manufacturing procedures (Rafiq et al., 2022).

B. Novel Feed Additives

Novel feed additives are compounds that have never been used in animal feed before, or they are modified versions of already-existing substances with new functional properties (Hayhoe et al., 2022). It offers potential advantages like enhanced immune function or better nutrient utilization while lowering environmental impact or other adverse health effects linked to conventional livestock animal feeding practices like antibiotic overuse, etc.

Regulations

Pertaining to these innovative additions mandate adherence to established protocols formulated by regional government agencies with the objective of guaranteeing production process safety standards and livestock animal consumption outcomes that are health-promoting (Sarpong, 2020).

C. Sustainable Feed Additives

Sustainable feed additives are those that have been made through environmentally friendly methods (Herrmann et al., 2024). Those include obtaining raw materials from sustainable sources, such as food waste products that have been recycled, rather than depending on conventional methods, which frequently entail intensive farming practices that contribute to deforestation, etc. Compliance with established parameters developed by local government agencies to ensure safety standards during manufacturing processes and ensure healthy outcomes when consumed by livestock animals is required by regulations pertaining to these sustainable alternatives (Saleh et al., 2021).

D. Nanoparticles

The potential advantages of nanoparticles, a type of feed additive, including enhanced nutrient absorption and decreased environmental effect, have drawn attention in recent years (Valletta et al., 2023). They are still being investigated for their safety for ingestion by animals as well as any potential long-term consequences on the environment and animal health (Alagawany et al., 2020).

Regulations

There are currently few regulations governing the use of nanoparticles in animal feed. Before their widespread usage is authorized, more study is required to ascertain their safety and effectiveness (Fedlheim and Foss, 2001).

Conclusion

In conclusion, feed additives and nutrition are vital instruments in contemporary animal husbandry and important cornerstones in the pursuit of ethical, efficient, and sustainable food production. The wide range of feed additives, their purposes, and the legal frameworks governing their usage have all been covered in this review.

Each category of feed additive offers distinct advantages targeted at maximizing animal health, performance, and product quality, ranging from vitamins and minerals to probiotics and sustainable substitutes. However, it is crucial to put sustainability, efficacy, and safety first when using feed additives as we traverse the complicated world of animal nutrition. It will be crucial for industry participants to work closely together, utilizing technological advancements, scientific research, and regulatory knowledge to guarantee the ethical use of feed additives in animal husbandry. We can continue to address the changing requirements of an expanding world population while preserving human health, the environment, and animal welfare by enforcing strict standards and welcoming creative solutions. Let's not waver in our resolve to push the boundaries of animal nutrition and agriculture as we set out on this innovative and discovery-filled journey. Together, we can ensure that feed additives and nutrition will pave the way for a more resilient, prosperous, and sustainable food system that will benefit future generations.

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Chapter 41

Natural Feed Additives for Sustainable Agriculture

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ABSTRACT

The agriculture industry is experiencing a major wave of transformation because of issues such as environment, people's health, and sustainability of the farming business. These natural feed additives are proving useful in an effort to increase cattle yield and reduce the adverse effects to the environment. This paper presents overview of sustainable agriculture with focus on the interactions between the economy, society and the environment. The benefits of natural feed additives for animal performance, welfare, and health are emphasized, along with their role in promoting sustainable agriculture. Various types of natural feed additives, are discussed, along with their mechanisms of action and potential to support sustainable farming practices. The study also examines the impact of natural feed additives on rural livelihoods, market competitiveness, and environmental sustainability.

KEYWORDS		
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INTRODUCTION

Recently the focus on production of agriculture sector has moved towards sustainable agriculture because of issues related to human live animal and environmental health. Natural feed additives have gained popularity among farmers and producers as they preferred to use additives that are not chemical based. These additives may have the ability of improving the health of the animal, reduce the effects that it has on the environment, and also improve the quality of the final product to be produced. This plants also supply food, fiber, and employment, as well as preserve the environment, and encourage sustainability (Harris and Fuller, 2014).

Still, the agriculture is threatened by climate change, loss of bio-diversity, decline in the land and water resources, and increasing cost of inputs; a continuously reducing number of farms, and tangled to that poverty and shrinking rural population (Hossain et al., 2020). Sustainable agriculture on its part seeks to feed the world's people in a fair manner and at minimal cost and impact on the environment (Brodt et al., 2011). It aims at fulfilling the current generation's wants and needs but not at the expensive of future generations (Fig. 1) (Robertson, 2015).

It involves observing social, ethical, and environmental standards in the use of resources when practicing agriculture (Harwood, 2020). It encourages practices such as intercropping, organic farming, agroforestry, IPM, and other, which are less hazardous to the environment than the industrialized agriculture that relies on chemical fertilizers and agrochemicals and uses high technology (Gomiero et al., 2011). These are measures that enhance soil, biological and ecological health; thereby minimizing adverse effects on the environment (Bommarco et al., 2018). There are also benefits in sustainable agriculture such as fair labor practices that influence the regional food economy and the performance of smallholder farmers (Berti and Mulligan, 2016). In summary, it is a systems approach of managing food production in a sustainable manner that addresses the triple bottom line of people, environment and profit for the long-term viability of agriculture.

Components of Sustainability

The fundamental components of sustainability—economic, social, and environmental factors—are widely acknowledged and are bolstered by an increasing amount of empirical research. The intricate connections among these elements are depicted by the overlapping circles in a three-part Venn diagram, emphasizing their interconnectedness and the comprehensive nature of sustainability (Fig. 2) (Robertson, 2015). The foundation of agricultural trade is economic sustainability, which is the ability of a system to consistently provide commodities and services at values higher than those of production. However, evaluating inputs and outputs, especially those that are externalized or taken for granted, such as nitrate pollution or soil biodiversity, creates difficulties, particularly in agriculture, necessitating extensive economic research (Swinton et al., 2007). Contrarily, social sustainability refers to a system's capacity to uphold societal norms for security and justice, including intergenerational parity. Food security, which guarantees a steady, sufficient, and accessible food supply, is crucial to this idea. The ability of a system to retain ecological balance and protect natural resources for future generations is the final aspect of environmental sustainability. This covers things like maintaining biodiversity, stabilizing the climate, and managing resources sustainably. Therefore, economic, social, and environmental components of sustainability are intertwined, necessitating a holistic approach to achieve lasting and meaningful sustainability outcomes (Collins et al., 2011).

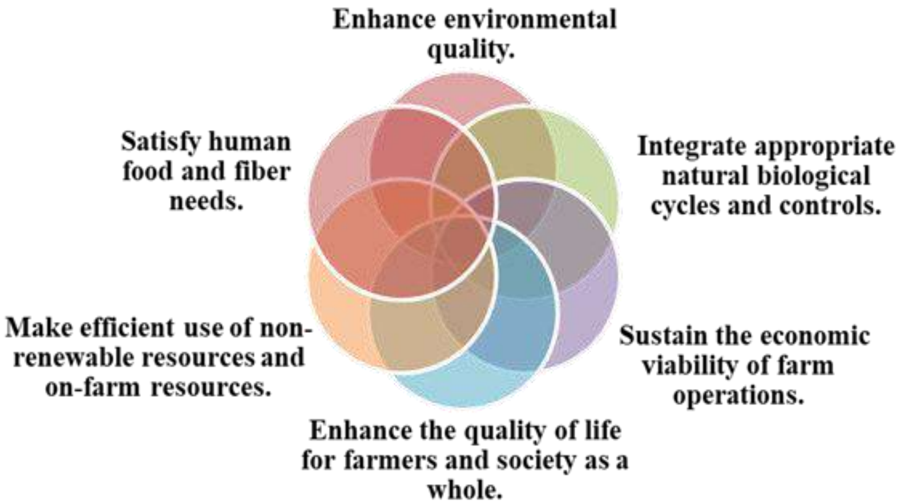

Fig. 1: Definition of sustainable agriculture.

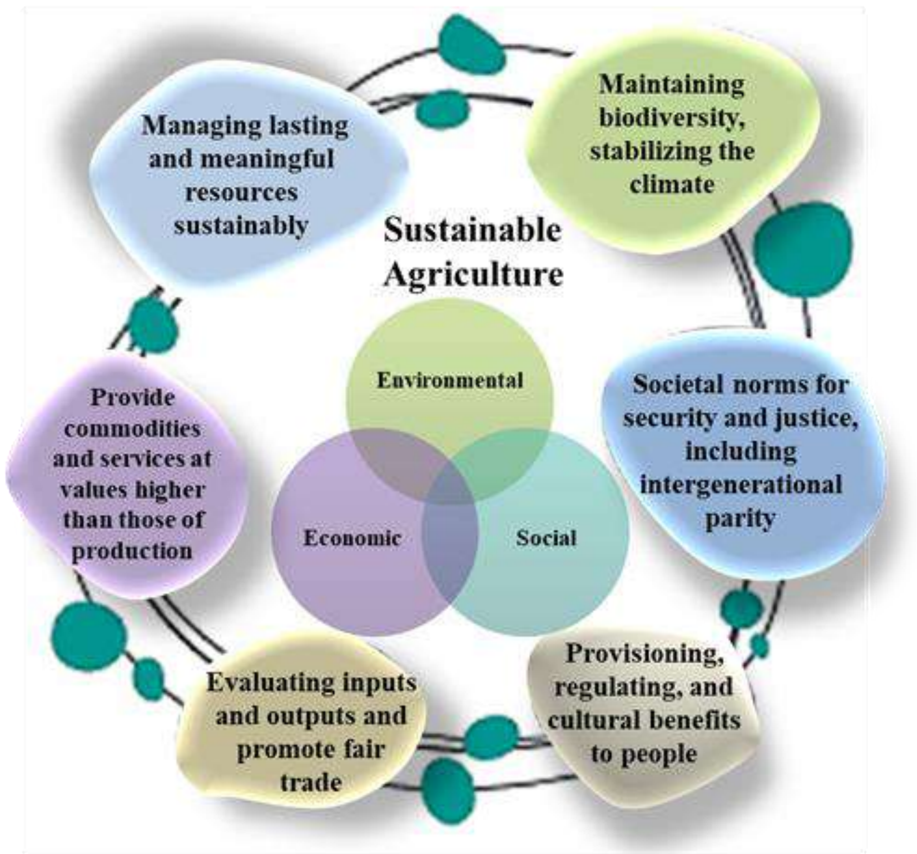

Fig. 2: Venndiagram showing Components of Sustainability.

Sustainability in agriculture relies on the relationship between ecosystem services and human well-being. A model developed by biologist Scott Collins and his team illustrates how interactions within cropping systems lead to ecosystem services that benefit people (Figure 3) (Collins et al., 2011). Social factors influence the perception and management of these services, while agricultural practices are determined by choices like crop selection and pesticide use. Adaptive management strategies are essential to address unforeseen challenges such as invasive pests and climate change. To address sustainability issues in agriculture effectively, it is crucial to requires an understand these complex interactions from social ecological perspective (Collins et al., 2011; Robertson, 2015).

Importance Sustainable Agriculture

The significance of sustainable agriculture in addressing critical global concerns related to food security, environmental sustainability, and climate change, cannot be overstated. Sustainable agriculture prioritizes methods that reduce environmental degradation, preserve natural resources, and enhance ecosystem services to ensure the long-term health and resilience of agricultural systems (DeClerck et al., 2016). By promoting practices that reduce the need for synthetic inputs, mitigate soil erosion and enhance improving soil structure, nutrient cycling, and water retention through the promotion of soil organic matter and biodiversity, sustainable agriculture plays a vital role in improving agriculture sustainability (Brodt et al., 2011). The conceptual network analysis of "Sustainable Agriculture" in Figure 4 highlights key themes such as sustainable food system development, plant growth from an environmental perspective, environmental quality (particularly air and water), and soil quality in the context of grain cultivation, with a specific focus on addressing ecological challenges in China (Polcyn el al., 2023).

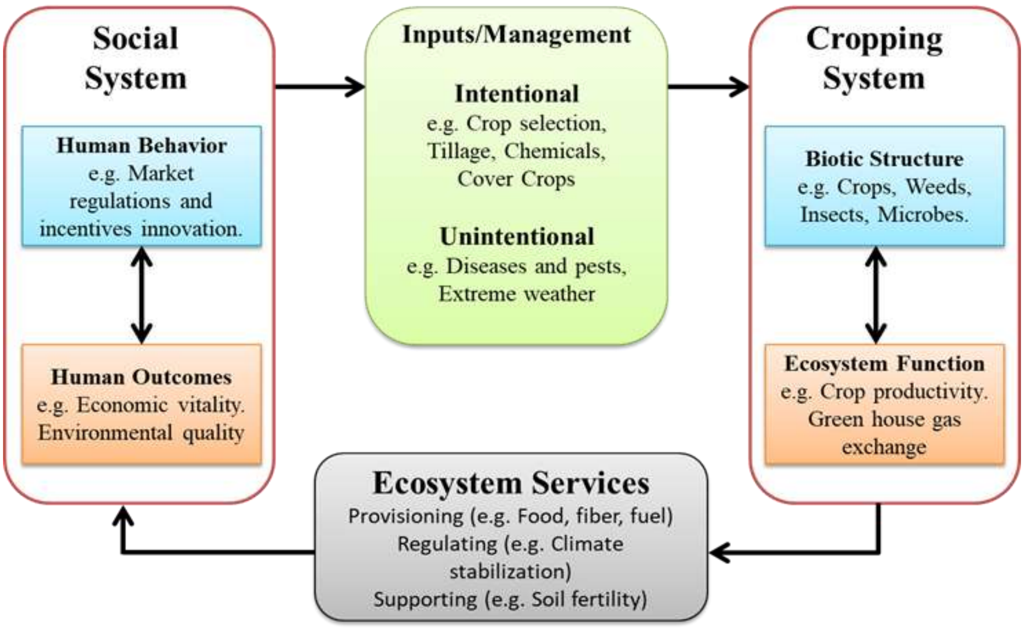

Fig. 3: Social-ecological model

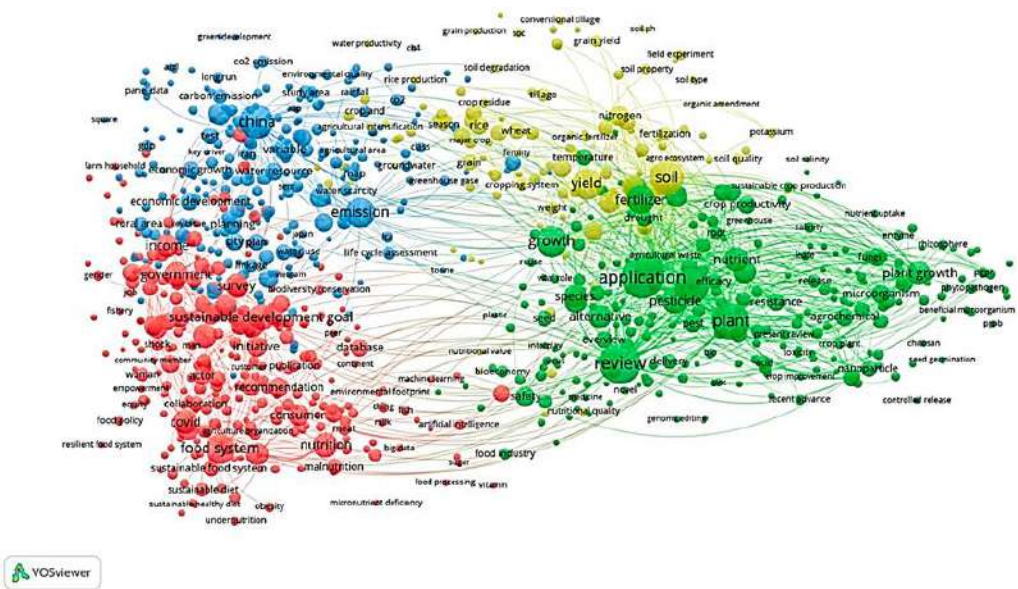

Fig. 4: Network visualization of the term “Sustainable Agriculture”

Feed Additives

Feed additives are compounds added to animal feed to improve its nutritional content, digestibility, palatability, and overall performance (Al-Jaf and Del, 2019). They serve various functions, including boosting growth rates, increasing feed efficiency, strengthening immunological function, and promoting general animal health (Pandey et al., 2019).

Natural Feed Additives

Natural feed additives are substances added to animal feed to promote growth, health, and well-being. They can be derived from plants, herbs, or other natural sources such as plant-derived compounds, essential oils and herbal extracts. These additives are used are used in livestock production to enhance animal health and reduce the reliance on synthetic chemicals and antibiotics (Alagawany and Abd El-Hack, 2020).

Types of Natural Feed Additives

They can be classified into several categories based on their origin and mode of action (Figure 5).

Phytogenic Additives

Phytogenic also known as phytobiotics, are plant-based materials used in animal nutrition to enhance health, well-being, and performance (Steiner and Syed, 2015). Phytogenic feed additives consist of bioactive substances like flavonoids, phenolic compounds, alkaloids, essential oils, and tannins, sourced from aromatic plants (e.g., peppermint, lavender), medicinal plants (e.g., ginseng, echinacea), spices (e.g., cinnamon, turmeric), and herbs (e.g., thyme, oregano) (Singh and Gaikwad, 2020).

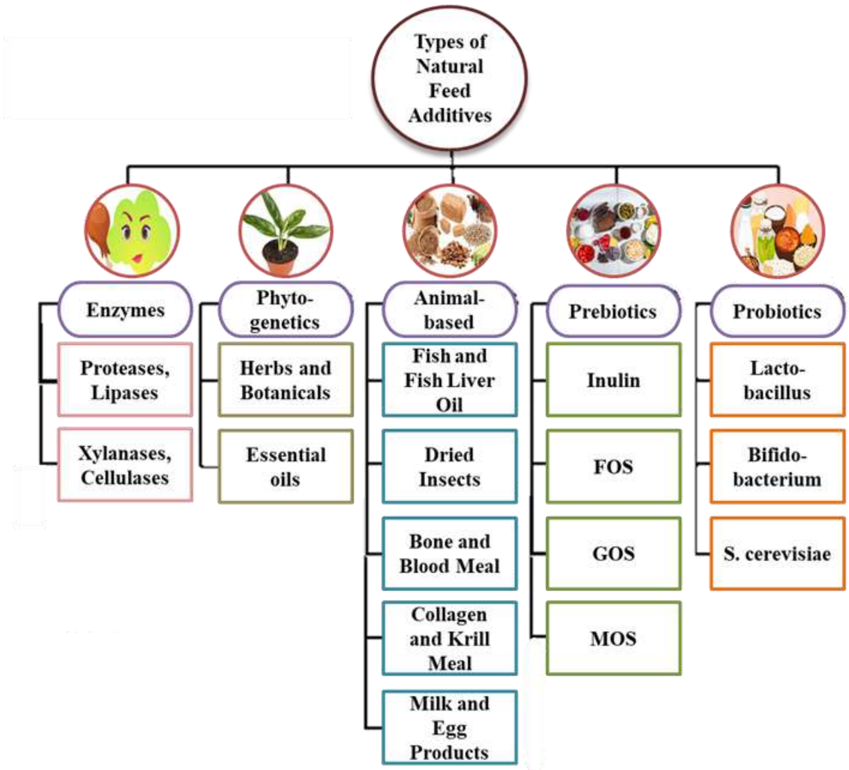

Fig. 5: Types of natural feed additives.

