Chapter 03

Probiotics and Innovative Feed Additives for Optimal Gut Health

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ABSTRACT

The livestock industry relies heavily on maintaining optimal intestinal health for maximizing productivity. However, concerns regarding antibiotic resistance and environmental impact have prompted the search for alternative feed additives. This comprehensive review explores the latest advancements in feed additives and their impact on animal health and sustainability. Various categories of feed additives are examined, including natural additives such as herbs and phytochemicals, technological additives like organic acids, and alternatives to antibiotic growth promoters such as tannins, Dicarboxylic acids, and ionophores. Additionally, the potential of phytogenic feed additives, Phytases, and nonstructural polysaccharides in enhancing nutrient utilization and animal health is discussed. Probiotics have emerged as a promising alternative to antibiotics, promoting gut microbiota balance and enhancing immune function. Recent research highlights the efficacy of probiotics in improving animal performance while reducing reliance on antibiotics. Furthermore, advancements in feed additives aim to mitigate environmental impact, with additives like zeolites and phyllosilicates showing excellent results in reducing enteric methane emissions and improving feed conversion efficiency.

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INTRODUCTION

Production of animals is the most important aspect of the economy, and maintaining intestinal health is crucial to their peak performance. The intestine is composed of a single layer of cells known as the intestinal epithelium (IEC). Maintaining an optimal state ensures proper nutrient absorption and digestion, intestinal barrier integrity, and gut bacteria balance (Ji et al., 2019). The GIT functions include defense against pathogens and non-pathogens, transportation of digested and ingested feed along the GIT, energy, and nutrient absorption, secretion of endogenous materials, hosting of intestinal microbiota, and excretion of digested feed and metabolic waste (Yegani and Korver, 2008). The gastrointestinal tract's homeostasis is developed and maintained by a variety of physiological and functional elements that make up gut health. These include the mucus layer's growth and maintenance, the control of barrier function, the synchronization of energy generation and host metabolism, appropriate nutritional uptake and digestion, and a variety of mucosal immunological responses (Kogut and Arsenault, 2016). It takes much more than simply probiotics and prebiotics to modify the gut microflora to maintain or improve "gut health". In contrast to commensal bacteria, which are essential to host health and metabolism, which might have detrimental consequences directly or indirectly, pathogenic bacteria interact with their host, with themselves, and with the host's nutrition (Yadav and Jha, 2019). Therefore, anything that impacts the condition of the gut will surely have an effect on the animal as a whole, changing its requirements for and ability to absorb nutrients. As a result, "gut health" is a very complicated terminology that includes the immune system's state, the micro- and macro-structural integrity of the gut, and the balance of micro flora (Kelly and Conway, 2001). To ensure optimal gut function feed additives must be used which include antibiotics, prebiotics, probiotics, enzymes, organic compounds etc. Antibiotics have been used extensively in livestock management to reduce disease, enhance performance, and boost output. Furthermore, probiotic, prebiotic, postbiotic, and symbiotic supplements have become the most widely utilized antibiotic substitutes (Hamasalim, 2016). Throughout the world, animal feed additives are used to improve feed utilization, support growth performance, and give livestock especially poultry vital nutrients. Industry norms and customer awareness are driving an increase in demand for natural and non-residual substitutes. Additives to herbal feed, such as ascorbic acid, prebiotics, probiotics, and herbal extracts, have therapeutic properties that improve immune-stimulant activity, digestibility, antibacterial, anti-inflammatory, and antioxidant traits. The key to sustained cow production is standardizing dose schedules (Pallauf and Müller, 2006).

Feed Additives

Feed additives are the products used in animal nutrition to improve the quality of feed and food obtained from animals or to improve the animals' overall health and performance. Increasing the digestibility of the feed ingredients is one of the examples. Sensory additives are a type of additive used to make a diet more appealing, thus encouraging voluntary consumption. They usually work by changing the diet's flavor or color. For instance, additives like vanilla extract can stimulate piglets to consume their feed. To improve the appeal of feed and zootechnical performance, sensory feed additives often include aromatic herbs, spices, and essential oils. These are commonly used in pig farming to stimulate consumption and promote growth. This approach leverages the natural appeal of these substances to enhance the effectiveness of animal feed (Clouard and Val-Laillet, 2014). Nutritional additives are additives that give animals the precise nutrition they need for healthy growth. A vitamin, amino acid, or trace minerals are a few examples. Vitamins have catalytic properties that aid in the synthesis of nutrients, regulating metabolism and impacting the well-being and productivity of poultry. Vitamin-supplemented diets are essential for the treatment and prevention of disease because they enable an animal to use proteins and energy for growth, reproduction, FCR, and overall health (Whitehead, 2002). Zoo technical additives are the additives that supply nutrients and facilitate the more effective utilization of the nutrients already present in the feed. These additions enhance the nutrient status and productivity of the livestock. An example of such an additive would be a direct-fed microbial product or an enzyme, both of which improve digestive tract conditions, making it possible to take nutrients from food more efficiently. Coccidiostats and histomonostats are the chemicals that have a direct influence on poultry health management. These substances are not categorized as antibiotics and are used to regulate the intestinal health of chickens. They work directly on the parasite organisms that live in the intestines (Amit Kumar Pandey, 2019). Technological additives are A set of additives that affect the feed's technological features are included in this classification. These additions may have an indirect impact on the feed's nutritional value by enhancing its handling or hygienic qualities, but they have no direct effect on it. An organic acid for feed preservation is an example of such an addition (Amit Kumar Pandey, 2019).

Importance of Feed Additives in Animal Health

Natural Feed Additives

Natural feed additives are important for nutrition and overall wellness. The emergence of microbial resistance to antibiotic medications and the ensuing health effects on humans, as well as consumer demands that animal diets be devoid of all non-plant xenobiotic substances, have led to an increased interest in the use of natural feed additives in livestock production(Muneendra Kumar, 2014). Feed additives enhance the flavor of farm animal's feed, and as a result, they can affect the feeding habits, digestive fluid output, and overall amount of feed consumed. Through their antimicrobial properties or by favorably stimulating the eubiosis of the micro biota, herbs or phytochemicals can specifically affect microorganisms. Most natural feed additives work by denaturing and coagulating proteins in the bacterial cell wall, which is how they have their antibacterial action(Muneendra Kumar, 2014).

Antibiotics as Feed Additives

Antibiotics are a class of natural, semi-synthetic, or chemical compounds that have anti-microbial activity. They are widely used to treat and prevent infectious diseases in humans and animals, and they are also added to animal feed as growth promoters to aid in the animals' development (Apata, 2009). Antibiotics are frequently used as a treatment, preventative measure, and growth stimulant. Because antibiotics have generally enhanced chicken performance both economically and effectively, farmers and the economy as a whole view the use of antibiotics in poultry and cattle production as beneficial (Apata, 2009). Animal welfare, quality and growth efficiency, feed efficiency boosters, economic output, carcass quality, and public health were the primary reasons why antibiotics were used in livestock production (Van Boeckel et al., 2015). Antibiotic growth promoters reduced the populations of potentially harmful bacteria such as Salmonella, E. coli, and Clostridium perfringens and enhanced their growth performance (ME, 2011). Feed additives enhance animals' energy balance by focusing on four key objectives: (i) shifting methane production towards propionate; (ii) minimizing protein degradation in feed to boost amino acid availability in the small intestine; (iii) slowing down the breakdown of rapidly fermentable carbohydrates like starch and sucrose, while managing lactic acid levels; and (iv) optimizing fiber digestion. Ionophore antibiotics in the rumen have been effective in achieving these goals, particularly in reducing acid production and preventing lactic acidosis when consistently given at low concentrations (20–40 p.p.m.) in meals (Osborne et al., 2004).They decreased the deamination of amino acids, which increased the passage of peptides from the rumen into the small intestine and decreased foamy bloat in cattle feeding on legume pastures; these actions alleviated methane generation by redirecting metabolic H use towards propionate production. There have also been reports of ionophores' post-ruminal effects. They have demonstrated efficacy against coccidiosis, for instance (Gallardo et al., 2005; Wallace, 1990).