Types of Phytogenic Feed Additives

Here are some examples of plant-based additives:

a. **Herbs and Botanicals:** Herbs and botanicals are plant-derived substances with therapeutic or aromatic properties. Medicinal plants and aromatic are plant products which have curative or aromatic values. They include many number of plants like turmeric, thyme, oregano, cinnamon and garlic etc. Scientific research conducted has indicated that herbs and botanicals possess antibacterial, anti-inflammatory and antioxidant characteristics which are important natural sources of feed (Wenk, 2003).

b. **Essential Oils:** The nature's fragrant oils, also known as essential oils, are natural compound produced by plants and derived through the use of distillation or expression. They consist of Bioactive compounds that exert several physiological actions on animals (Stevanović et al., 2018).

c. **Mechanisms of Action:** Phytogenic feed additives work through various physiological and biochemical pathways,

1. Antimicrobial Activity: Phytogenics and their bioactive substances eliminate pathogenic bacteria, fungi and protozoa in the GI tract and decrease the probability of infections as well as enhance the gut health (Valdivieso et al., 2019).

2. Anti-inflammatory Effects: some phytonutrients in green vegetables contribute to the decrease of inflammation in intestinal lining and other body tissues thus playing a role in maintaining the overall digestion and on relief of symptoms of gastrointestinal disorders (Carrera-Quintanar et al., 2018).

3. Antioxidant Action: Phenolic compounds and flavonoids in phylogenetic act as antioxidants, scavenging free radicals and reactive oxygen species to prevent oxidative damage to cells and tissues, thereby supporting overall health and immune function (Fig. 6) (Akbari et al., 2022).

Animal Based Additives

Animal-based additives are natural supplements derived from animals that are used in animal nutrition to enhance meat quality, improve health, and boost performance. These additives include material sourced from animal tissues, organs, or secretions such as ish oil, bone meal, dried insects, and gelatin, collagen, bone meal, blood meal, krill meal, milk product and egg products (Jouany and Morgavi, 2007; Kiczorowska et al., 2017).

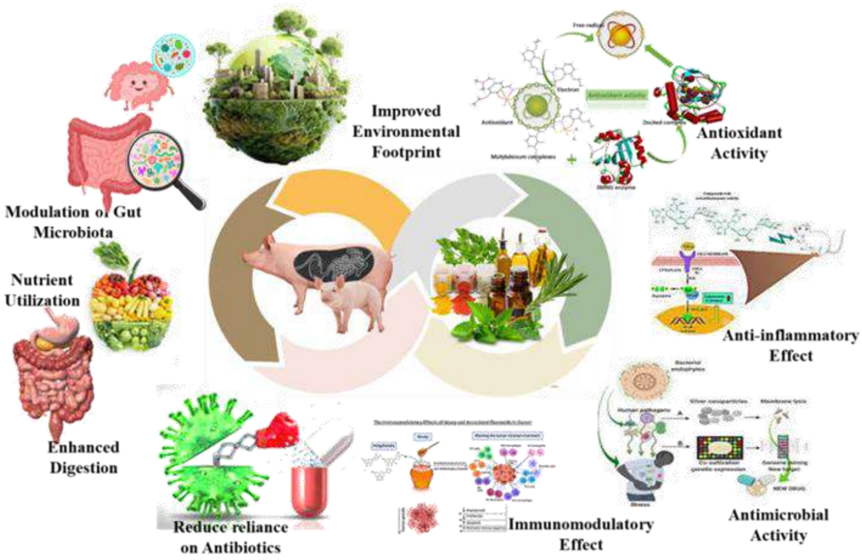

Fig. 6: Mechanism and Role of Phytogenic Feed Additives.

Types of Animal based Additives

a. Fish Oil: Fish oil from oily fish species like salmon and mackerelis rich in omega-3 fatty acids that support immune system function and cardiovascular health (Kiczorowska et al., 2017).

b. Dried Insects: Dried insects, such as mealworm and black army fly larvae, offer protein, amino acids, vitamins and minerals as sustainable protein sources in animal diets. (Kiczorowska et al., 2017).

c. Gelatin, derived from animal collagen, is used in feed formulations to enhance texture, digestability, and palatability of feed pellets, increasing nutrient utilization (Jouany and Morgavi, 2007).

d. Collagen: Collagen supplements can improve joint health in animals, reducing inflammation and arthritis symptoms (Bello and Oesser, 2006).

e. Bone meal and blood meal, are concentrated mineral sources that support bone strength and overall nutritional condition in animals (Leoci, 2014).

f. Krill Meal: rich in astaxanthin and omega-3 fatty acids, promotes joint function, cardiovascular health, cognitive function, and skin and coat health (Tou et al., 2007).

g. Milk Products: like lactose, casein, and whey, provide high-quality protein, amino acids, vitamins and minerals for growth, muscle development, digestive health, and immune system function (Pereira, 2014).

h. Egg Products: such as powdered egg yolk or white, offer protein, vitamins, and minerals that support muscle growth, tissue regeneration, immune system performance and feather quality in animals (Réhault-Godbert et al., 2019).

Enzymes

Enzymes are naturally occurring proteins that act as biological catalysts, speeding up chemical reactions in living organism. In animal nutrition, enzymes are added to feed as feed additives to enhance animal's ability to digest and utilize nutrients from feed ingredients. This method is gaining popularity due to its potential to reduce environmental impact, lower feed costs, and improve feed efficiency. Various types of enzymes are used as natural feed additives, each serving a specific purpose in the animal digestive system (Wenk, 2000).

Types of Enzymes Used as Feed Additives

a. Proteases: Amylases catalyse complicated carbohydrates such as starch and glycogen into simpler sugars; glucose. The inclusion of amylases in animal diets helps to improve the energy metabolism besides reducing the level of undigested carbohydrates in the intestine thus aiding the efficient digestion of starch (Sarica et al., 2005).

b. Lipases: Some of its uses include aiding in digestion of dietary lipids through hydrolysis of ester bond to produce glycerol and fatty acids which are required for cell synthesis and fat soluble vitamin assimilation. Adding lipases to animal feed improves the fat digestion and absorption, increasing energy utilization and overall performance (Liang et al., 2022).

c. Xylanases and Cellulases: d. Xylanases and Cellulases complex plant cell wall polysaccharides, such as xylan and cellulose, found in fibrous feed materials like grains and forages. These enzymes enhance the digestibility of fibrous materials, releasing nutrients and fermentable sugars for microbial fermentation in animal's hindgut (Paloheimo et al., 2010).

Mineral and Nutrient Supplements

Mineral and nutrient supplements are essential for animal's diet as they support healthy growth, development, and overall wellbeing. These supplements are often added to animal feed to ensure optimal nutrition and address any specific nutrient deficiencies. Natural feed additives containing minerals and nutrients play a crucial role in sustainable livestock production and help maintain of animals' physiological processes (Wenk, 2000).

Types of Mineral and Nutrient Supplements

a. Macro Minerals: Animals require sufficient amounts of macrominerals such as calcium, phosphorus, magnesium, potassium, sodium, and sulfur for various physiological functions like bone formation, muscule contraction, nerve transmission, and acid-base balance (Mateos et al., 2010).

b. Micro Minerals: Also known as trace minerals, example include iron, zinc, copper, manganese, selenium, iodine, and cobalt (Al-Jaf and Del, 2019).

c. Vitamins: Animals must obtain vitamins from their diet as they are organic compounds that cannot be synthesized in sufficient amounts. Essential vitamins include water-soluble (vitamin C) and fat-soluble (A, D, E, and K) vitamins, which are vital for immune function, growth, metabolism, and reproduction (Pandey et al., 2019).

Prebiotics

Prebiotics are food ingredients that the host animal cannot digest but promote the growth and activity of beneficial bacteria in the gastrointestinal tract (GIT). They serve as nourishment for beneficial microorganisms like lactobacilli and bifidobacteria, enhancing intestinal health and overall animal performance (Figure 7) (Markowiak and Śliżewska, 2018).

Types of Prebiotics

a. Inulin: Inuline is a type of dietry fiber found in plats like asparagus, garlic, onions, Jerusalem artichokes, and chicory root. It consists of fructose molecules linked by glycosidic bonds β (2-1) and promotes the growth of beneficial bacteria in the gut (Singh et al., 2017).

b. Fructo-oligosaccharides (FOS): FOS are short-chain carbohydrates with fructose molecule linked by β(2-1) glycosidic bonds. They are naturally found in fruits and vegetables like bananas, garlic, and leeks, and have prebiotic effects that support gut health (Ganguly et al., 2013).

c. Galacto-oligosaccharides (GOS): GOS are oligosaccharides composed of a glucose and galactose units linked by β(1-4) glycosidic bonds. They are present in legumes and human breast milk, promoting the growth of bifidobacteria in the gut as prebiotics (Singh et al., 2017).

d. Mannan-oligosaccharides (MOS): MOS are complex carbohydrates derived from fungi cell walls like Saccharomyces cerevisiae, consisting of mannose molecules linked by β (1-4) glycosidic bonds.. They act as prebiotics by binding to harmful bacteria, preventing their adherence to the gut lining, and supporting immunity and gut health (Ganguly et al., 2013).

Probiotics

Probiotics are live microorganisms that, when administered when given in sufficient amounts, provide health benefits to the host. When used as natural feed additives in animal nutrition, probiotics help improve gut health, enhance nutrient absorption, and boost overall animal performance (Figure 7) (Simon et al., 2005).

Fig. 7: Sources of Prebiotics and probiotics.

Types of Probiotics

a. Lactic Acid Bacteria (LAB): LAB Probiotics such as Lactobacillus and Bifidobacterium species, are commonly included in animal feed. In the gut, they ferment carbohydrates to produce lactic acid and other metabolites that create an acidic environment, inhibiting the growth of harmful bacteria (Patil et al., 2015).

b. Saccharomyces cerevisiae: Another probiotic type is the yeast species S. cerevisiae, known for its beneficial effects. It aids in fiber digestion, improves rumen quality in ruminants, and supports gastrointestinal health in various animal species (Elghandour et al., 2020).

Role of Natural Feed Additives in Sustainable Agriculture

Enhanced Animal Health and Welfare

Ensuring animal health and welfare is crucial for sustainable agriculture. Natural feed additives play a significant role in achieving this goal by improving immune system function, overall health, and welfare of livestock. Here are the key ways in which natural feed additives contribute to the health and welfare of animals:

Promotion of Growth and Development

Natural feed additives are sources of biologically active proteins, peptides, amino acids, fatty acids, vitamins and minerals that should be introduced into the system for good growth and improved production in animal farming. They facilitate growth and development of the tissues, bones and muscles, and other body organs for faster and better growth rates thus better feed conversion and performance in various Animation species of livestock.

Disease Prevention and Management

Herbal feed additives have active ingredients with anti-bacterial, anti-inflammatory and antioxidant effect for preventing and curing livestock diseases (Yang et al., 2015). Natural additives enhance immune status and pathogen opposition and therefore decrease the prevalence of infectious diseases and improve general health and disease tolerance in the animals.Lactis improves and sustains good intestinal microflora thus preventing infections and other bowel diseases (Kiczorowska et al., 2017).

Stress Reduction

Natural feed additives improve animal health of gut microbiota, which is known to have a central role in managing stress hormones in animals. There are some feed additives, which possess good adaptogenic effect that may help animals to mitigate the impact of heat, humidity, handling or transportation stresses (Kiczorowska et al., 2017).

Enhanced Reproductive Performance

It composes matters, such as zinc, selenium, and vitamin for the production of reproductive hormones, formation of embryo as well as animal reproductive systems. Natural supplements being feed additives can improve the reproductive performance of breeding animals through providing nutrition (El-Husseiny et al., 2008).

Improvement of Gut Health

Probiotics and prebiotics support a healthy intestinal microbiota and improve digestive function, essential for maintaining gut health (Kiczorowska et al., 2017). Probiotics produce enzymes that aid in the digestion of feed ingredients, enhancing nutrient absorption and utilization (Elghandour et al., 2020). Prebiotics act as substrates for beneficial bacteria, promoting their growth and activity in the gut, improving digestion and nutrient absorption (Kiczorowska et al., 2017).

Reduced Dependency on Medications

With regard to performance and health promotion that improved immunity can lead to, natural feed additives can contribute significantly in the prevention of diseases thereby minimizing the use of antibiotics and antimicrobials. To be specific, these rumours include: This type of rumours was defined by Yang et al., (2015).

Improved Feed Efficiency and Nutrient Utilization

It is therefore evident that to improve the livestock production systems in a sustainable manner they must be efficient in the use of nutrients as well as feed. There should therefore be natural feed additives which help in the improvement of feed conversion rate and nutrient acquisition, to the level of optimizing yields with the least input. Previous studies show that feed additives can improve nutrient intake while increasing the utilization factors and decreasing the proportion of excretion (Adegbeye et al., 2020).

Some of the Natural Feed Additives' natural composition that enhances feed conversion efficiency and nutrient utilization includes amino acids enzymes and organic trace minerals. Hence, by enhancing the conversion efficiency of available nutrients into productive outputs these feed additives help in making the livestock systems sustainable (Zampiga et al., 2021.

Reduced Environmental Impact

The use of natural feed additives is very important to minimize the harm that livestock farming creates to the environment. (Fig. 8).

Mitigation of Greenhouse Gas Emissions

It has been reported that specific feed additives which are natural chemicals like phytogenic and enzymes can lower the enteric methane losses from the ruminant animals. Some of the plant derived additives are capable of affecting the rumen fermentation and in the process slash methane emission. It is suggested that the utilizing of unconventional raw materials such as insect protein rather than the common feed ingredient soybean meal can help reduce the emission of greenhouse gases by as much as 70 percent (Chuang et al., 2021).

Minimization of Nutrient Runoff

Natural feed additives enhance the nutrient digestibility hence; the excretion of undigested nutrients is minimized in animal's feces. Supplementation with prebiotics improves gut integrity and feed conversion rate reducing nutrient losses in faeces thus minimizing environmental pollution resulting from nutrient leaching (Markowiak and Śliżewska, 2018).

Promotion of Sustainable Farming Practices

Integrated and sustainable farming practices are the practices, which will ensure sustained profits and production the impacts of which are not detrimental to the natural resources. In order to achieve such objectives, natural feed additives for livestock and poultry have the following benefits including enhancing soil health, decreasing the usage of chemical inputs, and enhancing bio-diversity as illustrated in figure 8.

Enhancement of Soil Health

Some examples of OM are organic fertilisers derived from plant residues, which help in determining the overall structure of the soils, ability to retain water and the level of microbial activity. These natural feed additives feed the soil nutrients and organic matters hence enhancing soil fertility and boosting sustainable farming. They improve the growth and yield of crops so that, they cut down the use of artificial fertilizers and pesticides (Singh, 2021).

Reduction of Chemical Inputs

Natural feed additives have avoided or greatly limited the application of synthetic chemicals on the farmland that leads to environmental pollution. Organic agricultural components can substitute chemical inputs and pesticides that lower chemical contaminants in food chain, water, and soil. Such a transition towards the environmentally friendly OFM lead to proper soil and environmental health due to the reduction in the cases of chemical leaching and running off into the water sources (Meena et al., 2020).

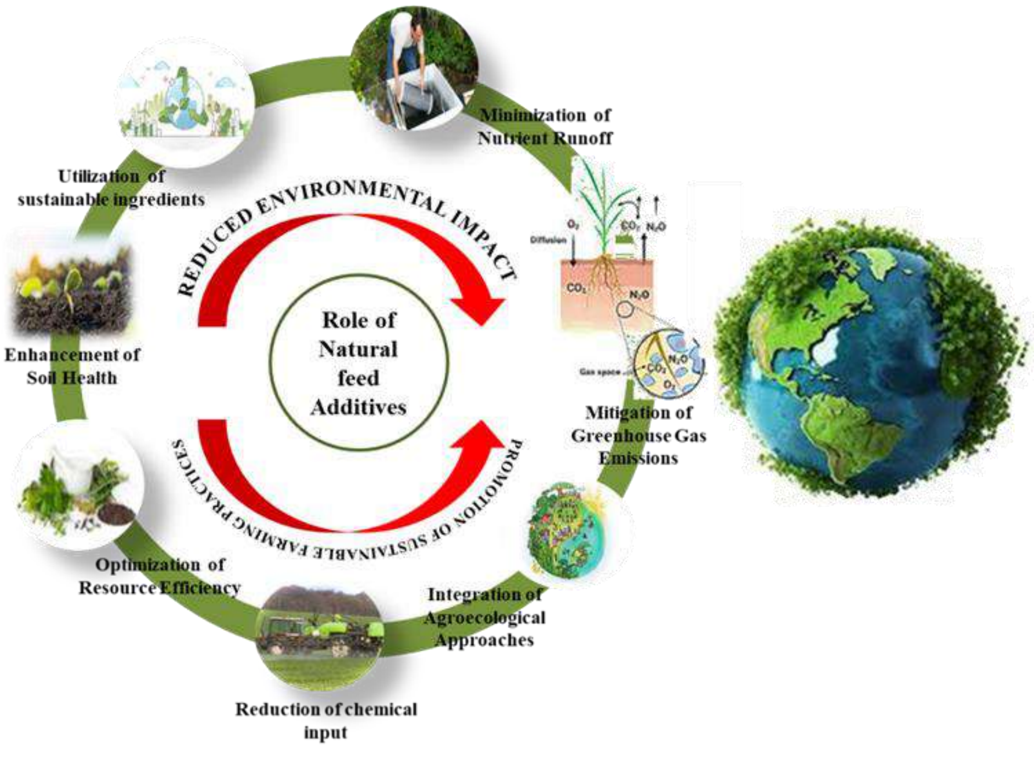

Fig. 8: Promoting Sustainability Through Natural Feed Additives

Support for Organic Farming Principles

Natural feed additives are compatible with the principles of organic farming because they encourage environmentally friendly and natural strategies for cultivation of the feeds. This addition boosts the well-being of plants, replenishes soil nutrient content and sustains the biological equilibrium which helps to foster the establishment of efficient progressive and qualitative methods of farming. (Seufert et al., 2017).

Integration of Agroecological Approaches

Natural feed additives have agroecological contexts relative to the promotion of other and various systems of farming and other ecosystem services. Most of these nutrients and minerals are crucial supplements in agroecological systems that have close linkages to agroforestry and integrated crop livestock systems through enhancing fertility of the soil as well as increasing the organic matter and biodiversity as well as strengthening the ecosystem (Wenk, 2000).

Compliance with Consumer Preferences

There is a demand from the consumer to embrace naturally, organic and sustainably produced food items in the agriculture sector. According to their source, natural feed additives contribute greatly in linking resource supply for farming with consumers' expected conducts by promotion of humane practice in farming, health of human beings, and conservation of the environment (Fig. 9).

Preference for Natural and Sustainable Products

As identified by the customers, organic and natural products that are eco-friendly have a gaining trend in the market (Siddiqui et al., 2022).The natural feed additives derived from natural products and have the similar meaning to synthetic chemicals are preferred by the consumer who takes organic produced foods and feeds (Escribano, 2018).

Preference for Organic Feed and Ingredients

Such consumption items and products that people perceive to be natural, organic and green get more market adoption with each passing day (Siddiqui et al., 2022). Organic feed additives are trendy among the customers who prefer foods which are produced with high ethical standards and do not threaten the environment as they are derived from natural sources and do not contain synthetic chemicals (Escribano, 2018).

Acceptance of Innovative Ingredients

This is because customers' attitudes towards sustainable and ethically sourced raw-materials determine the extent to which they accept new and innovative products such as insect derived feed additives. Consumers' willingness and choice to opt for sustainable consumption can be enhanced through educating the customers on the positive impacts that other protein sources such as insect protein have to the environment (Sogari et al., 2019).

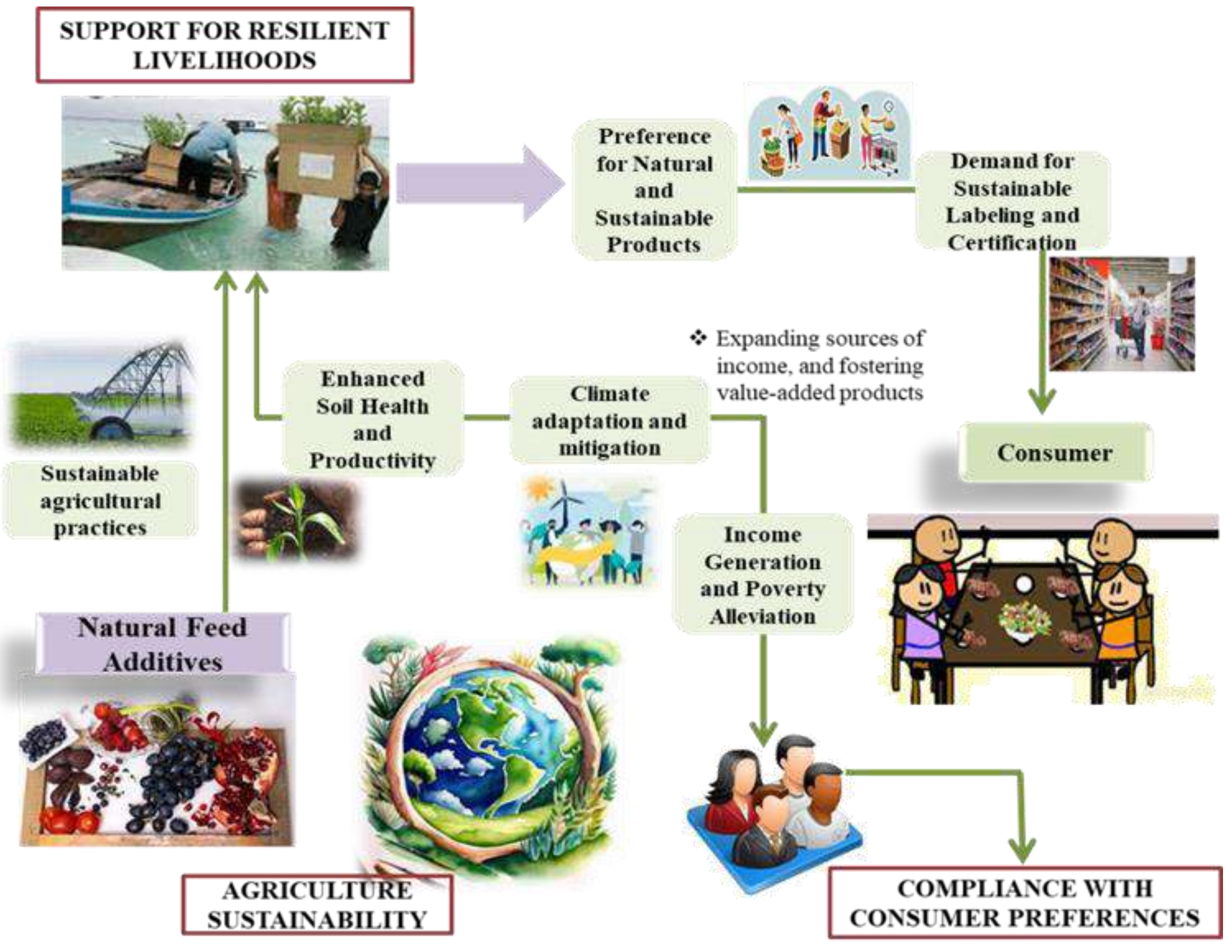

Fig. 9: Enhancing Livelihoods with Natural Feed Additives.

Demand for Sustainable Labeling and Certification

Sustainability certificates and labels that attest to the food items' ethical and environmental qualities are highly valued by consumers. Consumers' decisions to buy food goods are influenced by sustainability labels and organic certification, which reassure them about the products' ethical and environmental credentials (Seufert et al., 2017).

Support for Resilient Livelihoods

Resilient livelihoods are essential for rural communities, especially in the context of sustainable agriculture. Natural feed additives play a crucial role in increasing agricultural productivity, promoting sustainable farming practices, and ensuring economic stability, all of which are key element of resilient livelihoods (Figure 8).

Sustainable Agricultural Practices

Natural feed additives contribute to soil health improvement, reduced reliance on synthetic inputs, and environmental stewardship, making them essential for sustainable agricultural practices (Singh, 2021).

Enhanced Soil Health and Productivity

Natural feed additives such as organic fertilizers and soil conditioners enhance the soil health, fertility, and structure leading to Strong crop growth, higher yields, and sustained agricultural output. Healthy soils are fundamental for resilient livelihood, as they support agricultural systems by recycling nutrients and stimulating microbial activity (Dahal et al., 2016).

Diversified Livelihood Strategies

By utilizing natural feed additives, farmers can diversify their income sources of revenue beyond traditional livestock or crop farming (Rao et al., 2015).

Climate Adaptation and Mitigation

Climate-resilient farming techniques supported by natural feed additives help farmers adapt to changing climatic conditions and mitigate the effects of climate change (Dubey et al., 2020).

Income Generation and Poverty Alleviation

Sustainable agriculture with natural feed additives has the potential to increase revenue and alleviate poverty in rural areas. By boostingagricultural output, expanding income sources, and promoting value-added products, natural feed additives contribute to economic resilience and improved living standards in rural communities (Dubey et al., 2020).

Conclusion

In conclusion, the use of natural feed additives presents a promising path towards sustainable agricultural practices. These additives derived from plant, animal, and microbial sources offer numerous benefits for both cattle and the environment. By reducing reliance on artificial chemicals and antibiotics, natural feed additives enhance animal health, welfare, and performance leading to increased productivity and profitability for farmers. Moreover, their use promotes resource efficiency, minimizes nutrient runoff, and helps mitigate greenhouse gas emissions, aligning with principles of environmental sustainability. By incorporating natural feed additives, farmer can enhance market competitiveness and consumer trust by meeting demands for ethically and sustainably produced food products. Overall, the incorporation of natural feed additives in livestock production has the potential to drive resilient livelihoods, sustainable agriculture, and address the challenges facing the agricultural industry in the modern era.

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Chapter 42

Exploring Advanced Nutrition: Beyond the Basics

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ABSTRACT

Health and disease prevention depends much on nutrition hence determining physical strength and mental capacity. Basic nutrition on the other hand, is about taking rightful nutritional substances which are needed by the body to support its activities while advanced nutrition defines macronutrients and micronutrients, and also explain how they work in relation to metabolism and overall health. Functional foods that are defined as foods that also have health benefits over and above providing the identity nutrient of interest are especially significant; examples are carrots containing phytochemical compounds. In this regard, an understanding of the types of carbohydrates, proteins and fats as well as their impacts on the health of a human being is vital, particularly in patients suffering from chronic diseases such as obesity, diabetes, and cardiovascular diseases. Also, more progressive diet-related plans, such as the intermittent fasting, presents different strategies towards controlling diseases. Last but not the least, sleep and circadian rhythms are the vital components of metabolism and health related issue. Such a holistic view of nutrition explains why nutrition is a critical factor and determinant of disease prevention and a healthy life.

KEYWORDS		
Nutrition, Health, Disease prevention, Functional foods, Metabolism	Received: 08-Jun-2024 Revised: 07-Jul-2024 Accepted: 06-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Nutrition, or the study of food and its effects on human health, is a critical component in promoting health and illness prevention. Nutrition is critical to human health and well-being, influencing everything from physical stamina to cognitive ability. In recent years, a number of research and publications have underlined the importance of nutrition in improving overall health and avoiding chronic diseases. Fundamental food is required for optimal health and well-being. It refers to the intake of critical nutrients necessary for the body's numerous physiological activities. Certain foods go beyond nutrition and give extra benefits, therefore qualifying as functional foods. These foods, such as carrots of varied colors, not only provide basic nutrition but also contain accessible phytochemicals with health advantages (Arscott and Tanumihardjo, 2010). Functional foods play a role, in enhancing health by addressing deficiencies through the use of whole food approaches (Roberfroid, 2002).

Definition of Advanced Nutrition

Advanced nutrition is described as the specialized study and application of principles governing nutritional intake, absorption, metabolism, and utilization in the human body. It extends beyond fundamental nutrition principles to a deeper understanding of macronutrients (carbohydrates, proteins, and fats), micronutrients (vitamins and minerals), and their functions in numerous metabolic processes. Advanced nutrition in clinical practice refers to the assessment and management of nutritional demands in people with unique health conditions or diseases (Brody et al., 2012).

Understanding Macronutrients in Depth

Understanding macronutrients in depth requires a thorough understanding of their importance in human nutrition and health. Macronutrients are vital nutrients that supply energy and support a variety of physiological functions in the body. Carbohydrates, proteins, and lipids all play various functions and follow different metabolic pathways. Carbohydrates are the body's principal energy source, supporting important functions and physical activity. They can be found in foods such as cereals, fruits, and vegetables. Understanding the different types of carbohydrates, such as simple sugars and complex carbohydrates, is critical for controlling blood sugar levels and achieving total energy balance. Proteins are essential for tissue growth and repair, immunological function, and enzyme and hormone production. Protein sources include meat, chicken, fish, dairy products, beans, and nuts. A thorough grasp of protein quality, amino acid composition, and protein synthesis pathways is required for optimal muscle growth, recovery, and health. Fats have important functions in energy storage, insulation, and absorption of fat-soluble vitamins. They also act as structural components of cell membranes and participate in hormone synthesis (Muth and Park, 2021). Saturated, unsaturated, and trans-fats have different impacts on cardiovascular health and metabolism. Understanding their sources and effects on lipid profiles is crucial for improving heart health and weight management. Furthermore, evidence indicates that the macronutrient balance in the diet might affect a variety of health outcomes, including obesity, cognitive function, and metabolic problems (San Cristobal et al., 2020).

Carbohydrates

Carbohydrates are and essential macronutrients which is the major source of energy for the human body. It can be obtained from grains, fruits, vegetables, leguminous seed, and other starchy and Cereals products. Carbohydrates provide glucose in the body to the cells for energy through the processes like glycolysis and cellular respiration according to Seal et al. (2021). It was not the amount of carbohydrates that affected their general health negatively it was the quality. The (HHS) has found that carbohydrates from whole grains, fruits, and vegetables are healthy and that their consumption lowers the risks of chronic diseases like obesity, diabetes, and cardiovascular diseases (Sievenpiper, 2020).

Simple vs. Complex Carbohydrates

Complex and simple carbs are two classifications of carbohydrates which have chemical makeup and the manner in which it is metabolized in the body. These are known as the refined carbohydrates, or simple sugars, and include glucose, fructose and sucrose as these carbohydrates contain only one or two units of sugar. They are channeled quickly into the bloodstream and this leads to rise in blood sugar levels. They can also be gotten from items such as soft drinks, sweets and baked and processed foods (Holesh et al., 2023). Simple carbohydrates are also referred to as simple sugars and include sugars that are made of one or two molecules of sugar while complex carbohydrates are also referred to as polysaccharides and are lengthy chains of sugar molecules that include starch and fibre (Mustad et al., 2020). They take time to be digested and are progressively converted into glucose and thus release energy slowly and sustainably (Clemente-Suárez et al., 2022).

Glycemic Index and Glycemic Load

Glycemic Index (GI) and Glycemic Load (GL) are measures of how carbohydrates impact on blood glucose levels. GI of a diet sweetened by carbohydrates depends on the rate at which its blood sugar rises above glucose level, which has a GI value of one hundred. GL take into account not only the portion size and the quality of carbs consumed in a portion of food but their amount as well which provides a more complete picture of the effects they have on the blood sugar (Vlachos et al., 2020). Based on the study there is an intake of meals with the low GI and GL that may help enhance postprandial hyperglycemia of type 2 diabetes patients (Vlachos et al., 2020).

Carbohydrate Timing and Performance

The timing of carbohydrate consumption is a very sensitive issue that determines both sports performance and training recovery. Carbohydrate consumption before and after exercise is of significant effect to the actual performance as found by Arent et al. 2020. For this reason, endurance athletes must ensure themselves high glucose availability prior and post long periods of training (Nielsen et al., 2020). Also, carbohydrate feed just after exercising enhances glycogen restocking and muscle recovery in training, thereby enhancing training adaptation (Sigler, 2023). Carb intake with regard to its appropriate timing has also been identified as enhancing the rates of recovery as well as athlete's performance (Moore et al., 2022). Therefore, it is of great importance that high carb diets be integrated around exercise so that increased performance and post exercise recovery can be achieved (Dhiman and Kapri, 2023). Carbohydrate dietary pattern (CDP) index and the rate of prevalence of obesity is shown in (Fig. 1).

Proteins

Protein on the other hand is an essential nutrient that has several roles in body system such as in the building of new muscles, in manufacture of enzymes and in the immune system. It has been ascertained that both plant and animal products fit well in term's meeting nutritional needs and supporting good health. These nutrients also have significance to human food requirements, and added function in animals' diets, hence helping in growth and wellbeing of animals (Gasco et al., 2020).

Essential Amino Acids

Conditionally indispensable amino acids are a part of protein structure and play a very significant role in various physiological processes. Nine amino acids are considered essential which are required from food sources because the body cannot synthesize them well (Church et al., 2020). HC resists proteolysis, the breakdown of proteins by enzymes, and those amino acids include: histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine.

Conditional nutrients retain body proteins especially muscles, immune system and act as precursors to neurotransmitters in the body (Lopez and Mohiuddin, 2023). They are particularly important for the body especially athletes and those who involve in frequent exercises since they are useful for muscles repair and building (Church et al., 2020).

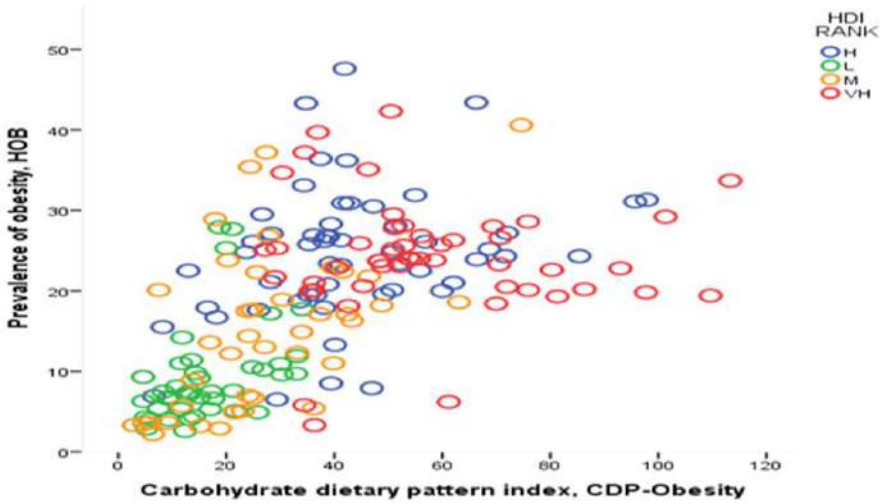

Fig. 1: Carbohydrate dietary pattern (CDP) index and the rate of prevalence of obesity (Ferretti and Mariani, 2017).

Protein Quality and Digestibility

Nutrition quality and quality available are two determinant attributes in defining the foods nutritional value. Digestibility of protein, means the extent to which the protein ingested by the human body has been utilized by breaking them and in turn; the term quality of protein comprises of the quantity of amino acids present in the protein and the ability to assimilate the mentioned amino acids. Preparation techniques can influence protein solubility and other qualities, (van den Berg et al., 2022). Methods that have been used in the evaluation of protein quality include in vitro techniques such as protein digestibility warranting indices especially in chicken diets. In addition, stable isotope methods give information about the means of determining the consequences of digestibility in human beings which in turn supports the claims towards protein content (Bandyopadhyay et al., 2022).

Protein Synthesis and Muscle Growth

Muscles require proteins for growth a repair hence the need to produce them in the body. Short term muscle atrophy is accompanied by decreased muscle protein synthesis; therefore, it is mandatory to maintain protein synthesis rates for muscles (Brook et al., 2022). Protein food especially essential amino acids in the diet enhances muscle protein synthesis thus leading the muscular repair and growth after exercise (Churchward-Venne et al., 2020). Some of the conditions for muscle protein synthesis include amino acids like phenylalanine which is an important substrate for muscle protein synthesis besides helping in the muscle and overall body response to meals as stated by Church and his colleagues (2020).

Fats

As it is known fats are required in human diet the main reason being that they constitute one of the most important components needed for the provision of energy besides that fat soluble vitamins cannot be absorbed in the body without fats. Some of the dietary lipids consist of animal fats and vegetable oils and they have distinct nutritional characteristics (Sanders, 2024). It is an essential parameter to identify nutritional nutrients and to manage diseases for example; obesity (Short and Hahn, 2023). In addition, fat replacers in food products result in nutritional modifications, thereby promoting desirable nutrition behaviours (Fontes-Candia et al., 2023). In total, fats are involved in a number of processes within the body from metabolic efficiency to dietary requirements (Lin et al., 2023).