Negative Effect of Antibiotics as Growth Promoters

The development of "antibiotic alternatives" has been spurred by concern about the growing number of bacteria that are resistant to antibiotics as a result of the overuse of antibiotics and a decline in the number of innovative antibiotics (Cheng et al., 2014). The reduced activity of bile salt hydrolyase, an enzyme generated by gut bacteria that negatively affects host fat digestion and utilization, was linked to the growth-promoting action of antibiotics (Lin, 2014). Concerns about the emergence of resistant bacteria and the potential for these bacteria to spread from animals to people have been provoked by the overuse of antibiotics. Resistance to drugs that were never used on farms is among the multidrug-resistant (MDR) infections that are associated with non-therapeutic antimicrobial usage (Cheng et al., 2014). The health and feed efficiency of farm animals has improved due to the use of antibiotics as growth promoters in commercial animal production, which has increased overall growth performance by about 18% (Duckett and Pratt, 2014).

Alternatives to Antibiotic Feed Additives

Concerns about the use of antibiotics as feed additives in animal agriculture are growing among the scientific community and the public. Many human pathogenic microorganisms are becoming resistant to antibiotics, which is a cause for concern (Manero et al., 2006; Parveen et al., 2006). The possibility that meals derived from animals may include antibiotic residues that promote growth. Due to all these factors, the European Union (EU) decided, on September 22, 2003, by EU regulation no. 1831/2003 of the European Parliament and the Council, that the use of antibiotics in cattle as production enhancers would be prohibited as of January 1, 2006. This prohibition essentially puts an end to the non-therapeutic usage of antibiotics for almost 50 years. It includes all types of antibiotics, including ionophores, a class of compounds widely employed in chicken production as coccidiostats and in ruminant agriculture as growth promoters or productivity enhancers (Gallardo et al., 2005; McDougall et al., 2004; Melendez et al., 2006).To lessen the risk of drug resistance in human health, and experts have searched for natural substitutes for feed additives.

Tannins

Plants rich in tannins have been explored as potential ruminant feed additives. These plants, high in protein and available during hot, dry seasons when other feeds are scarce, play a crucial role in animal nutrition (Yang et al., 2015). Many forage species contain high levels of tannins, a type of plant-based phenolic compound (Han-Chung Lee, 2005; Makkar, 2003). Tannins are naturally occurring secondary plant chemicals that have varying molecular weights. They are found in nearly all vascular plants and are typically given to ruminants(Wang et al., 2015). There are two types of tannins: condensed tannins (CT) and hydrolyzable tannins (HT).

Particularly, tannins have strong anti-bloat properties that prevent proteins from being broken down by the rumen and lower intestinal parasites, urine nitrogen excretion, and enteric methane emission (greenhouse gas). These benefits can then be transferred to increased milk production, wool growth, immunological responses, and reproductive efficiency (Attia et al., 2016; Aufrère et al., 2012; Min and Hart, 2003; Ramírez-Restrepo and Barry, 2005; Waghorn, 2008).

Dicarboxylic Acid

Additives to acidifier feed are thought to be essential for promoting rumen fermentation, which enhances animal health, productivity, and product quality. Acidifiers are often used as alternatives to antibiotic development marketers because of their ability to create an ideal digestive environment for beneficial microbes that may lead to increased nutritional digestibility, increased growth performance, and decreased diarrhea (Vassilis Papatsiros and Billinis, 2012). Since they function as "hydrogen sinks" during the conversion of Dicarboxylic acids e.g. aspartate, malate, and fumarate to propionate, some of the significant acidifying chemicals that dairy producers now utilize have been studied for use as feed additives (Newbold and Rode, 2006).