Types of Fats: Saturated, Unsaturated, Trans

Fats are categorized into three types: There are three types of fats, namely; saturated fats, unsaturated fats, and trans fats; each one containing different chemical properties as well as affects the human body. Total fats are found in butter and pork, which are solid at the room temperature and are said to raise the cholesterol levels (Clavijo-Bernal et al., 2023). Traditional oils and nuts are examples of unsaturated fats which are at room temperature and are said to be beneficial to heart when taken in moderate portion (Shahi et al., 2023). Hydrogenated oils and fats which are most commonly used in processed foods have been found to cause adverse health related effects (Darioli et al., 2023).

Omega-3 and Omega-6 Fatty Acids

These are essential poly unsaturated fats essential for good health and are classified as omega -3 and omega-6 fatty acids. Omega-3 fatty acids in fatty fish include eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA), both of which are anti-inflammatory (Egalini et al., 2023). Omega-6s including linoleic acid are present in vegetable oil and they are important for proper cell operation (Redruello-Requejo et al., 2023).

Fat Metabolism and Health Implications

Products of fats play a critical role in health outcomes since it is at the center of several metabolic diseases. Probiotics found in the intestines have a role to perform in lipid metabolism the potential of which is in the therapeutic context (Song et al., 2023). Oil gels used instead of fat has abusable effects on metabolism; it changes the nutritional quality of high fat diets in a way (Tan et al., 2023). Metabolic health clusters have stressed more on their heuristic ability when it comes to the early identification and management of cardio metabolic threats (Stefan and Schulze, 2023). Moreover, there are more understandings of SCFA and its involvement in the process of intestinal gluconeogenesis that closely related to obesity and diabetes treatment (Anachad et al., 2023).

Micronutrients: Going Beyond Vitamins and Minerals

The Micronutrients are not just the vitamins and minerals but they also include certain necessary materials that are needed for various functions in the body. Apart from traditional nutrients, they consist of other constituents that are relevant to energy and immune systems coherence, and synthesis of tissues and organ coat (Abd Rahim, 2023; Fawzy et al., 2024). An appreciation of its use encompasses matters related to pharmacology or drug-interaction, nutritional supplementation, and methods of biofortification (Laight, 2023).

Phytonutrients

Definition and Types

Phytonutrients that or derived from plants compounds include a large number of bioactive phytochemicals with a positive impact on health. Among these are flavonoids, polyphenols, carotenoids, glucosinolates and others which have gained much attention due to their multipotent health benefits. The phytonutrients are antioxidant, anti-inflammatory and anticancer which assist in disease prevention and overall wellbeing (Adetunji et al., 2023). They exist in plant produce in their natural states such as fruits and vegetables, whole grains, nuts and seeds. Biomarkers help to assess their bioavailability and effectiveness in epidemiological studies according to Zhang et al., (2023). It is all clear that to fully exploited their medicinal properties it is concluded to understand their biosynthesis and efforts to standardize them (Khan et al., 2023; Saadullah et al., 2023).

Health Benefits and Food Sources

Or derived from plants Phytonutrients that include a broad list of bioactive phytochemicals that are beneficial in maintaining human health. Some of them are as follows; flavonoids, polyphenols, carotenoids and glucosinolates among others. Phytonutrients encompass antioxidant, anti-inflammatory and anticancer properties that assist in resistance to diseases as well as enhance overall health and wellbeing (Adetunji et al., 2023). It can be consumed in products of plant origin, and specifically in vegetables and fruits, whole grains, nuts and seeds. Bioactive compounds' bioavailability and efficacy are possible to assess with biomarkers in epidemiological research studies according to Zheng et al. (2023). Such knowledge enables to improve usage of these compounds and their standardization to achieve optimal medicinal effect (Khan et al., 2023; Saadullah et al., 2023).

Antioxidants

Role in Health and Disease Prevention

Antioxidants combat free radicals and lower oxidative stress that leads to diseases like cancer, heart diseases, Alzheimer, Parkinson's disease and so on (Kıran et al., 2023; Halliwell, 2024). They possess cellular structure and DNA, which improve life span and general body health as revealed by Jena et al., (2023). The consumption of natural sources of antioxidants from fruits, seeds and whole foods offer a profound health benefits including anti inflammation, anti-cancer, and neuroprotection (Laurindo et al., 2023; Rahaman et al., 2023). Therefore, incorporating this type of foods in one's diet is very important in determining one's health and the ability to avoid diseases (Pujol et al., 2023).

Foods Rich in Antioxidants

Fruits, seeds and natural products containing antioxidants have manifold and immunomodulative effects and shield against chronic diseases and cancers including cardiovascular disease (Rahaman et al., 2023; Wu et al., 2023). Such fruits that are highly packed with antioxidants include blackcurrants that are medium calorie fruits and can be used to prepare functional meals to enhance athletic performance (Redha et al., 2024). S solid food waste from the Brazilian Amazon also contains bioactive compounds such terpenes and flavonoids that may benefits the body, particularly those suffering from cancers and dental diseases. It's important to understand that antioxidant containing foods are good for overall health of the body (Lima et al, 2023).

Trace Minerals

Importance of Trace Minerals

Microminerals include zinc, copper, iron and selenium and these are used in the enhancement of biological functions and cure of ailments including anxiety as listed by Totten et al. in its Global publication in the year 2023. They play immunological, antioxidant and anti-inflammatory roles in animals; they are critical to the animal's health, and any form of deficiency result in illness (Khan et al., 2024). Organic trace elements are very effective in increasing the antioxidant status and nutritional absorbability (Xiong et al., 2023). The supplementation of trace elements in the meals as well as in the organic forms leads to increase in production and reproduction of animals (El-Hamd et al., 2023).

Common Deficiencies and Health Effects

Lack of some necessary minor minerals including zinc, copper and iron have various effects on the body such as stunted growth, formation of bone abnormalities, anaemia and reduced body immunity. Besides, deficiency of these minerals may lead to some problems with teeth and may result in developmental anomalies (Islam et al., 2023). In contrast, the consumption of some trace elements might be toxic to one's health and therefore the importance of moderation cannot be overemphasized (Keen, 2023). Therefore, in an attempt to mitigate the effects of these trace minerals and any other health complications that may be linked to them, it is very important to check and regulate the levels of these nutrients (Jenkins et al., 2023).

Advanced Dietary Approaches

Contemporary methods of dieting encompass a number of innovative strategies aimed at enhancing the quality of life and at managing certain diseases. The steps for instance the Dietary Approaches to Stop Hypertension (DASH), which involves increasing the intake of nutrient dense foods in a bid to reduce hypertension. Some scholars, including Aljuraiban et al., (2023). Moreover, the publications in phytotherapy offer potential tactics for handling illness like diabetes mellitus with specific blends of herbs (Alburyhi and El-Shaibany, 2024). These approaches feature a paradigm shift towards the prescription of individualized nutrition plans and comprehensive healthy living programs which incorporate diets, lifestyles and therapeutic strategies for enhancing general well-being and disease prevention (Klonoff et al., 2024).

Intermittent Fasting

Health Benefits

Metabolic syndrome (MetS) has gradually become an important disease in international health care. Life style modification especially in diet should include guidance on energy balance and weight loss strategies to fit the management of the MetS risk factors. Fasting, in particular IF is a novel dietary approach that is widely recommended for weight loss and reduction of cardiovascular risk. A number of studies, nevertheless, have reported positive impact of IF on CV risk factors. To this end, this study aims to review the impact of different types of IF on BMI, glycemia, lipid profile and blood pressure, besides the treatment considerations (Naous et al., 2023).

Implementation Strategies

Optimizing IF practices can lead to the enhancement of its benefit in different health related situations. This is evident from other professionals with Hansen et al., (2023) research where Healthcare professionals embraced IF as a therapeutic option for chronic pain. According to Lange et al., (2024) they suggested that IF regimens should be personalized according to the demands which have physiological effects. The multiple applications of IF was also emphasized in relation with the different therapies. Cultural integration, like the practice of ramadan fasts is highlighted to assist in nutrition as proven by Sucholeiki et al., (2024). Some studies conducted in the field are presented by Valentina et al., (2023). These include hereby the concept of personalised techniques, continuous research as described by Pieper et al., (2024) and education regarding lifestyle modification, as explained by Naous et al., (2023).

Beyond Nutrients: The Role of Lifestyle Factors

Sleep and Circadian Rhythms

Sleep and circadian cycles have a significant impact on health, affecting several areas of physiology and disease susceptibility (Lane et al., 2023). Sleep patterns and circadian rhythms combine to influence episodic memory in older persons (Carlson and Wilckens, 2023). Lifestyle choices, especially sleep habits, can have a substantial impact on cardiovascular health by influencing circadian rhythms (Figueiro and Pedler, 2023). Sleep deprivation and circadian disruptions are strongly associated with metabolic problems, emphasising the complex relationship between sleep, metabolism, and health (Russell et al., 2023). Sleep disorders and the circadian rhythm disturbances play important roles in neurodegenerative diseases, with possible implications for disease treatment (Kunz et al., 2023). In addition, a circadian imbalance caused by lack of sleep leads to adiposity via hormonal dysregulation (Chaput et al., 2023).

Impact on Metabolism and Appetite Regulation

Sleep and circadian cycles are tightly linked to metabolism and hunger (Chaput et al., 2023). Sleep and circadian cycles both regulate ghrelin, an appetite-stimulating hormone (Chaput et al., 2023). Circadian misalignment can disturb hormone rhythms and affect metabolic processes (Meléndez-Fernández et al., 2023). The hypothalamus mediates the link between sleep, circadian rhythms, and food regulation (Oster and Colwell, 2024). The circadian clock controls daily eating cycles, which influence appetite and metabolic regulation (Chamorro et al., 2023).

Strategies for Improving Sleep Quality

Multiple techniques are effective for enhancing sleep quality. Physical activity is linked to better sleep duration and quality (Monteiro et al., 2023). Therapies based on mindfulness improve sleep quality and reduce insomnia symptoms

(Fazia et al., 2023). Sleep hygiene techniques, mindfulness, and reducing electronic device use before bedtime are also recommended (Cunha et al., 2023). Non-pharmacological treatments, like as cognitive behavioural therapy, can considerably improve sleep quality in older people (Sella et al., 2023). Increased physical activity, combined with better sleep quality and reduced sedentary behaviour, enhances well-being, especially among older women living alone (Jang and Yang, 2023). Psychoeducation focused on aspects of sleep hygiene and CA-AM results in enhanced subjective sleep quality (Almeida et al., 2023).

Integrating Advanced Nutrition into Daily Life

- Setting Realistic Goals
- Creating Balanced Meal Plans
- Monitoring Progress and Adjustments
- Seeking Professional Guidance when Necessary

Conclusion

Advanced nutrition is a remarkable overview of working of the nutritional plans of the human body and how various food choices affect the health of the human body most effectively. Error emphasis is not only on the primary functions of macronutrients such as carbohydrates, proteins and fats but also on their interrelated metabolic functions and physiological effects. Carbohydrates on the other hand are necessary for energy but what is important is the quality rather than the quantity because they do impact blood glucose levels and chronic diseases. Protein plays a very important role in the building and repair of muscles and, as such, the quality and the readiness of the proteins to be digested and assimilated into the body effectively is very important in determining the overall health and rate of recovery. Carbohydrates which supply energy for the body and serves as for cellular functions also need a proper intake; one has to think about the types of carbohydrates that are good and bad for heart health. Additionally antioxidants and trace elements, and phytonutrients all known as micronutrients contribute to the prevention of diseases and boosting of health. Phytonutrients are nutrients that interfere with the body's nutrient metabolisms and are obtained from plant-based foods; they have benefits that include acting as antioxidants, anti-inflammation, and anticancer. Besides the genetic factors, two other aspects of lifestyle, sleep and its regularity, or chronobiology, interfere with and affect metabolism and appetite. Introducing such scientific approaches into nutrition based on meal planning and fasting provides a boost to the health of a person.

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Chapter 43

Strategies for Enhancing Animal Feed Quality and Productivity

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ABSTRACT

A higher growth rate and feed efficiency result from feeding at the proper level. In order to produce more meat, milk, and eggs, it is imperative to increase the intensive production of farm animals. Proteins are needed for tissue growth and repair, fats are concentrated energy sources, carbohydrates provide energy, and vitamins and minerals are essential for many metabolic functions as well as structural integrity. There are two main types of traditional methods used to evaluate the quality of meat: subjective methods, which use human senses to evaluate the meat, and objective methods used scientific methods to evaluate the meat. Methods such as neurogenetics, blockchain, gene editing and selection, and alternative sources of protein are among these strategies to produce animal feed. Feed components can improve animal productivity by improving nutrition utilization, digestion, and metabolism. Feed components improve feed conversion ratios by maximizing nutrient absorption and lowering waste, allowing animals to produce more with less feed. According to current policies and guidelines, producers must submit comprehensive protection and efficacy statistics to the regulatory body for evaluation prior to approval for feed components. These tests are intended to verify that components adhere to environmental, buyer, and animal health protection regulations.

KEYWORDS		
Animal nutrition, Feed ingredients, Digestibility, Metabolomics, biological preservative, Food biosecurity	Received: 03-Jun-2024 Revised: 01-Jul-2024 Accepted: 07-Aug-2024	A Publication of Unique Scientific Publishers

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INTRODUCTION

Animal nutrition is critical to sustaining peak health and performance. The impact of diet on development, reproduction, and overall health is greater. Feed efficiency optimization reduced production costs and environmental impacts. Animal performance has increased through the use of several feed additive strategies. Feed consumption at its appropriate level leads to an increased growth rate and feed efficiency. Animal immunity has also improved as a result of feed supplements. In order to produce more meat, milk, and eggs, it is imperative to increase the intensive production of farm animals. However, in order to accomplish this, the animals' diet must not compete with that of humans and instead must be nutrient-rich and highly digestible (Ugwuanyi, 2016). A good substitute protein source should have many qualities, including being digestible, aesthetically pleasing, economically feasible, and meeting nutritional needs (Gatlin et al., 2007). Plant proteins make up a percentage of these ingredient sources, with soybean products being among the most commonly used in diet formulations for a variety of fish species (Glencross et al., 2020). A study on amino acids in rainbow trout (*Oncorhynchus mykiss*) found that, in addition to hormones and neuropeptides, the gastrointestinal sensory perception of nutrients also affects feed intake (Calo et al., 2023). Additives can boost feed intake, helping to compensate for the less appealing aspect of vegetable protein-rich diets (Bai et al., 2022; Hossain et al., 2024). Aquaculture diet development has focused on substituting environmentally benign and economically viable plant proteins for fish meals (Li et al., 2019). In particular, crustaceans like *Litopenaeus vannamei* can have altered behavioral responses in response to low temperatures, as well as changes in feeding, growth, survival, and reproduction (de et al., 2016). The ability of Japanese black cattle, sometimes known as Wagyu, to accumulate intramuscular adipose tissue sets them apart (Motoyama et al., 2016).

Feed Requirements of Animals

The correct growth, development, and maintenance of animals depend on essential nutrients such proteins, lipids, carbs, vitamins, and minerals. Energy is provided by carbohydrates, vitamins and minerals are needed for various metabolic processes and structural integrity, proteins are needed for tissue growth and repair, and fats act as concentrated energy sources. Animals have different dietary needs based on their species, age, sex, stage of development, and degree of activity. Furthermore, due to differences in physiology and metabolic rates, different species may require different kinds of food. All things considered, knowing these elements is critical to creating balanced meals that satisfy the dietary requirements of animals under various physiological and living circumstances. In order to investigate how biotic and abiotic factors affect organismal health and stress response in the environment, metabolomics is used (Nguyen et al., 2022). The flavor of food is influenced by a multitude of chemical components. Biomarkers from a wide range of metabolites have been found using metabolomics analysis. Therefore, in an effort to identify components related to quality, the relationship between metabolomics profiling and food quality has been investigated. Previous research demonstrated that the metabolomics profiles of foods such as fermented alcoholic beverages, soybeans, and tomatoes had a considerable influence on their taste (Sugimoto et al., 2010; Malmendal et al., 2011; Takahashi et al., 2016). Approximately 40 trillion microorganisms make up the human gut microbiota, which is the total genomic content of microorganisms. Numerous unique microorganisms, including bacteria, viruses, fungi, protistas, nematodes, and phages, comprise the complex ecosystem known as the human intestinal microbiota. These microorganisms are all crucial to the metabolism of their hosts. It has been discovered that the main mechanism through which the gut microbiota converts indigestible carbohydrates into short-chain fatty acids (SCFAs) has several implications on energy homeostasis and is crucial for intestinal health (De et al., 2016).

There are two main types of traditional methods used to evaluate the quality of meat: subjective methods, which use human senses to evaluate the meat, and objective methods, which use scientific experiments and instruments to evaluate the meat's physical, chemical, and microbiological qualities (Wu et al., 2022; Shi et al., 2021). The food industry, particularly the chicken industry, can greatly benefit from metabolic technology since it can be applied at every stage of the supply chain, from breed identification to the final product. This method provides important details about food safety, nutritional value, processing phases, and sensory attributes. To comprehend how raw materials become finished goods, as well as the chemical and sensory alterations brought about by different processing and operations in the food industry, metabolic analysis is essential (Utpott et al., 2022). The importance of metabolomics research in identifying the biomarkers required for food authenticity across different dietary matrices (Mialon et al., 2023). Customers still base their decisions on the eggs' valuable physical characteristics, even though they now prefer free-range chicken eggs because they think they have a higher nutritional value (Yogeswari et al., 2024).

Recommended Feed Additives

Following recommended dosages of feed additives in livestock diets is essential for ensuring maximum animal health and output. The National Research Council (NRC), the European Food Safety Authority (EFSA), and feed additive producers all support this approach. For typical feed additives, the following guidelines are often advised:

Sr. No	Feed Additives	product	Recommended dosage
1	Amino acids	Lysine	0.5-1%
		Methionine	0.3-0.6%
2	Enzymes	Phytase	500-1000 FTU/kg
		Carbohydrase	500-1000 ppm
		Protease	200-500 ppm
3	Organic acid	Citric Acid	5-10 g/kg
		Fumaric Acid	5-10 g/kg
4	Prebiotics	Mannan-oligosaccharides (MOS)	1-2 g/kg
		Fructo-oligosaccharides (FOS)	2-4 g/kg
5	Probiotics	Lactobacillus spp.	1x10^9 to 1x10^11 CFU/kg
		Bifidobacterium spp.	1x10^8 to 1x10^10 CFU/kg

Types of Feed Additives

Antibiotics and Antimicrobial Products

Antibiotics and antimicrobials are used to keep growth normal and treat illnesses. A turning point in the development of modern medicine was reached when antibiotics were first used as a means of treating and managing infectious diseases. Unfortunately, overuse of these drugs has led to the widespread emergence of antibiotic resistance (ABR) in a range of species, including bacteria that cause spoiling and illnesses (Founou et al., 2016; Nelson et al., 2019; Hughes et al., 2021). The growth of bacteria that cause diseases in humans and animals can be inhibited by the use of natural, synthetic, or manufactured antibiotics. When medications that once effectively treated a particular bacterial infection are no longer able to stop the infection-causing bacteria from growing and developing, antibiotic resistance naturally develops (Founou et al., 2016; Nelson et al., 2019; Cahill et al., 2017). The prevalence of resistant bacterial illnesses has increased as a result of the growing number of antibiotic-resistant bacteria decreasing the therapeutic efficacy of various antibiotic therapies. The economic and social facets of public health systems are negatively impacted by this issue (Wu et al., 2023).