Ionophore

The most researched and utilized substances in cow diets are ionophores, which are primarily used to optimize fermentation pathways, change the ruminal microbiota, and lower the incidence of digestive problems (Duffield et al., 2012; Nagaraja and Lechtenberg, 2007; Tedeschi et al., 2003). Ionophores are naturally occurring antibiotics that are carboxylic polyethers, generated by a strain of Streptomyces spp. Utilizing ionophores to alter the ruminal environment and fermentation dynamics also enhances the absorption of protein and dietary energy (McGuffey et al., 2001; Russell and Strobel, 1989; Weimer et al., 2008). As a result of the diet's inclusion of rapidly fermentable carbohydrates, ionophores also help to prevent bloat and the buildup of short-chain fatty acids (SCFA), which includes lactic acid (acidosis) (Nagaraja and Lechtenberg, 2007; Tedeschi et al., 2003). As a result, ionophores have been utilized to enhance beef cattle's health, ruminal fermentation characteristics, and performance. Ionophores in diets improve feed efficiency and performance in ruminants by modulating the rumen microbiome and fermentation routes, increasing energy and nitrogen efficiency metabolism. However, their effects may vary depending on dosage, animal, and diet. In feedlot diets, ionophores improve body weight gain and reduce feed intake, while in forage-based diets, they increase body weight gain but increase feed intake (Tedeschi et al., 2003).

Phytogenic Feed Additives

An increasing amount of research has demonstrated that adding plant-based feed additives or phytogenic feed additives (PFAs) to diets improves zoo technical and animal health indicators. This suggests the potential of PFAs in animal nutrition. Herbs, spices, essential oils, and non-volatile extracts from plants like clove, anise, thyme, fennel, or Melissa, among many others, are examples of phytogenic compounds used in PFAs (Steiner and Shah, 2015). A primary benefit of PFAs is thought to be enhanced digestibility and feed conversion. PFAs affect several parameters, such as the release of digestive juices and enzymes, immune system modulation, alterations in intestinal morphology, and enhanced nutrition utilization, all of which lead to increased performance. Reduced amounts of microbial metabolites in the digestive tract as a result of intestinal microbiota stabilization soothe the immune system and increase the amount of energy available for muscle accretion (Steiner and Syed, 2015).