Astaxanthin (AXT)

AXT is approved as a food color by the Food and Drug Administration (FDA). Natural AXT is preferred in the food, pharmaceutical, and cosmetic industries over manufactured AXT due to the unknown effects on human health. The primary source of AXT for ingestion by humans and animals is thought to be the green alga *Haematococcus pluvialis* (Pashkow et al., 2008; Kidd, (2011); Guerin et al., 2003). AXT can be synthesized from a variety of sources, including microbial, plant, and animal. One of the most significant microbiological sources of naturally occurring AXT is the green microalga *Haematococcus pluvialis*, which can accumulate up to 38% on a dry weight basis (Martínez et al., 2020; Rao et al., 2013). AXT has minimal clinical applications because of its poor drug stability, even with its strong pharmacological potential (Liu et al., 2019).

Probiotics and Prebiotics

Probiotics are live microorganisms that enhance the microbial balance in the animal's stomach and have a positive effect on the host**.** Prebiotics are indigestible chemicals that boost the immune system and overall health of the digestive system by encouraging the growth or activity of good bacteria in the gut (Zhou, Chen, Patil, and Dong, 2024). The use of probiotics as functional feed additions has enhanced the absorption of critical nutrients such vitamins, vital amino acids, and fatty acids (Simón et al., 2021). Lactic acid bacteria (LAB) and bifidobacteria, two forms of commercial probiotics used in aquaculture, can be found in fermented or dairy foods (Fenster et al., 2019). Due to conflicting data and a lack of knowledge about long-term effects, the effects of probiotics and prebiotics on human metabolism, in particular obesity, are currently being vigorously debated in the scientific literature (Butel et al., 2016; Parekh et al., 2017).

Enzymes

All living things depend on chemical reactions to proceed normally within their cells, and proteins known as enzymes, or biological catalysts, are able to accelerate these reactions (Velázquez et al., 2021). Enzyme supplements increase feed efficiency and nutritional availability by dissolving complex nutrients into simpler forms, which improves digestion. They are especially helpful in diets with a lot of plant-based foods. When applied to agro-industrial and agroforestry wastes utilized as animal feed, exogenous enzymes have been found to improve nutrient bioavailability and digestibility while also helping to remove some anti-nutritional elements. Exogenous enzyme therapy is a trend that has positive effects on animal yield and productivity because, although animals have endogenous enzymes involved in digestion, they are unable to digest them and absorb all of their nutritious components (Ojha et al., 2019). The most often used enzymes to enhance animal feed are those that have carbohydrase, protease, phytase, and lipase activities. The biocatalyst needs to be able to withstand changes in the gastrointestinal tract and extrusion and granulation caused by feed processing in order to be used (Debyser et al., 1999, Velázquez-De Lucio et al., 2021). ANF (anti-nutritional factor) can worsen nutritional absorption, increase the viscosity of digesta, and even raise the risk of pathogenic diseases like necrotic enteritis, which can harm chicken health and raise production costs (Raza et al., 2019).

Antioxidants

Antioxidant supplements improve general health and lower the risk of oxidative stress-related diseases because they counteract free radicals and protect animal tissues from oxidative damage. Numerous clinical conditions that affect the productivity, welfare, and health of animals are also linked to oxidative stress (Buchet et al., 2017). Animals must adapt to physiological changes during certain productive times, such as lactation and farrowing, as well as environmental changes, like weaning or high temperatures. Stress of all kinds also lowers an animal's antioxidant status (Guo et al., 2021). The impact of plant additions on poultry nutrition has been evaluated through a survey of the literature published during the previous 20 years (Righi et al., 2021; Pitino et al., 2021). Stress is a major issue in the poultry industry, so researchers have also looked at how heat stress affects broiler antioxidant status and inflammatory responses (Saracila et al., 2021). Since amino acids are involved in cellular oxidative equilibrium, early nursing sheep were used to test the effects of dietary rumen-protected methionine and lysine, either separately or in combination. The findings demonstrated that lysine decreased the oxidative stability of milk while methionine increased the antioxidant state (Mavrommatis et al., 2021).

Buffer and Acidifier

Acidifiers operate by lowering the pH of the digestive tract, reducing the chance of harmful microbes surviving and enhancing nutrient absorption. Buffers serve to keep the pH of the digestive system at a healthy level, lowering the risk of digestive illnesses. Tricarboxylic acids (TCA), medium chain fatty acids (MCFA), and short chain fatty acids (SCFA) are the three functional groups into which organic acids are divided (Grilli, and Piva, 2012). TCA are Krebs cycle metabolic intermediates, which means they are involved in energy metabolism. These acids influence the microbiota positively and enhance the structure and function of the gut barrier (Li et al., 2019). The lower intestines of animals produce SCFAs, or carboxylic acids with up to five carbon atoms, through microbial fermentation of indigestible carbohydrates and amino acids (Mroz, 2005). The aliphatic chains that comprise MCFA have six to twelve carbon atoms each. These acids are readily absorbed into the phospholipid membrane, and they play a vital role in the diet of neonatal pigs by providing a vital source of energy (Zentek et al., 2011).

Flavor Enhancer

These modifications make the feed more appealing, encouraging animals to accept and consume it. This is especially useful in encouraging the consumption of bland or medicated foods. A complex mixture of proteins, peptides, amino acids, nucleic acids, B vitamins, minerals, carbohydrates, and other substances is yeast extract (Tomé, 2021). The food industry has paid close attention to yeast extracts because of their potential as natural flavor enhancers and masking agents in foods with low sodium or reduced salt content (Tao et al., 2023). This study shows that yeast extracts can mitigate sensory losses associated with lower salinity levels in marinated shrimp while maintaining bacterium safety. The global issue of excessive salt consumption is addressed by these findings, which help to create seafood products that are more appetizing and nutritious (Şen, 2023).

Food Production Technologies

1. Precise Livestock Agriculture

Precision Livestock Farming (PLF) combines the concepts of precision agriculture with the use of PA in livestock systems to assist farmers in managing large-scale livestock farming through the use of sensors and actuators (Vaintrub et al., 2021). The demands of today's large-scale livestock production may not be met by traditional management techniques, which only take into account the observations, judgment, and experience of farmers. As a result, thanks to information technology, precision farming has emerged as a necessary trend in modern cattle farming (Jiang et al., 2023). A new era of integrated fusion innovation is rapidly emerging in China's animal husbandry sector, driven by the urgent need to combine information technology, data science, artificial intelligence, and innovative animal husbandry development (Li et al., 2023). Three areas of focus for PLF research are intelligent systems, animal behavior, and precision dairy and cattle technologies. Popular terms are categorized using PLF technology (Jiang et al., 2023).

2. **Gene Selection and Editing**

The agricultural industry of today is changing quickly, bringing with it new difficulties like environmental impact reduction and the safety of breeding practices. Breeding and biotechnology also saw rapid advancements in applied genetic engineering. Agricultural animals such as cattle, sheep, goats, pigs, rabbits, chickens, and fish have been genetically modified (GM) in spite of these obstacles (Singh and Ali, 2021). The primary goals of farm animal gene engineering research have been to improve the efficiency of food production while also improving the health and welfare of animals. The effects of livestock products on the environment and human health are also reduced, whenever possible (Van, 2019). The engineered nucleases known as zinc finger nucleases (ZFNs) combine a DNA cleavage domain with a zinc finger protein domain for DNA binding, resulting in the formation of an artificial restriction enzyme (Carroll, 2017).

3. Alternative Sources of Protein

The use of products derived from insects in poultry and other monogastric animals' diets has drawn a lot of attention from researchers in recent years (Schiavone et al., 2018; Sogari et al., 2019). Studies have indicated that the nutritional value of insects is adequate to support the growth, health, and nutrient digestibility of poultry (Gariglio et al., 2019). A high biological value, a highly variable ether extract (EE) content (15–49% DM), and a high crude protein (CP) content (ranging between 35 and 57% on a dry matter basis, DM) are among the characteristics of black soldier fly (BSF, *Hermetia illucens*) larvae that have demonstrated a nutritional composition that is suitable for poultry diets among species of insects. Although the fatty acid composition of the rearing substrate determines the fatty acid content of BSF larvae, the larvae seem to have high levels of lauric acid (20–40% of total lipids), palmitic acid (11–16% of total lipids), and oleic acid (12–32% of total lipids) (Barragan et al., 2017).

4. Blockchain in Conjunction with Traceability

The growing global population and the need for adequate, secure, and high-quality agri-food products are putting pressure on the agriculture sector today. Simultaneously, the modern food supply chain has become more globally interconnected (Bhagwani and Govindaraj., 2020). A wide range of players with various demands, roles, and responsibilities are involved in agri-food supply chains, or AFSCs. The AFSC management and traceability tasks become extremely complex and challenging due to this system (McEntire and Kennedy, 2019; Keogh et al., 2020). Customers need a quick and reliable method to obtain the information they need about food products because of these concerns about food quality and safety (Bosona and Gebresenbet., 2023). Information is essential for cutting expenses, raising employee productivity, improving yield and quality (while cutting waste), and improving customer service. It contributes to increasing the supply chain's (and its stakeholders') market competitiveness (Rahman et al., 2021; Madumidha et al., 2019).

5. **Nuerogenetics**

Animal feed manufacturers have been using LPL, which is produced from the phospholipase hydrolysis of soy lecithin, as a feed additive for more than 20 years. Its ability to improve animal growth performance while reducing feed expenses is well known (Haetinger et al., 2021). As in mammals, the somatotropic axis, which includes growth hormone (GH), growth hormone-releasing hormone (GHRH), insulin-like growth factors (IGF1 and IGF2), growth suppressors (SS), their corresponding carrier proteins and receptors, and other hormones, is primarily responsible for controlling growth and development in chickens. Muscle and bone cells can proliferate and differentiate when exposed to growth hormone. Many of GH's growth-promoting effects in chickens are mediated by the peptide hormone IGF1 (Anh et al., 2015; Renaville et al., 2002; Kühn et al., 2002). An additional investigation revealed that the intestinal epithelium's gene expression is triggered by LPL supplementation, resulting in increased collagen deposition and villus length. Conversely, these responses are not mimicked by pure LPC alone as a supplement (Brautigan et al., 2017). Mammalian target rapamycin, or mTOR, is a protein synthesis regulator, energy, nutrient, and redox sensor that is highly activated by insulin signaling. It also governs cellular metabolism, growth, and proliferation (Yoon, 2017; Menon et al., 2017).

Risk and Benefits Associated with Feed Additives

Feed components can improve animal productivity by improving nutrition utilization, digestion, and metabolism. This results in a faster weight advantage and improved manufacturing performance, which leads to increased profitability for companies. Feed components improve feed conversion ratios by maximizing nutrient absorption and lowering waste, allowing animals to produce more with less feed. This not only saves production costs, but also minimizes environmental stress associated with feed processing and waste disposal. Certain feed components, such as antibiotics, probiotics, and antioxidants, can help save and manage illnesses in animals by assisting immune function and preserving intestinal health. This results in a decrease in the prevalence of diseases and a decrease in the need for clinical interventions. Feed components that improve feed efficacy and reduce waste production contribute to a more sustainable farm animal manufacturing system. They reduce feed ingredient demand, greenhouse gas emissions from feed manufacture, and nutrient excretion into the environment, as well as nitrogen and phosphorus runoff. Overuse of certain feed components, particularly antibiotics, can lead to increased antimicrobial resistance in bacteria, posing a threat to both animal and human health. Furthermore, a few components can contribute to environmental pollution by releasing metabolites or residues into soil and water systems. It is vital to exercise caution while using feed components in order to reduce risks while also optimizing their benefits in animal manufacturing.

Animal health and its connection to biosecurity are receiving more attention as a result of the prevalence and difficulty of controlling major animal diseases. Food safety, environmental protection, and sustainable agriculture are all intrinsically linked to biosecurity, according to the Food and Agriculture Organization (FAO) (Alarcón et al., 2021; FAO, 2003). Research that has already been conducted on farmers' actions to prevent epidemics has mostly concentrated on specific traits. The first step in preventing and controlling animal epidemics is the proactive actions of farmers. Improved feeding conditions, the use of vaccinations and veterinary care, reporting animal epidemics, and the treatment of sick and dead animals are the four main epidemic prevention behaviors that farmers frequently engage in (Li et al., 2016). More assistance and direction for large-scale farming is necessary to advance large-scale agricultural models. Animal husbandry and veterinary departments should release epidemic information in a timely manner. By using new media technology to build a smart platform for animal epidemic prevention and control, timely epidemic information can be released, making it possible for farmers to learn about epidemic information through their mobile phones (Wang and Hu., 2023).

Methods for Preservation of Food

Feed preservation is the practice of using methods to maintain the nutritional value, safety, and quality of animal feed over time. Feed can be preserved in a variety of ways, such as by heating it, adding chemical preservatives, reducing moisture content to inhibit microbial growth, storing it in a hermetic environment to reduce oxygen exposure, fermenting the feed to produce organic acids that inhibit spoilage, and monitoring for pests to avoid contamination. The health, performance, and overall productivity efficiency of animals are enhanced when high-quality feed is provided, and this is made possible by these strategies. One of the biggest environmental issues facing the world today is the production and disposal of food waste (FW). Population growth and rising living standards are positively correlated with increased FW production ((Zheng et al., 2020; Sheppard and Rahimifard, 2019). FW is a major global contributor to issues with social justice, health, the environment, and the economy (Teigiserova et al., 2020). To further prevent environmental damage, any technology used for reuse or recycling must also adhere to the principles of sustainability and the circular economy (Noori et al., 2022). Since it causes food and agricultural products to spoil, water content is the most crucial factor (Karam et al., 2016). Drying of single-source wastes, such as olive pomace and mango waste, has been the main focus of research in the field of FW drying (Wilkins et al., 2018).

Regulatory Framework

Producers are required to submit complete protection and efficacy statistics to the regulatory government for assessment before approval in current policies and guidelines for feed components. The purpose of these exams is to ensure that components meet protection requirements for animal health, purchaser protection, and environmental protection (Sorbo et al., 2022). Approval methods vary based on location, but they usually involve thorough clinical statistics, such as toxicological studies, residue analyses, and discipline trials. Once approved, feed components can be difficult to track and evaluate to ensure continued protection and efficacy in animal production.

Techniques of Application

Feed additives can be added to feed formulas in a variety of methods, including premixes, top dressing, liquid application, and inclusion in full feeds. Each approach provides significant advantages in terms of mixing homogeneity, additive stability within the feed, and ease of administration (Asrar et al., 2023).

Feed additive dosage must be correct to ensure effectiveness and prevent undesirable consequences. In addition to the additive employed, dose considerations take into account the animal's species, age, weight, and overall health. To get the desired results, manufacturers' dosage recommendations, which are based on product labeling and scientific research, must be rigorously followed (Karam et al., 2016). The effectiveness of feed additives must be monitored and evaluated on a regular basis to identify how they affect animal performance and health. This could require measuring characteristics such as growth rates, feed conversion ratios, disease prevalence, and overall production. Producers can optimize performance and ensure cost-effectiveness by regularly monitoring these variables and making appropriate changes to feed compositions and management approaches.

Conclusion

For animals to continue performing at their best, they must eat well. Diet has a bigger influence on growth, reproduction, and general health. Animal performance has increased through the use of several feed additive strategies. These strategies are precise livestock agriculture, gene selection and editing, alternative source of protein, blockchain and neurogenetics. Food contains different type of ingredients that have short duration and feed become spoilage. To obtain the good result, we use different preservatives techniques for long term use of food products. These preservative methods are Drying, chemical preservatives, fermentation and microbial inoculants. Stakeholder and producer should follow the guidelines properly to confirm that parts fulfill the standards for animal health protection. Advances in enzyme technology are improving feed efficiency and nutrient use, which bodes well for the future of feed additives. Probiotics, prebiotics, and synbiotics are being examined more and more as potential antibiotic substitutes for enhancing gut health and immunological regulation. Furthermore, in order to lower methane emissions and lessen their negative effects on the environment, sustainability-driven additives are being developed.

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Chapter 45

Preventive Feed Additives in Poultry Diet

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ABSTRACT

Feed additives are any sort of organic, inorganic, or synthetic compounds or substances added to poultry feed to enhance its nutrition and efficiency. Feed additives play a pivotal role in the poultry industry and are very crucial for the health of birds. Moreover, these additives are also pre-eminent in preventing many diseases and controlling morbidity, as well as mortality. Feed additives impart various benefits to birds' good gut health, carcass gain, increased production, and ultimately favor a better economy. Feed additives can be classified according to their manufacturing process, their impact on the health and performance of birds, and their nutritional value. Different manufacturing agents include antifungals, antioxidants, pellet binders, and flavors, which are also important for increasing the shelf life of feed and its palatability. Moreover, different enzymes, acidifiers, vitamins, amino acids, antibiotics, minerals, etc. can also be added to feed for nutrition and preventive purposes. Different approaches are used worldwide regarding the addition of feed additives in poultry feed to improve the efficiency of the poultry industry, while many are under research.

KEYWORDS
Poultry nutrition, Poultry feed, feed additives, Nutrition, preventive Additives, Health, Prevention, Prebiotics, Feed efficiency, Growth promotors, Oxidative stress reducers

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INTRODUCTION

Feed additives are substances that can be added to the food of an animal, bird, or any human to enhance its nutrition and effectiveness. These can be nutrient or non-nutrient compounds. We can refer to these feed additives as supplements that act as a substrate for these feed items and their nutrients that can affect the gut health of birds. These feed additives can have potential benefits to birds' health. It works by decreasing the feed intake and enhancing the utilization of its nutrients in the body and proper weight gain, thus improving the FCR of the bird. This will ultimately lead to good health of the bird, its improved carcass quality, and dressing percentage. It aids in enhancing the growth rate and production, enhancing health and immunity, and preventing disease, thereby elevating the profit margin (Pandey et al., 2019). As we are aware, there are many challenges in food production today, such as safety, climatic and environmental problems, quality standards, and the effect on gastrointestinal health, and along with it, it costs about 60 to 75% of total production, and there is no margin for any upheaval, that's why we use feed additives that play an important role while combating these challenges. Moreover, feed additives can be used to maneuver feed to increase the FCR so our birds can gain proper weight with less feed intake (Gangadoo et al., 2016).