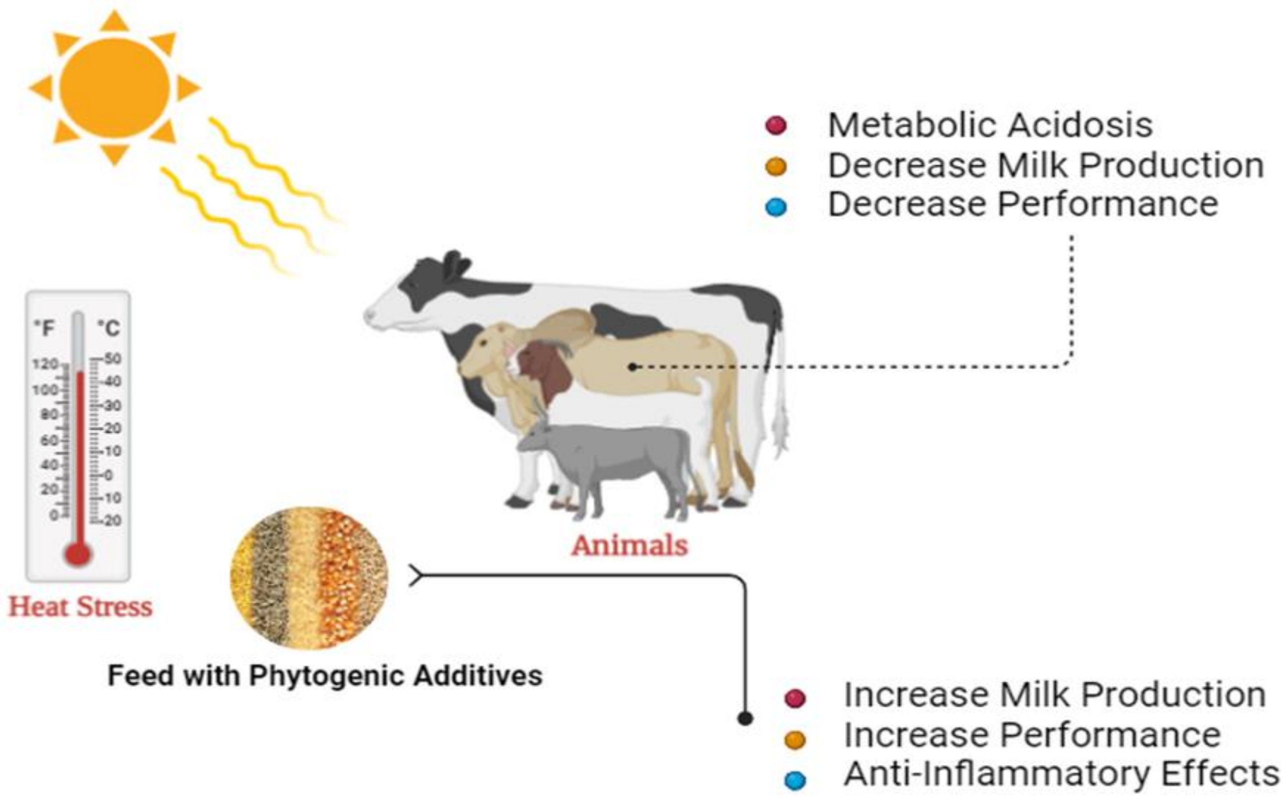

Fig. 1: Effect of phytogenic feed additives on the heat stressed animals (Swelum et al., 2021)

Phytases

Enzymes may cut feed costs by enhancing feed use, which will result in less feed being consumed. Enzymes are also necessary to enhance the sustainability of meat and egg production due to the higher feed utilization efficiency(Bundgaard et al., 2014). Phytase is added to animal feed to counteract the antinutritional effect of phytate, increase the availability of myoinositol, decrease phosphate emissions to the environment, and make use of an existing phosphorus source in the feed (Selle and Ravindran, 2007). The usage of phytate has increased after the use of animal protein sources, such as meat and bone meal, was prohibited. In poultry, it raises the digestion of phytate from about 25% to 50–70% (Papadopoulos and Lioliopoulou, 2023).

Nonstructural Polysaccharides (NSPs)

Nonstructural polysaccharide includes all plant polysaccharide except starch. NSPs can make up as much as 90% of a plant's cell wall (Selvendran and Robertson, 2005), are primarily found in plant cell walls as structural polysaccharides where they are associated with and/or substituted for other polysaccharides, proteins, and phenolic compounds like lignin (Kumar et al., 2012). Typically, they make up less than 10% of the grain's weight. The three NSPs that are most prevalent in plant cell walls are cellulose, hemicelluloses, and pectin; fructans, glucomannans, and galactomannans are the storage polysaccharides that are part of the less prevalent NSP category. When combined with water, soluble NSPs can create dispersions and increase the viscosity of digesta; insoluble NSPs, on the other hand, cannot do this but are distinguished by their capacity for fecal-bulking(Davidson and McDonald, 1998; Habte-Michael Habte-Tsion, 2018). Cereal-based diets have high concentrations of soluble NSPs, which have a negative impact on animal performance and the effectiveness of the digestive system. Animal diets are frequently supplemented with marketed exogenous enzyme combinations, which include NSP enzymes, to lessen the adverse effects of dietary NSPs. These enzymes can partially hydrolyze NSPs, lower the viscosity of the gut's contents, and enhance the digestion and absorption of nutrients (Almirall et al., 1995; Bedford and Apajalahti, 2001; Sternemalm et al., 2008). By decreasing undigested substrates and antinutritive factors and maybe by generating oligosaccharides from dietary NSPs with possible prebiotic effects, dietary added enzymes can benefit the ecology of the digestive microbial population (Habte-Tsion and Kumar, 2018).

Probiotics for Optimal Animal Health

The use of growth promotants and antibiotics, however, has raised concerns about the emergence of food-borne allergies, an increase of bacteria resistant to these drugs, and the harm that these substances due to the environment, including runoff from agriculture. Moreover, growing concern among consumers regarding the impact of growth promotants and antibiotics on human health is a factor that is still being discussed. Researchers employed Probiotics supplementation as a substitute, either as a single strain or multiple strains in the diet of animals to solve this issue (Lipsitch et al., 2002).

Probiotics are defined as mono or mixed strains of living microorganisms that, when used appropriately, confer a desirable health benefit on the host (*FAO/WHO. Guidelines for the Evaluation of Probiotics in Food.*, 2002). A microorganism is considered probiotic if it is nonpathogenic, able to produce a viable cell count, beneficial to the host's health, and improves intestinal tract functioning. Probiotics must meet certain requirements to be used and stored: (i) Probiotic bacteria must be prepared in a viable way and on a large scale; (ii) they must be able to survive in the digestive tract; (iv) the probiotics must have both direct and indirect positive effects on the host (better intestinal microflora); and (v) their safety must be obvious (Vanbelle et al., 1990). Probiotics can be made as capsules, paste, powder, granules, fermented feed, pelleted feed, and more. It has recently been suggested that inactivated bacteria should be broadly classified as probiotics since they too have probiotic effects, especially immunological ones (Tsukahara T, 2005).

Common Probiotics

Lactobacillus acidophilus, Lactobacillus lactis, Lactobacillus plantarum, Lactobacillus bulgaricus, Lactobacillus casei, Lactobacillus helveticus, Lactobacillus salivarius, Bifido bacteria, Enterococcus faecium, Enterococcus faecalis, Streptococcus thermophilus, Escherichia coli bacteria, and other probiotic fungi like *Saccharomyces cerevisiae* and *Saccharomyces boulardii* are the most widely used probiotics(McFarland, 2006; Naseem et., 2023). The assertion is that microbial products enhance performance and feed conversion for the targeted species, lower morbidity or mortality, and benefit consumers by improving the quality of the product. Genetically modified organisms (GMOs) are being used for biomedical purposes in a novel way, with recombinant probiotics and alternative gene therapy as their basis. There are no clinical adverse effects from probiotic therapy.

Mechanism of Action of Probiotics

Since Lactobacillus and Bifidobacterium are not pathogenetic, they are typically regarded as beneficial bacteria for health. As a result, fostering these beneficial bacteria may enhance host health. The use of live bacterial supplements improves the intestinal microbial equilibrium of the host animal, which has a positive impact on the animal's health(Ohashi and Ushida, 2009).

Pathogens struggle to survive in the gut because probiotics compete with them for nutrition and receptor-binding sites. Short-chain fatty acids (SCFA), organic acids, hydrogen peroxide, and bacteriocins are produced by probiotics and serve as anti-microbial agents, reducing the number of harmful bacteria in the gut. Probiotics also help the intestinal barrier.

Function by promoting the synthesis of mucin proteins, controlling the expression of tight junction proteins like claudin 1 and occluding, and controlling the immunological response within the gut (Latif et al., 2023).