Following is the role of feed additives used in feed production. It improves digestion, strengthens the function of the immune system and its response, improves the absorption of minerals, gives texture to the feed (Pandey et al., 2019), combats infections and diseases (Pirgozliev et al., 2019), preserves the nutritional value and improves palatability (Pirgozliev et al., 2019). Moreover, it also provides antimicrobial effects and buffer effects, promotes growth, and maintains the wholesomeness of feed.

Need of Feed Additives in Poultry Feed

In recent years, the global poultry industry has looked at remarkable and subsequent growth. The production of poultry has increased by 2 times in the past 30 years. This transition is controlled by expanding the requirement for protein sources. The urging rise, set in motion by an increase in population, incomes, and shift of dietary bias, has fastened poultry as a foundation of the world's food supply. Prime producers all over the world have jumped onto advanced technologies and efficient production systems to meet this demand. The innovations are also helpful in combating the rising threats of different disease outbreaks like new castle disease, avian influenza (Qureshi et al., 2022). Poultry products like feed additives, supplements, antibiotics, etc. are also innovated to ensure the takeover of all the above-described challenges.

Factors Affecting the Feed Intake of Poultry

The following are the important factors affecting the feed intake of birds (Chadd, 2007). It depends upon the birds' requirements. These requirements are influenced by the age, sex, and genotype of the birds. Maintenance of eggs and meat production is influenced by nutrient adequacy of diet, or diet composition. Environmental factors also affect the feed intake (Ferket and Gernat, 2006). Physical and physiological feedback mechanisms (hormonal mechanism, environment, and feed composition), and metabolism (circulating metabolites and liver metabolism) are the other factors affecting the feed intake of our birds (Barzegar et al., 2020). Feed additives in the feed can help in enhancing the efficiency of feed, production maintenance, nutrition improvements, and controlling the metabolism of birds. Different types of feed additives are present in the market, made by different manufacturing companies, to combat all the above challenges.

Classification of Feed Additives

Feed additives can be categorized into 4 major classes. These are classified as feed manufacturing agents, performance-enhancing additives, nutritional additives, and health-improving agents (Okey, 2023).

Feed Manufacturing Feed Additives

Antifungal Feed Additives

Unluckily, ingredients like corn, soybean, etc. are apt to get contaminated by the fungi and their secondary metabolites i.e., mycotoxins, particularly during their storage. Moisture also contributes to the production and proliferation of various fungi. Fungal impurities in feed can also lead to different diseases, bad health impacts as well as economic losses. There are different antifungal feed additives present in the market, and many others are under study. These can be natural or can be prepared synthetically in the laboratory. Here are some different antifungals added as feed additives in our birds 'diet.

Fermented whey in the presence of kefir grains @ 1 liter/kg can be used as an antifungal preservative against *Aspergillus spp., Rhizopus, and Penicillium* (Londero et al., 2014). Metal nanoparticles like ZnO, and Fe_2O_3 are effective antifungal agents (Nabawy et al., 2014). Poultry feed is prone to fumonisins, a mycotoxin produced by fungi of class *Fusarium* spp. *Lactobacillus plantarum MYS6* can be used as a potential antifungal agent against fumonisin-producing *F. proliferatum* MYS9 and can act as an auspicious replacement for chemical preservation of poultry feed (Deepthi et al., 2016). Addition of *Saccharomyces cerevisiae* yeast cell wall in poultry diet can act as an absorbent of mycotoxins (Aflatoxin B1) and cannot have any detrimental effect on birds' health (dos Santos et al., 2021). Cinnamaldehyde and carvacrol both have antifungal and antibacterial properties. Carvacrol and trans cinnamaldehyde can be used in poultry feed as an additive to inhibit the growth of fungi like *Aspergillus flavus*, and *Aspergillus parasiticus* (Yin et al., 2015). Mycotoxin detoxifiers as a feed additive in feed of birds can improve the FCR, and bring antibodies level against different viruses like *New Castle* to normal that can be decreased by aflatoxins in the feed (Afzal and Zahid, 2004). Barberine can also be used as a preservative in food. It helps prevent the growth of different fungi, and molds. Barberine concentration of at least 0.03g/kg in poultry feed can be effective in controlling the growth of different fungi (Geerlofs et al., 2019). *Glycyrrhiza glabra*, a traditional medicinal herb, can also be used as an antifungal, as well as antimicrobial (Gowthaman et al., 2021). Complex of propionic acid, formic acid, and ammonia can be recommended for the treatment of fungal diseases in poultry chicks (dos Santos et al., 2009).

Antioxidant Feed Additives

As we know, stored poultry feed is prone to oxidation. Vitamins, fats, lipids, and proteins present in the feed are degenerated by this oxidation. The degeneration of important compounds in the feed leads to reduced intake of feed, decreased performance, and ultimately reduced production. There are different natural, and artificially synthesized substances present already, and some are being studied to prevent this oxidation of feed materials. Some important antioxidants are discussed below, that can prevent spoilage of the feed ingredients of poultry. Antioxidants are either water-soluble like vitamin C, uric acid, and glutathione, or these can be fat-soluble like vitamin E, and coenzyme Q. Other antioxidants include zinc, vitamin A, selenium, saponins, flavonoids, and tannins.

Different extracts of essential oils like thymol, carvacrol, eugenol, cinnamaldehyde, grapes extracts, and rosemary can be used as antioxidants and can reduce oxidative stress on birds' bodies (Righi et al., 2021). But these can affect the organic functions of the body, depending on the metabolism of the bird. Stored feed for above 30 days (about 4 and a half weeks) is viable for lipid peroxidation. Thymol can prevent this lipid peroxidation of feed, and its rancidity (Luna et al., 2017). Different birds fed with natural photogenic vegetables, and herbs in their feed, showed increased antioxidant quantity in their carcasses, hence protecting it against unfavorable oxidation (Zdanowska-Sasiadek et al., 2019). Vitamin E, a powerful free radicals scavenger, has a favorable impact on the carcass quality of poultry meat.

Pellet Binders

Pellet binders are the binding vehicles that give strength to pellets and provide integrity and stability. These are used to enhance the durability of feed pellets so that they can be available to birds in their best form. These are thought to be reliable agents to prevent any kind of feed impairment during storage or transportation. Pellet binders are added to the feed to enhance the physical quality of poultry feed, the growth of poultry birds, to improve the carcass quality, and dressing percentage of birds, as well as profits and economy. Both kinds of pellet binders, organic and inorganic, are used. Organic pellet binders include lactase monohydrate, sodium lignosulfate, hemicellulose, carboxymethyl cellulose etc. Other inorganic binders include hydrated aluminum silicate (bentonite), and clay. Wheat gluten @ 10g/kg, or a wheat average of 150g (about 5.29 oz)/kg can increase weight in the broiler chicken as well as improve the quality of pellets (Moradi et al., 2018).

Feed Flavors

Feed flavors added in poultry feed to reform its intake is a hot topic in research nowadays. Feed reforming or modification stated by (Balog and Miller, 1989) includes reduced feed intake in the rearing of broiler breeders (reduced fat deposition that is not favorable), and molting stage (forced molting) of layers. It also includes increasing the feed intake in commercial broilers. Feed flavors work by increasing appetite through enhanced nice aroma and color, and in this way feed with low palatability can be fed to birds easily to raise weight (Okey, 2023). The use of different flavors like anise oil, garlic oil, vanilla oil, oregano extracts, molasses, yucca, salts, and different essential oils are under study, but no significant result can be proven in reforming until now.

Performance-enhancing Feed Additives

Enzymes

Enzymes are characterized as non nutritional dietary elements that are added to poultry feed to enhance the accessibility of substrate thus improving proteins, energy intake, and nutrient digestion (Koryagina et al., 2019). These include non-starch polysaccharides (NSP), lectins, phytates, and protease inhibitors (Fig. 1). Phytase has a positive impact on energy utilization in birds, showing increased growth and performance (Selle et al., 2007). Phytases work by breaking phytic acid present in poultry feed and releasing bound inorganic phosphorus for better utilization, absorption, and digestion. NSP plays an important role in improving the GIT health of birds and their performance, but still, its use in feed formulation is scarce (Nguyen et al., 2021). NSPs are referred to as hydrolyzing enzymes that work by enhancing nutrient digestibility, small intestine modification, and decreasing digesta viscosity (Simon, 2000). The use of lectin is controversial due to its anti-nutritional impacts. Protease supplementation in diet can result in enhanced performance of birds, it works by breaking down both stored proteins and anti-nutrient proteins (Erdaw et al., 2016).

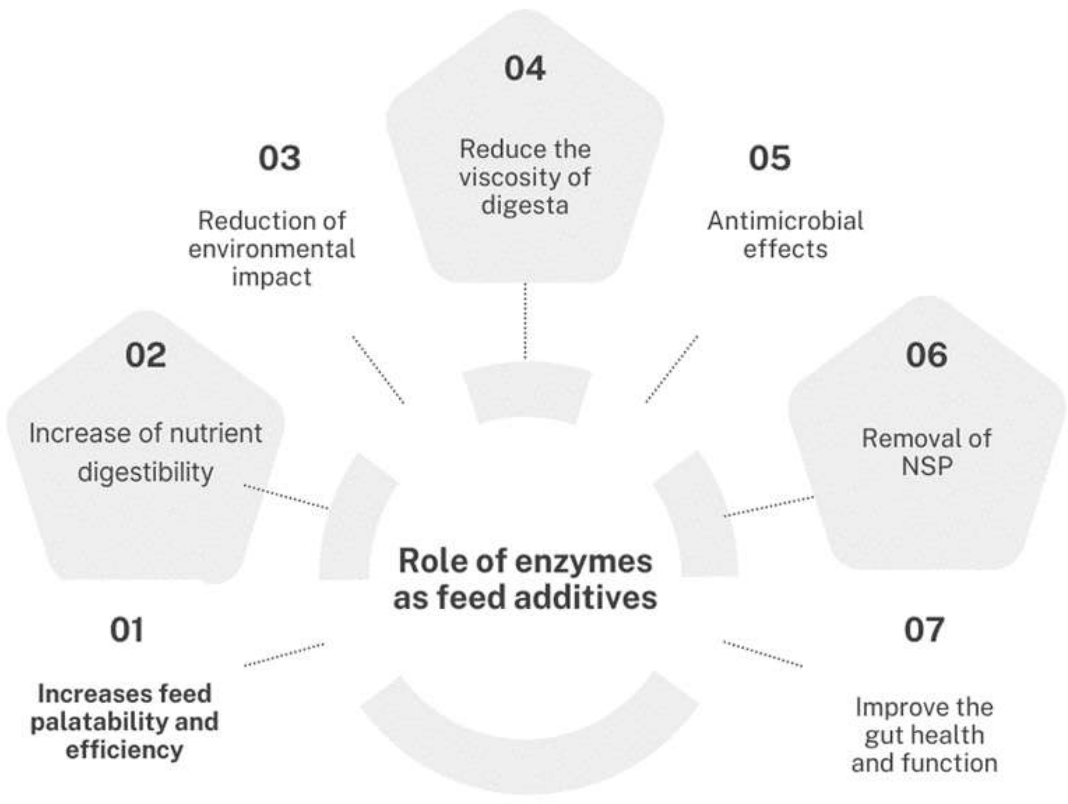


Fig. 1: Role of enzymes as feed additives

Prebiotics and Probiotics

Different prebiotics and probiotics are added to poultry feed with beneficial effects on the performance and production of birds. Prebiotics include lactose acid bacteria (LAB), lactulose, insulin, oligosaccharides of fructose and galactose, xylose, and soya etc. Lactose inhibits the multiplication of *salmonella* and other pathogenic bacteria in the GIT of chicken by altering pH, but excess of lactose can cause watery droppings (diarrhea) (Alloui et al., 2013). Moreover, probiotics commonly used in poultry feed are *Bacillus subtilis, Lactobacillus, Lactococcus lactis*, etc. These microbiota work by altering pH in GIT, making survival of most pathogens impossible (Fig. 2). *Yeast* can also be used as a probiotic. Enhanced growth, performance, and production can be availed by providing a mix of *lactobacillus* and *yeast* (Choudhari et al., 2008).

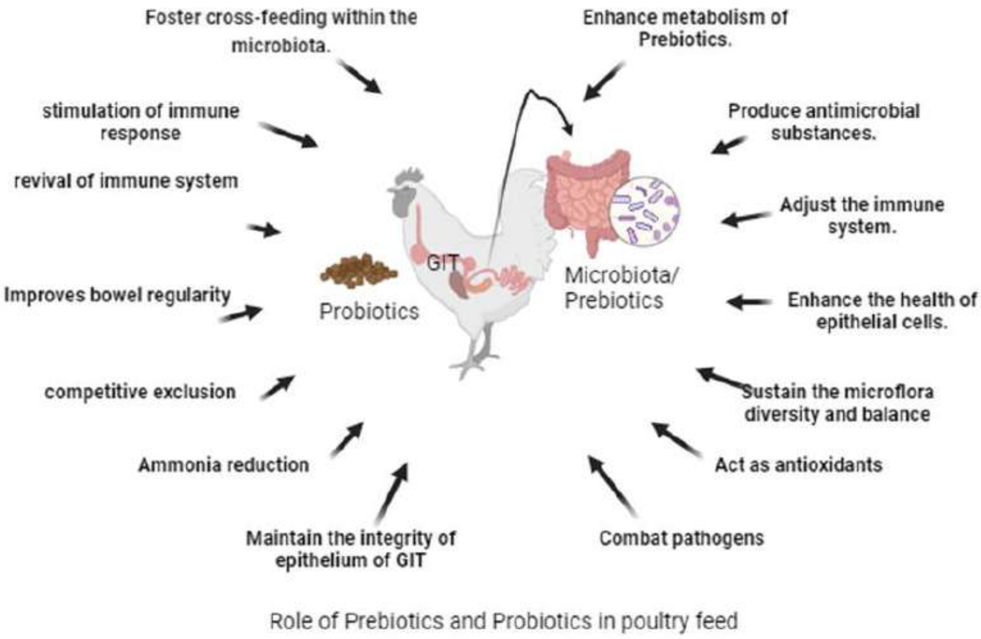


Fig. 2: Role of prebiotics and probiotics in poultry feed

Xanthophylls

These are added to the feed to improve the color of the products obtained from poultry to meet the consumer's demands, e.g., xanthophylls are added to feed to get golden yellow egg yolks (Fig. 3) (Breithaupt, 2008).

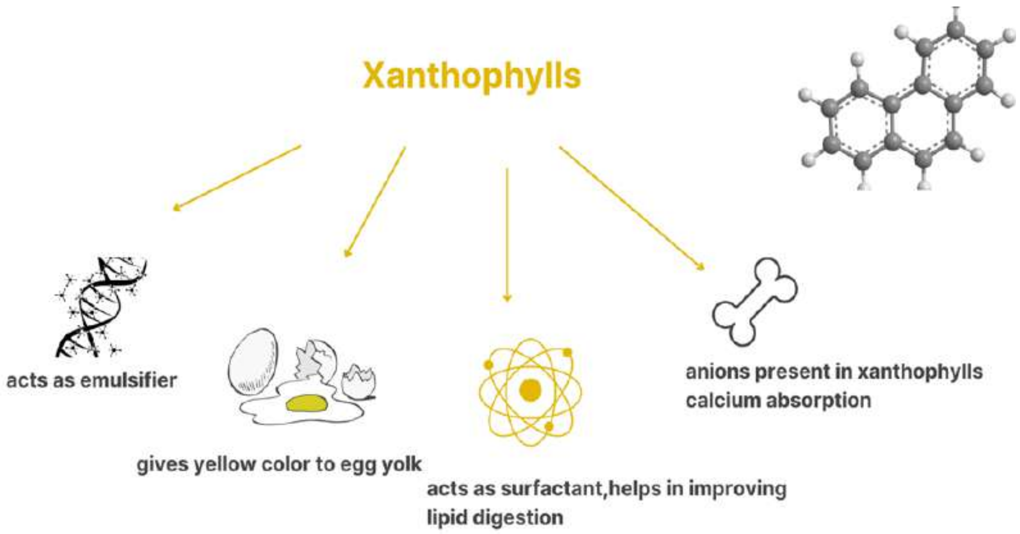
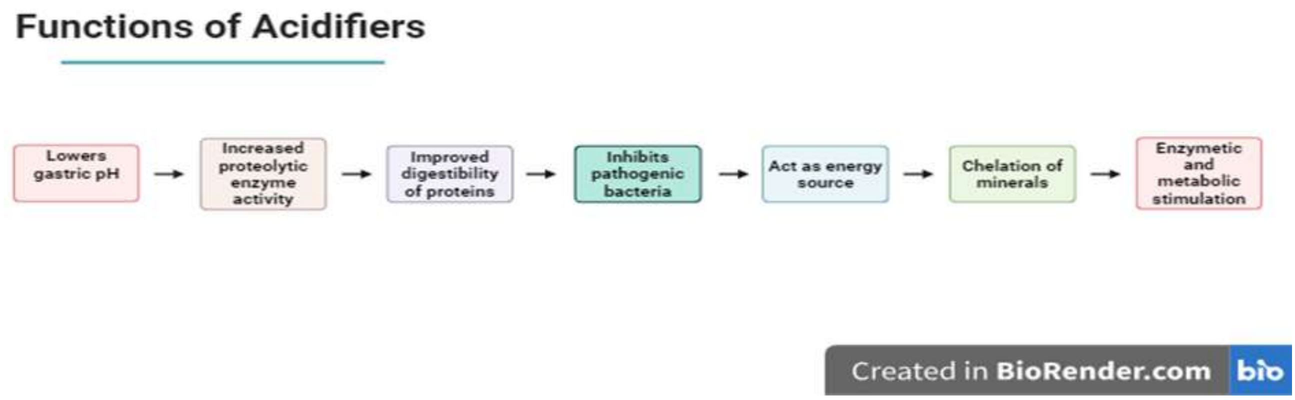


Fig. 3: Role of Xanthophylls in poultry

Antibiotics

In the poultry industry, antibiotics are used for the prevention and treatment of different bacterial diseases that can result in high mortality rates and ultimately lead to loss and poor economics. Antibiotics were used as feed additives in the past but nowadays, their use as a feed additive in poultry feed is banned due to the present scenario of antibacterial resistance or antimicrobial resistance. Various strategies like immuno-stimulation, intestinal integrity protection, and control of harmful bacteria via biosecurity, vaccination, and prevention measures are used to lessen the use of antibiotics. Different alternatives to antibiotics like prebiotics/probiotics, enzymes, photogenic, organic acids, peptides, antibodies, and metals are in use and more are under study and research.

Acidifiers



Acidifiers are mainly used as an alternative to antibiotics. Balanced acidifiers blend (0.1%) of a trio of lactic acid, formic acid, and propionic acid can be used to increase the efficiency of broilers (Hedayati et al., 2013).

ACIDS	EFFECTS
Fumaric acid	Growth, enhancce immunity, aids in digestion, improves health of the intestines of birds, and an antioxidant (Reda et al., 2021).
Propionic acid (Buffered)	Antimicrobial,elevates the GIT health of birds, enhances dressing percentage in female birds, reduces abdominal fat in males to improve performance(Lakshami et al., 2016).
Malic acid	Antimicrobial, improves carcass quality, acidifiers,antioxidant, reduces production of lactate (Qiu et al., 2022).
Sorbic acid	Antimicrobial, improves the efficiency of birds, molds and fugus inhibitors, meat preservatives (Stopforth et al., 2005).
Lactic acid	Improves FCR, enhances the performance of birds, antimicrobial (Polycarpo et al., 2017).
Formic acid	Antibacterial against coliforms and salmonella, enhances the production, improves FCR (El-Faham et al., 2018).
Benzoic acid	Antimicrobial, antifugal, improves the function of gut, regulates enzymatic activity (Mao et al., 2019).
Butyric acid	Maintains the performance, intestinal health, and carcass quality of chicken (Panda et al., 2009).
Tartaric acid	Chelating agent that improves FCR, preservative pH control agent (Al-Tmimy, 2022)..

Phytogenic Compounds

The addition of phytogenic feed additives helps in improving the microbiota of birds' gut, increasing digestibility, and performance, ultimately leading to increased yield and profits. These additives also improve the oxidation status, and immune status of birds. These are mostly used as substitutes for antibiotics (Fig. 4). These additives work by improving nutrient digestion and absorption in small intestines (Amad et al., 2011). These additives involve different herbs like oregano, thyme, carvacrol, and different essential oils. Some of these are also described below (see essential oils as feed additives).

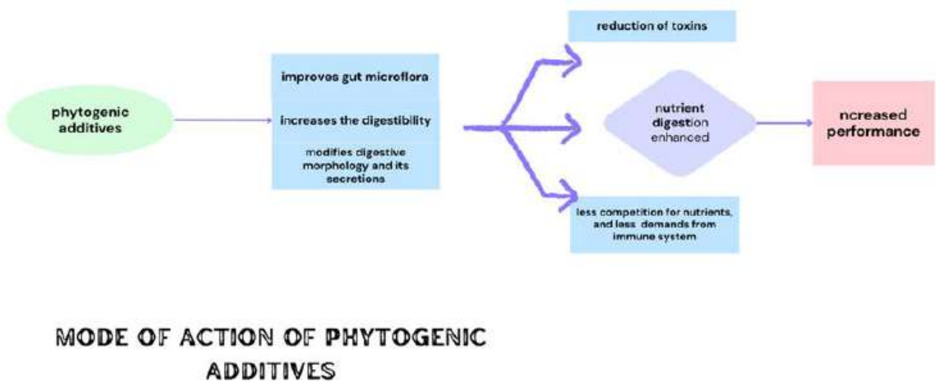


Fig. 4: Mode of action of phytogenic additives

Nutritional Feed Additives

Vitamins

Vitamins are organic compounds present in natural feed as well as can be present in synthetic feed. These can be water-soluble as well as fat-soluble. Water soluble vitamins contain vitamin C, and vitamin B complex including thiamine, riboflavin, pantothenic acid, niacin, pyridoxine, biotin, cobalamin, and folate. B complex is essential for the normal growth of the body and its development. Fat-soluble vitamins contain vitamins A, D, E, and K. These vitamins also provide aid in the health maintenance of chicken and good egg quality. Deficiency of these vitamins can cause different diseases and syndromes in poultry.

Table 1: Different roles of vitamins

Vitamins	Role
Vitamin C	Improves the performance of birds, reduces heat stress, modulates the immune system by responding to infections and inflammations, helps in growth and development (Van Hieu et al., 2022).
Thiamine (B1)	Regulates basic metabolism, essential in nerve functioning, thiamine co enzymes synthesized artificially are used in treatment of coccidiosis, and fungal infections (Tylicki et al., 2018).
Riboflavin (B2)	Modulates the microbiome of intestines, improves intestinal functions, an an energy source, stimulates the proliferation of cells of epithelium, antimicrobial, act as immunity boosters, beats different kinds of pathogens (Biagi et al., 2020).
Niacin (B3)	Maintains optimum performance, and reduces the risks of infections and diseases, mediates the transport, necessary for skin, ayes, and inhibits cancer cells growth, antioxidant (Hrubsa et al., 2022).
Pantothenic acid (B5)	Antioxidants are involved in producing several neurotransmitters, and hormones for growth and development (TURAL and TUZCU, 2023).
Pyridoxine (B6)	Weight gain, improves FCR, improves carcass quality (Tagar ,2005).
Biotin (B7)	Improves metabolism (Zhao et al., 2024).
Folate (B9) and Cobalamine (B12)	Improves growth performance of chickens, enhances the carcass and meat quality, boosts the metabolism (Giguere et al., 2005).
Vitamin C (Ascorbic acid)	Improves the health of chicken, helps in growth and development, acts as an antioxidant and an anti-inflammatory, enhances the eggshells, quality, reduces the risk of broken eggs in layers, improves immunity of the birds, helps in regulating the stress (Van Hieu et al., 2022).
Vitamin A	Essential for vision, growth, and development, maintains optimal performance, acts as an antioxidant, enhances the rate of laying and egg production, increases the egg mass and weight, helps in improving hatchability (Khan et al., 2023).
Vitamin D	Improves the performance of birds, immunity, and bone health. It also maximizes the digestion of minerals thus enhancing the growth (Swiatkiewicz et al., 2017).
Vitamin E	Improves the growth and performance of broilers, enhances the composition of carcass and meat quality, reduces heat related stress and mortality (Calik et al., 2022).
Vitamin K	Helps in promoting bone health, aids in modulating metabolism of calcium and phosphorus (Guo et al., 2020).

Amino Acids

Amino acids are characterized as breakdown products of proteins and are essential for the existence of living beings. These are also classified as essential as well as non-essential. Essential amino acids include histidine, leucine, isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. Other non-essential or conditional amino acids include alanine, arginine, alanine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, proline, serine, and tyrosine. All these amino acids are necessary for a proper portion of the poultry diet. In poultry feed, these amino acids have a positive impact on egg mass and yolk weight and should be provided in the laying phase of layers (Alagawany et al., 2021). Tryptophan, valine, isoleucine, and arginine added in feed can dispense functional outcomes. These amino acids can help reduce thermal stress, oxidation, intestinal challenges, and feathering, thereby improving efficiency and high yield (Lee et al., 2023).

Feed Additives for Health Improvement

Coccidiostats

Coccidiosis is a parasitic disease caused by the *Eimeria species* and has always had dangerous impacts on the lives of chickens, causing excessive mortality, and severe economic losses. To wage the war against coccidiosis, several anti-coccidia drugs known as coccidiostats, several vaccinations along with some alternatives, and control approaches are used worldwide. Several synthetic coccidiostats include halofuginone, clopidol, amprolium, and sulfoquinoxaline, while some authorized ionophores including monensin, salinomycin, naracin are also used (Martins et al., 2022). Although live vaccinations have good results against coccidiosis, biosecurity breaches in introducing live parasites at farms have limited its application, and various other alternative approaches have been used (Peek and Landman, 2011). Essential oils can also be used in diet to prevent coccidiosis (see essential oils as feed additives).

Feed Additives and Nanoparticles

It has been suggested by scientific studies in various fields that nanoparticle feeding helps in improving digestion, immunity, and efficiency in the performance of livestock as well as poultry. Nanoparticles refer to minute entities ranging in size from 1 to 100 nanometers, and their sizes can vary according to the bulk (Hasan, 2015). These can be organic, inorganic, or carbon-based, and can be in more than one dimension (Khan et al., 2022). We can prepare them in physical, chemical, or mechanical ways (Ealia and Saravanakumar, 2017). We can use these minute particles for therapeutic, preventive, and diagnostic approaches (Youssef et al., 2019). We can use these nanoparticles to provide supplements, nutrients, vitamins, minerals, antibiotics, and vaccinations in our poultry birds. We can use some nanoparticles to reduce bacterial growth and contamination in feed, to stimulate the proliferation of useful bacteria in their guts, and others to enhance the efficiency of production (Gangadoo et al., 2016). We can also identify the adulterations in feed using these nanoparticles (Abd El-Ghany et al., 2021). These nanoparticles can also help us in the diagnosis of different poultry diseases, and for biosecurity purposes. The most important and useful application of these nanoparticles is their antimicrobial effect as antivirals, antibacterials, and antifungals (Abd El-Ghany et al., 2021).

Classification of Nanoparticles

Nanoparticles can be classified as organic, inorganic, and carbon-based (Khan et al., 2022). Organic nanoparticles include polymers, ferritin, micelles, dendrimers, and liposomes (Ijaz et al.,2020). Inorganic nanoparticles can be metal-based (Al, Cd, Cu, Au, Fe, Pb, Ag, Zn) (Patra and Lalhriatpuii, 2020), or metal oxides (FeO, ZnO, Al2O3, TiO2). Carbon-based nanoparticles include Fullerenes, Graphene, Graphene oxide, carbon nanotubes, carbon nanofibers, activated carbon, and charcoal. These can also be immune-invigorating edifices, virus-like particles, or self-gathering proteins (Youssef et al.,2019). These are also present in the form of emulsions and dispersions (Singh, 2016).

Application of Nanoparticles in Poultry

Copper nanoparticles are widely used in the poultry industry. As they are not found in bulk in the body of birds, copper nanoparticles can be given to birds, hence providing an alternative for antibacterials and growth promotors (Sharif et al., 2021). To improve growth rate, body weight, and FCR, silver NPs are widely used in poultry feed at the dose rate of 900 ppm (Anwar et al., 2019). Thyme essential oil-loaded chitosan NPs regulate the intestinal microbiota and can be used instead of antibiotics as growth promotors (Hosseini and Meimandipour, 2018). Curcumin nanoparticles are also used in the poultry industry to increase productivity, as curcumin is a good antioxidant, can modulate immunity, and can improve the dietary intake of birds (Geevarghese et al., 2023). Nanotechnology has a wide scope in improving poultry feed production and combating all production challenges related to different poultry diseases like Salmonellosis and campylobacteriosis etc. (King et al., 2018). Methionine-coated zinc NPs can be used to enhance digestion, performance, and bone density (Alkhtib et al., 2020). Selenium NPs can enhance reproductive performance as well as immunity of broiler, Zn NPs can be used to improve FCR, Montmorillonite – composite NPs can reduce aflatoxin toxicity, and Bio complex of glutamine and nano-diamond NPs in chicken can help in weight gain and growth (El Sabry et al., 2018). Nanocapsules of aloe vera, nettle root, and dill extract can enhance growth, and as antibiotics replacements (Meimandipour et al., 2017). Metallic nanoparticles can be used to ingress the quality of feed, and the presence of any pathogen, allergen, or toxin in feed (Couto and Almeida, 2022). ZnO is an excellent antibacterial against *Salmonella gallinarum, Pseudomonas aeruginosa, and Bacillus anthracis* in the poultry industry (Raguvaran et al., 2015). Alginate-based nanoparticles coated with cellulose derivatives can be used against bacteria that have multi-drug resistance, or antimicrobial resistance (Roque-Borda et al., 2021). Activated carbon NPs are widely used as toxins absorbents in poultry feed (Colovic et al., 2019). Polymeric nanocapsules are widely used for antioxidant delivery to the target site in safe mode (Horky et al., 2018).

Essential Oils as Feed Additives

Essential oils are oily extracts of different parts of plants like their flowers, fruits, buds, roots, branches, bark, and seeds obtained by methods of distillation, extraction, or crystallization. There are thousands of essential oils present worldwide, extracted from different plants, but only about 300 are of commercial importance (Anuranj et al., 2022). Essential oils which are the secondary metabolites of plants can be used in the feed industry for poultry and livestock as a replacement for the antibiotic growth promotors. These EOs are not just used as antibiotic growth promotors, but these oils also have antiviral, antifungal, insecticidal, antipyretic, antioxidant, cytotoxic, and antiparasitic effects as well (Stevanovic et al., 2018). EOs promote the growth of birds by amplifying the secretions in their guts, and by intensifying the absorption of essential nutrients, eliminating the harmful and nosy microorganisms in their digestive tracts, and by reducing stress factors (Zeng et al., 2015). These oils also can stimulate immunity and blood circulation (Brenes et al., 2010). EOs are used in a blend with other transit oils in poultry feed to boost the production performance of birds (Krishan and Narang, 2014). These oil blends can reduce the risk of diseases like coccidiosis (*Eimeria*), and necrotic enteritis (*Clostridium perferingens*) (Amerah and Ouwehand, 2016). Moreover, Mesophilic bacteria, Enterobacter, and Enterococcus can also be controlled through EOs dietary therapy in poultry (Stamilla et al., 2020). These can also be used against gram-negative bacteria like *E. coli, Mycoplasma gallisepticum, M. synovia, Pseudomonas aeruginosa, Salmonella enteritidis*, fungi like *Aspergillus fumigates,* and toxins like Aflatoxin B1 (Adaszynska-Skwirzynska and Szczerbińska, 2017). The Hypercholesteremic effect is also seen in broilers (2% lowered serum cholesterol concentration) (Lee et al., 2004), which is a good merit of EOs to prevent joint diseases in chickens. The use of EOs in poultry diets makes the meat lean which has reduced the hyperlipidemia risk in end users (Marappan Gopi et al., 2013). Essential oils can also act as coccidiostats (VLAICU et al., 2022).

Different Essential Oils as Feed Additives

Thyme oil *(Thymus vulgaris)* @ 100mg/kg along with carvacrol @ 200mg/kg helps in digestion by increasing the small intestines' villi length, thyme oil extract supplementation @ 100ppm enhances the immunity, and peppermint oil @ 200mg/kg increases the protein digestion (Mandey and Sompie, 2021). Essential oil blends @ 0.25 or 0.5g/kg can increase the weight gain of quails in poultry by lowering feed intake and enhancing FCR (El-Shenway and Ali, 2016). Essential oil supplementation in the diet has a positive impact on the gut microbiota of broiler chickens, and ultimately increases their growth rate (Tiihonen et al.,2010). Basil EOs, thyme oil, rosemary oil, and sage EO contain many phenolic compounds, acids, and other derivatives that can act as antioxidants (VLAICU et al.,2022). Eugenol (0.5-1%) clover extracts essential oil works in a similar way as other essential oils by reducing feed intake and improving FCR (Tahir et al., 2019). Thyme oil and anise can have additive or maybe synergistic effects on weight gain, improved FCR, and low serum cholesterol levels (Al Mashhadani et al., 2011). Recommended the dose rate of 0.3g/kg of cinnamon oil in the diet can accelerate the growth performance of chickens (Choudhury et al., 2018).

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Chapter 46

Additives in Fish Feeds: Non-Conventional Way for Improving Fish Health

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ABSTRACT

More than half of the world's population gets their protein from fish, which is an affordable and effective source of lean meat. Nevertheless, aquaculture has financial loss, fish health issues, and viral illnesses. Proper nutrition accounts for 50–80% of the costs associated with aquaculture output. If growth performance and feed efficiency are improved in commercial aquaculture, production costs should go down. Fish would have significantly lower total production costs if their ability to survive increased. Aquaculture feeds are composed of various substances to give fish the nutrition they require for normal physiological functions such as growth, reproduction, and the upkeep of a strong natural immune system. To ensure that the dietary elements are taken in, broken down, absorbed, and given to the cells, an increasing number of feed additives are being employed in aquatic diets. Chemicals added to fish diets in trace amounts are known as feed additives. Additives can be Essential (Vitamins, minerals), non-essential (antibiotics, prebiotics, enzymes) and Auxiliary (binders, Color enhancers) additives, each having specific functions. To guarantee sustained growth in aquaculture, the right amount of chemicals must be employed.

KEYWORDS			
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INTRODUCTION

Feed additives have been used since the past, with salt added to animal feed to make it more palatable. The application expanded in the early 1900s, with vitamins discovered in the 1920s to boost growth rates and prevent deficits. Additional feed additives, including minerals, amino acids, and enzymes, were created. Governmental organizations control the use of feed additives to ensure their effectiveness and safety (Bai et al., 2022).

Since fish are a cheap and efficient source of lean meat, more than half of the world's population depends on them for their dietary protein needs (Oramary et al., 2016). However, aquaculture suffers difficulties like financial loss, health problems with fish, and infectious infections (Awad and Awaad, 2017). In aquaculture, 50–80% of output costs are related to proper nutrition (Ogunkalu, 2019). The term "feed additives" describes substances added to a diet or feed in trace amounts to aid in nutritional quality preservation (Abdelhamid et al., 2010; He et al., 2012), feed pelleting or ingredient dispersion, and ease of feed ingestion and consumer acceptance and nutrients availability or remove an anti-nutrient presence (Ebru and Cengiz, 2016).

Selection of Feed Additives

Each feed additive in feed should be present for a specific reason as described Kruger and Mann, (2003)

- Designed to identify, treat, reduce, cure, or avoid illnesses
- Pharmacological and physiological actions
- Other than dietary effects, no intentional effects on the body
- Impact on feed functionality
- Biologically active
- Exposure throughout life

Additionally, Wani et al., (2023) also defined selection of feed additives as follows.

- The material needs to be reasonably priced
- Readily available in sufficient quantities
- It shouldn't have an unfavorable effect on the meat of the animal

Classification of Feed Additives

The primary goal of feed additives is to promote faster, healthier growth that will increase yield. European legislation on animal feed provides a framework for ensuring feedstuffs do not pose environmental or human health risks, including laws on genetically modified food, feed material usage, hygiene standards, and addressing unwanted substances in feed. Feed additives tend to fall into certain categories which describe their action in the feed or in the animal (Yadav et al., 2021).

1. Essential additives.
2. Growth-promoting but non-essential additives.
3. Auxiliary additives

Essential Additives

According to Revesz and Biro (2019), these additions are also referred to as nutritious supplements. The formula contains small amounts of vital substances to improve nutritional balance and promote healthy growth. Deficient sickness may arise from prolonged abstinence from feeding (Luo et al., 2005).