Probiotics have several important methods of action, including modifying the gut microbiota by feeding some helpful bacteria and preventing harmful bacteria from colonizing the gut, which preserves the integrity of the gut mucosa. Probiotics provide a food supply for host-beneficial bacteria like Lactobacillus (LAB) and Bifidobacteria in the lower GIT rather than being digested or absorbed in the upper GIT(Adhikari and Kim, 2017).In the end, this prevents infections, such as Salmonella, from attaching and fosters gut flora. Certain sugars can prevent infections from adhering to the mucosa. For instance, MOS can attach to the mannose-specific lectin of gram-negative bacteria, including E. coli that produces Type-1 fimbriae, causing the bacteria to be expelled from the intestine. Yeast and the outer cell of yeast are common sources of MOS. It has been discovered that MOS alters the immune system and gets rid of infections in the digestive tract. (Adhikari and Kim, 2017)

Recent Advancements in the Feed Additives

As grazers, livestock production also contributes significantly to the restoration of carbon (C) to grassland ecosystems, as well as to the improvement of biodiversity and wildlife habitat. Therefore, strategies for reducing enteric CH4 emissions must be developed without compromising cattle output. In addition to adding to the greenhouse gas emissions from the production of livestock, enteric CH4 emissions also represent an energy loss of up to 11% of the gross energy intake from food (Moraes et al., 2014). Enteric CH4 emissions can be effectively reduced by changing the diet and adding feed additives. Since feed additives may be more economical, they might end up being an effective approach (Roque et al., 2019). Feed additives can reduce enteric CH4 emissions from ruminants by directly interfering with the methanogenesis process, which prevents the production of CH4. Chemical inhibitors are the term for these additives (Kelly and Kebreab, 2023). Numerous studies have demonstrated that adding zeolites to the diet increases feed conversion and/or average daily gain in pigs, sheep, and broiler chickens. Zeolites also improve sows' ability to reproduce, raise dairy cows' milk yields and laying hens' egg output, and have positive impacts on egg weight and internal egg features(Filippidis et al., 1996; Mumpton and Fishman, 1977). Zeolites supplementation appears to be an effective, supplementary, supportive strategy in the prevention of certain diseases and the improvement of animals' health condition, aside from the good impacts on animals' performance(Placinta et al., 1999). Because they have layered crystalline structures and comparable physicochemical properties to zeolites, phyllosilicates like bentonite and hydrated sodium calcium aluminosilicates (HSCAS) have been successfully applied to poultry, pigs, sheep, cattle, and lab animals for this reason (Papaioannou et al., 2005) represented in table 1.