Vitamins

Animal development, reproduction, survival, and health all depend on vitamins. Because they cannot synthesize most vitamins, animals must get them from their diet. Both fat-soluble and water-soluble vitamins have distinct functions (NRC, 2011). Table 1 shows vital water and fat soluble vitamins and their significance

Table 1: Vital water and fat soluble vitamins and their significance

Vitamins	Functions
Water Soluble Vitamins	
Thiamine (B1)	Cofactor for the enzymatic processes that produce energy.
Riboflavin (B2)	Protein, fat, and carbohydrate metabolism.
Nicotinic acid (B3)	NAD and NADP are components of a coenzyme that synthesizes cholesterol and fatty acids.
Pantothenic acid	Part of the acetyl coenzyme A
Pyridoxine (B6)	Protein and carbohydrate metabolism, mRNA and acetyl coenzyme A production.
Biotin (B7)	Carbohydrate and fat metabolism has a role in the urea cycle and protein synthesis.
Inositol (B8)	Cell growth in the liver and bone marrow, RNA synthesis
Folic acid (B9)	Amino acid metabolism and the creation of nucleotides, purines, and pyrimidines.
Cyanocobalamin (B12)	Maturation, erythrocyte development, and nerve tissue preservation (NRC, 2011).
Choline	Lipid transport and nerve impulse transmission.
Ascorbic acid (Vitamin C)	Participate in bone and cartilage production (Kraus et al., 2004) and immunological response (Barros et al., 2014).
Fat Soluble Vitamins	
Retinol (A)	The development of embryos, epithelial cells, and cell differentiation are all impacted by vision.
Cholecalciferol (D)	creation of calcium-binding proteins is involved in the creation of melanin, the stress response, and muscular function.
Tocopherol (E)	Antioxidant activity, including intracellular and extracellular, gene expression, and cell selection.
Phylloquinone (K)	Transport of calcium and blood coagulation (NRC, 2011)

According to Revesz and Biro (2019), vitamin premixes are concentrated blends of key vitamins in a steady state with base feed that is frequently added at amounts above dietary needs to comprehensive practical fish diets. Because choline has been shown in tests to decrease the stability of other vitamins, it is not included in these premixes. The addition of these premixes ranges from 0.5 to 4% (Demott et al., 1995).

Minerals

Minerals, often known as inorganic elements, are essential nutrients for fish life. Maintaining health and stress tolerance necessitates a diet with roughly twenty components. These elements are separated into macro- and micro-elements based on their concentration, ensuring that fish can tolerate stress and resist disease (NRC, 2011; Webster and Lim, 2015). Table 2 lists significant macro and micro minerals along with their purposes.

Fatty Acids

PUFA-rich fish oils like cod liver, sardine, squid, and clam oil have antibacterial and antioxidant properties, improve intestinal health, increase feed palatability, and stimulate growth (Sutili et al., 2018). All cellular and subcellular membranes rely on lipids for proper function (FAO, 2014). Fish oil is added to meals at a rate of two to three percent to increase growth and food conversion ratio (Deng et al., 2013). Fish muscle uses triglycerides, including free fatty acids, as its primary aerobic fuel source for energy metabolism. It also serves as a carrier for fat-soluble vitamins during absorption. Lipids maintain neutral buoyancy and support essential body organs (FAO, 2014).

Table 2: Important macro and micro minerals and their functions

Macro minerals	Functions
Magnesium (Mg)	The development of muscle and nerve tissue, as well as bone and cartilage (Webster and Lim, 2015)
Calcium (Ca)	Nerve impulse transmission, control over the permeability of cell membranes, vital components of bone and cartilage, and blood clotting.
Potassium (K), Sodium (Na)	Osmoregulation and the body acid-base equilibrium
Chloride (Cl)	The principal component of hard tissues like scales and bone
Phosphorus (P)	Blood oxygen and carbon dioxide transport, osmoregulation, and the body's acid-base balance (Lall, 2002)
Micro minerals	
Cobalt (Co)	Component of vitamin Bl2 (Lall, 2002).
Copper (Cu)	Iron metabolism, cellular energy production, protection of cells from free radical damage, collagen synthesis and melanin production (Linder, 2002).
Iodine (I)	An essential constituent of the thyroid hormones T3 and T4 (Lall, 2002).
Iron (Fe)	Electron transfer reaction, gene regulation, binding and transport of oxygen and regulation of cell growth and differentiation (Bury et al., 2003).
Selenium(Se)	Involved in hydrogen peroxide signaling, detoxification of hydro-peroxides and maintaining cellular redox homeostasis (Roman et al., 2014).
Zinc (Zn)	The catalytic role, stabilizes the tertiary structure of enzymes and regulates gene expression (McCall and Huang, 2000).

Phospholipid

In fish, phospholipids can function as an energy source under specific conditions, such as embryonic and early larval development, although triacylglycerols are the main type involved in lipid storage and energy provision (Salze et al., 2005). In young fish, dietary phospholipids improved digestibility (Kasper and Brown, 2003). Soybean lecithin, when added to the diet at a rate of 1-2 percent, accelerates growth and increases feed conversion ratio. According to Heo et al. (2013), phospholipids are physiologically significant for the body's lipid transportation system.

Growth-promoting but Non-essential Additives

Also called a zootechnical additive (Revesz and Biro, 2019). Feed additives include plant and animal-based materials, single-cell proteins, and some synthetic materials that help feeds develop and produce more quickly. They won't result in any deficiency diseases if they are left out of the diet (Apenuvor, 2014). However, when added to feed, they have advantages. These are attractants and growth boosters. Additionally, zootechnical additives can lessen the negative effects of animal production on the environment (Revesz and Biro, 2019). Ex. Probiotics, Animal materials, enzymes, Antibiotics, Drugs etc.

Antibiotics

Antibiotics do not reduce parasites, fungi, or viruses, however medicated feed is frequently advised to manage bacterial illness outbreaks in farmed fish (Kelly, 2013). Antibiotics act by decreasing or eliminating the activity of pathogens, getting rid of bacteria that create toxins that stunt growth, encouraging the growth of helpful microorganisms that synthesize nutrients, and lowering microorganisms that compete with the host for nutrients—all of which promote growth in young animals as opposed to adults (Hardy and Barrows, 2003). Table 3 includes a list of antibiotics that are authorized for use in medicated fish feed. The U.S. Food and Drug Administration (FDA) has approved only four antibiotics for use in food fish, including Terramycin, Romet, and Florfenico. Fish can be treated with antagonists via bath, flush, oral route, dip, bio-encapsulation, and injection (Haya et al., 2005).

Antibiotics function by one of two methods:

(a) Bactericidal, which kills bacteria by interfering with cell wall formation or cell contents.

(b) Bacteriostatic, which stops bacteria from multiplying by interfering with protein production, DNA replication, or other aspects of bacterial cellular metabolism (Romero et al., 2012).

Antimicrobial

Aquaculture uses both synthetic and natural antimicrobial medicines are rarely used as growth promoters; instead, they are mostly employed as preventative and therapeutic agents (Shao, 2001). These substances exhibit precise cellular targeting and can function as selective ligands for targets associated with disease, which can influence disease-related pathways and maintain a healthy biological network (Chin et al., 2006; Lagunin et al., 2010). Natural ingredients make up over half of FDA-approved medications (Chin et al., 2006; Kingston, 2011), with plants providing 25% of these. Herbal remedies are more accurate and less expensive than chemotherapy drugs, making them suitable for aquaculture-related issues such as immunological stimulants, growth promoters, appetite stimulants, tonics, and anti-stress agents (Rates, 2001). Fish medications are rarely derived from animals (Berger et al., 2005), and synthetic medications mimic naturally occurring drugs (Romero et al., 2012). The two most popular ways to administer antimicrobials in aquaculture are medicated feed and water medication (Singh and Singh, 2018). Table 4 shows FDA-approved pharmaceuticals are safe and efficient and have few unanticipated side effects (US FDA, 2017).

Table 3: Antibiotics Approved for use in Medicated Feed for Food Fish (kelly, 2013)

Antibiotics	Treatment
Terramycin	Furunculosis and Enteric septicemia
Romet	Furunculosis, Bacterial hemorrhagic septicemia, Pseudomonas illness, and Ulcer sickness.
Florfenico	Furunculosis, Enteric Septicemia, Columnaris and Streptococcal septicemia.

Table 4: FDA-approved aquaculture drugs (permitted for application in fisheries and aquaculture) (US FDA, 2017)

Drugs	Treatment
Formalin	For limiting the propagation of monogenetic trematodes, protozoa, and fungi.
Florfenicol	For the decrease in intestinal septicemia-related catfish mortality.
Papain	To improve hatchability and reduce disease incidence, fish egg masses should have their gelatinous matrix removed.
Onion	Used to treat external crustacean parasites and stop sea lice from reaching the outside surface
Calcium chloride	Utilized to increase the water's calcium concentration to guarantee proper egg hardening
Fuller's Earth	To reduce the stickiness of fish eggs to improve hatchability
CaCO3	To maintain the osmotic balance of fish throughout storage and transportation, the water should be made harder.
Garlic	Used to get rid of helminth infections and sea lice

Hormones

Hormones are chemical messengers that facilitate communication between various cell types that identify and act through protein structures called receptors that are trained in molecular identification (Chrousos, 2007). In aquaculture, hormones are utilized for sex reversal (Taranger et al., 2010) and growth promotion. The goal of using hormones in fish farming to reverse sex is to create a monosex population to accelerate growth or cause weight gain. Raising individuals of the most profitable gender is beneficial from a commercial standpoint as it leads to more uniform lots and reduces unwanted breeding (Singh, 2013). Hormones like 17β-estradiol, estradiol valerate, 17α-methyl testosterone, or 17α-methyl dihydrotestosterone (via food and immersion techniques) to feminize a population. Conversely, testosterone is utilized by masculine females (Piferrer, 2001). In species where males grow faster than females and attain larger sizes, tamoxifen, 17α-methyl testosterone, 17α-ethynyl testosterone, and 17α-ethynyl estradiol have all been used to produce an all-male population (Liao et al., 2014).

Hormones are utilized in aquaculture for artificial reproduction, controlling ovulation and maturation in the gonad. They can induce, accelerate, or stop fish development, and extend reproductive periods for more flexibility in marketability. Fish breeding hormone procedures involve intramuscular or intraperitoneal injections (Mylonas et al., 2010). The pituitary gland extract from mature fish is the oldest and most commonly used hormone, while gonadotropin-releasing hormone (GnRH) is produced by salmon and mammals. Various species use analogs, dopamine antagonists, and synthetic hormones (Almeida, 2013)

Enzyme

Biological catalysts, or biocatalysts, are substances that accelerate biochemical reactions in living things. They can be isolated from cells and utilized as catalysts for a variety of significant commercial activities (Robinson, 2015). The detrimental effects of anti-nutritional variables have an impact on fish development performance and how well they absorb dietary components. Exogenous enzymes can help solve these issues (Mazurkiewicz, 2008). Enzymes are utilized in the digestion of other feed ingredients, collagen in the skin and bones, and complex carbohydrates. Table 5 shows Different enzymes and their effects on various fish species. Generally speaking, temperatures exceeding 65° C denature enzymes. According to Strobel et al. (2012), enzyme supplements are therefore usually applied to meals following pelleting.

Prebiotics

Prebiotics are any substance, fiber, long-chain sugar, vitamin, or substrate that provides sustenance for the good bacteria in the digestive tract of the host (Mountzouris, 2022). To improve the host's health, prebiotics were employed to encourage the growth of microbes already present in the gut of the organism (Rohani et al., 2021). By functioning as a receptor, a modulator of the host immune system, and an inflammatory controller, a prebiotic can inhibit the attachment of pathogenic microorganisms to epithelial cells and eradicate them from gut epithelial cells (Mohammadi et al., 2021). Table 6 lists the effects of various probiotics on fish.

Table 5: Different enzymes and their effects on various fish species

Enzymes	Effects
Microbial phytase	Enhanced phosphorus and energy availability (Cheng et al., 2002)
Pepsin, papain, amylase	Increased feed utilization and growth efficiency (Alemayehu et al., 2018)
Non starch polysaccharides (cellulose, Xylans)	Increased the aquatic animals' digestibility (Sinha et al., 2011).
Glucanase, cellulase, xylanase	Increased nitrogen retention, feed conversion ratio and feeding efficiency ratio, decreased ammonia excretion (Ai et al., 2007)
Alpha - amylase	According to Kumar et al. (2006), starch digestibility improved growth and had a protein-sparing impact.

The following criteria should be a must for prebiotics, which is used in feed:

i) vulnerability to the fish upper digestive tract.

ii) The gut bacteria should be able to ferment it with ease.

iii) The host's health ought to benefit (Lee and Salminen, 2009).

Table 6: Effects of different probiotics on fish

Prebiotics	Effects
Fructo-oligosaccharides	improved the digestibility and uptake of feed (Grisdale-Helland et al., 2008)
Inulin	Enhanced the concentration of RBC, magnesium, calcium, and iron; also, it lengthened the intestinal villi and boosted lysozyme activity (Tiengtam et al., 2015)
Mannan	thickens the intestinal muscle layer and raises the height of the intestinal fold (Yuji-Sado et al., 2015)
Fermacto prebiotic	increased feed conversion ratio and growth (Mazurkiewicz et al., 2008)

Auxiliary Additives

Also known as technological additive (Revesz, and Biro, 2019).). Certain ingredients added to feed formula function as components to the physical qualities of feed, according to Shahidi et al. (2019). This ultimately contributes to improved feed utilization and increased feed efficiency. These substances could be categorized as supplementary substances. These include fats, molasses, binders, and feed color. For example, color, glue, molasses, etc.

Feed Colorants

To improve fish color, which is a crucial characteristic for aquaculture and the trade in ornamental fish, color enhancers are added to fish feed (Naeem et al., 2021). They have also been shown to enhance fish survival and growth (Yadav et al., 2021). Animals and plants of many kinds contain more than 300 pigments. Carotenoids and xanthophyll are the two most significant types of pigments. Fish and crustaceans contain carotenoid pigments, while plants contain the majority of xanthophyll (Wagde et al., 2018). Additional examples of color enhancers are blue-green algae called spirulina, which has natural pigments like phycocyanin and chlorophyll. The naturally occurring pigment beta-carotene is present in a variety of fruits and vegetables, including sweet potatoes and carrots. It is used to bring out the orange and yellow hues of fish, such as goldfish. To guarantee that synthetic colorants are safe for fish and consumers, strict regulations are in place. It is used to certain fish species to accentuate their blue and green hues. It's crucial to remember that there are certain disadvantages to using color enhancers in fish feed. The ecology and fish health may suffer if these enhancers are used excessively (Naeem et al., 2021).

Binders

Aquafeed production requires the use of binders because they keep the feed cohesive and stop it from dissolving. Materials that can be used to make binders include synthetic materials, plant- and animal-based products, and more (Karim et al., 2022). Used at a level of 2 to 8% to increase pellet stability (Hardy and Barrows, 2003).

Binders may be:

1. In the manufacturing of fish feed, plant-based binders including starches and gums are frequently utilized. Manufacturers choose these binders because they are affordable and easily accessible. They might not, however, offer as strong of a binding as synthetic or animal-based binders.

2. The manufacturing of fish feed also makes use of binders derived from animals, such as collagen and gelatin. These binders have a high binding strength and are made from animal byproducts. They might not work well with all kinds of fish feed, though, since certain fish species might respond negatively to these binders.

3. In the process of making fish feed, synthetic binders including carboxymethyl cellulose and polyvinyl alcohol are

gaining popularity. When compared to binders derived from plants and animals, these binders are much more efficient and can offer higher binding strengths. But compared to other types of binders, they could be more expensive and harder to get. (Arthithan et al., 2012).

Preservatives

Fish feed frequently contains preservatives to lengthen its shelf life and stop it from spoiling (Prokopov and Tanchev, 2007). Also known as antioxidants. The food to be preserved and the microbe it targets dictated which antibiotic to use as a preservative (Davidson and Branen, 2005). These preservatives, which are added to the feed during the manufacturing process, might be synthetic or natural. To guarantee that fish feed stays fresh and nutrient-rich for fish to eat, preservatives are used in it (Yadav et al., 2019).

Ethoxyquin and butylated hydroxyanisole are common preservatives in fish feed. Both are synthetic antioxidants that prevents oxidation, spoilage, and degradation of fats and oils. Butylated hydroxyanisole also maintains the nutritional value of fish feed (Lundebye et al., 2010). Feeds commonly use fat-soluble Vitamin E (Frank, 2004), ascorbic acid (Bou et al., 2001) and carotenoids (Escalante et al., 2001), as antioxidants. Dihydroquercetin is a potent antioxidant that blocks the lipid peroxidation processes in cell membranes, can enter the cytoplasm of a cell to shield it from the damaging effects of free radicals (Ponomarev et al., 2022).

Benefits of Feed Additives

Fish feed additives has following advantages (Dawood et al., 2018; Bharathi et al., 2019):

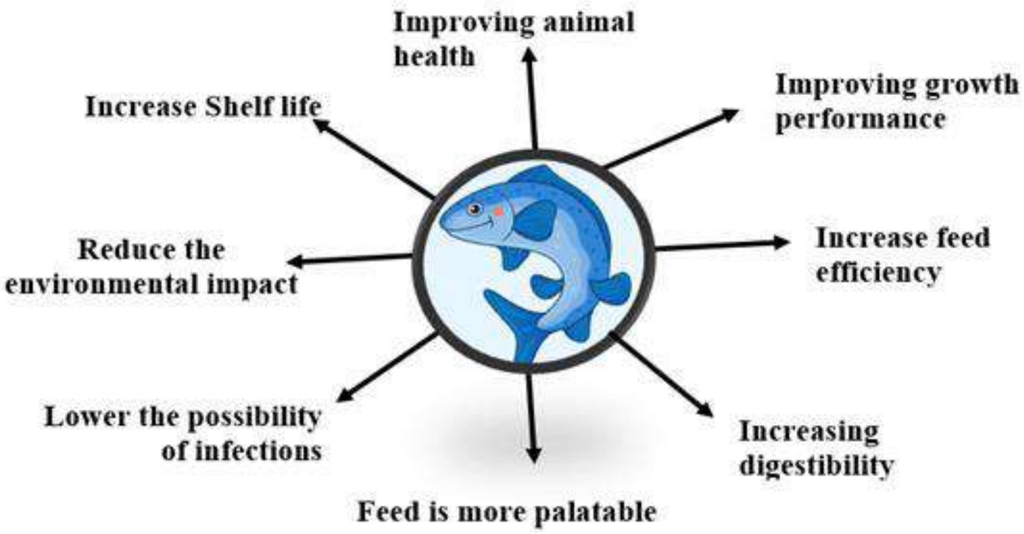

Fig. 1: Benefits of feed additives

Conclusion

In order to maximize nutrient uptake and boost productivity, feed additives are crucial to the production of poultry and animals. Since the turn of the 20th century, these additives—such as vitamins and salt—have been utilized to raise the quality and growth rates of animal feed. They fall into three categories: growth-promoting non-essential additions, auxiliary additives, and essential additives. Vitamins, minerals, and fatty acids are examples of essential additives that are necessary to sustain disease resistance, healthy growth, stress tolerance, and food conversion ratio. Aquaculture uses non-essential additives, including as hormones and antibiotics, to improve feed digestibility, cure illnesses, and create monosex populations. To increase feed utilization and efficiency, auxiliary additives such as carotenoids, binders, and feed colorants are crucial parts of fish feed formulae. In conclusion, feed additives enhance growth and production, make diets more attractive, palatable, and digestible, and increase digestibility.

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