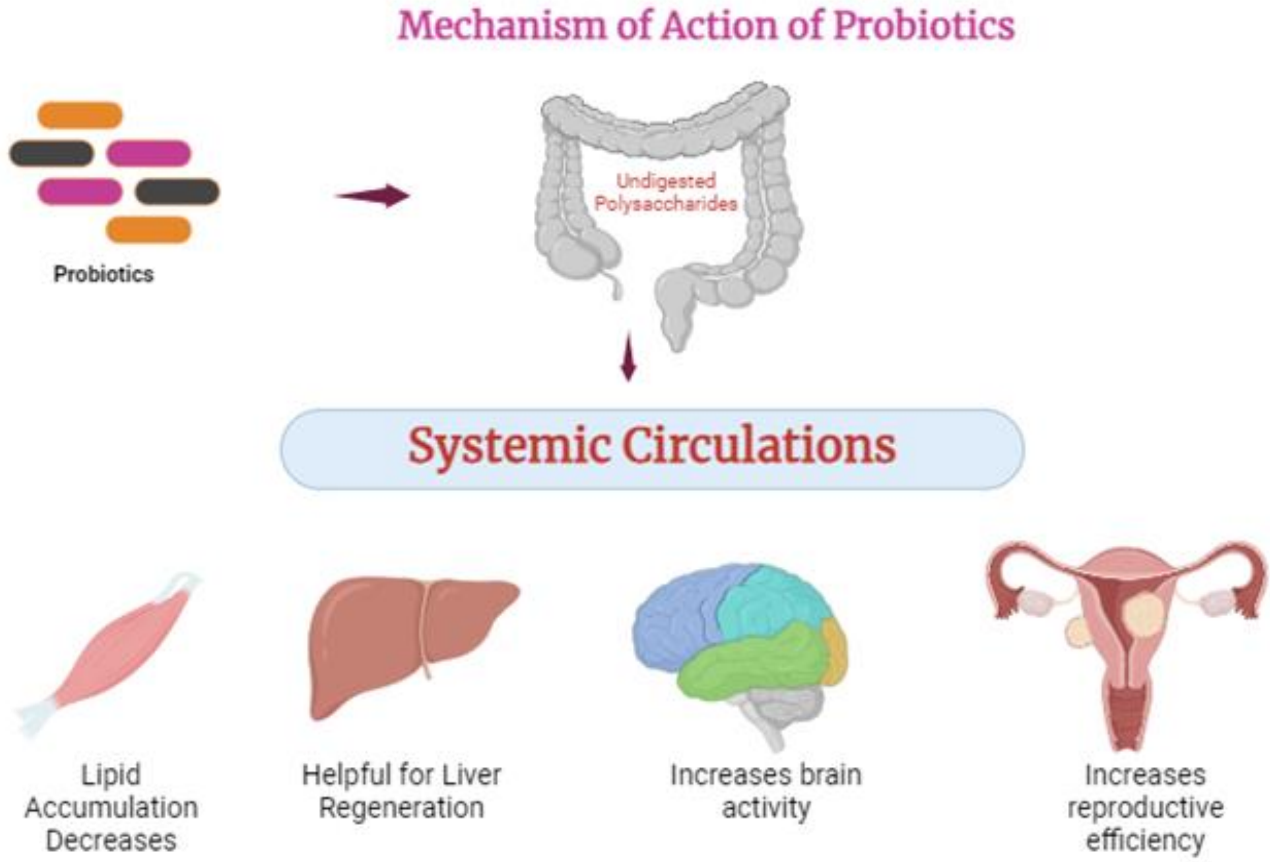

Fig. 2: Mechanism of action of probiotics.

Table 1: Effects of Various Feed Additives on Ruminant Health and Performance

Feed additive	Source	Effects	References
Essential oils	Anise, thymol, eugenol, cinnamon	Decrease protozoa Increase *S.ruminatum, R.albus, B.fibrisolvens* fungi	(Cardozo et al., 2006; Fraser et al., 2007)
Condensed tannins	*Calliandra calothyrsus*, waterdock roots, persimmon fruit	Decreased cellulolytic and proteolytic bacteria, strong antiparasitic properties	(McSweeney et al., 2001; Mueller-Harvey et al., 2019)
Saponins	Chinese chives, tea, yam tubers	Decreased protozoa, decreased CH4, improved feed digestion and ruminal fermentation	(Ramdani et al., 2023)
Ionophores	Monensin, lasalocid, narasin, salinomycin	Improve ruminal fermentation, decreased acidosis and bloat, reduced methane production	(de Sales Silva et al.)
Probiotics	*Aspergillus oryzea, S. cerevisea,B.cereus, E.facieum*	Increase weight gain and feed conversion, decrease incidence of diarrhea	(Al-Jaf and Del, 2019)

Conclusion

In the commercial livestock industry, ensuring sustainable animal production requires addressing several important issues, including environmental protection, public acceptance, consumer safety, animal welfare, and sustainability. Protein, phosphate, and water resources can be maintained, contaminants can be decreased, and performance can be improved by raising feed conversion. So, further advancements in Supplements containing probiotics, prebiotics, and probiotics lead to the stimulation of animal development, boosting immunological function and improving health in animals. Probiotics such as Lactobacillus and Bifidobacterium help to maintain gut microbiota. The development of animals' digestive tracts depends on pro- and prebiotics, metabolic modifiers, and antibacterial agents. Metabolic modifiers affect the metabolism of antimicrobial drugs, but pro- and prebiotics have distinct effects on digestive processes. Enzymes enhance general health, decrease digestive problems, and facilitate digestion. They can be applied to elderly animals to improve on-site feedstuffs with high dietary fiber content or nutrients that are poorly digested, while also reducing nutrient release. Additive feeding appears to have a promising future. To boost meat production, conserve feed, and resist disease, nutritionists are always creating new and improved additives.

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