Chapter 01

Recent Trends on Probiotics and Prebiotics in the Gut Health of Animals

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ABSTRACT

In the past two to three decades, efforts to enhance human health have concentrated on developing live microbial supplements, or "probiotics," that can alter the body's natural gut flora. Probiotics constitute a significant and continuously expanding portion of the global functional food market, accounting for around 65% of this enormous industry with a projected value of US$75 billion. Lactic acid bacteria, which include bifidobacteria, enterococci, and lactobacilli, are the most common active ingredients in probiotic products. Probiotics have been linked to a wide range of health benefits, like immune system stimulation, reduction of lactose intolerance, maintenance of normal and healthy intestinal flora, and protection from infections. Probiotics are a group of strains that have been shown to have positive effects and can be found in products in rather large quantities. Furthermore, typically present in the human gastrointestinal tract, bifidobacteria and lactobacilli are thought to be advantageous. They can be promoted by non-digestible food elements such as oligosaccharides, which are referred to as prebiotics. Probiotics and prebiotics can be combined to create a food product known as a synbiotic, which is likely intended to target two "target regions" of GIT.

KEYWORDS
Probiotics, Prebiotics, Synbiotics, Gut disease

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INTRODUCTION

Probiotics were first proposed in 1908 by Nobel Prize winner Eli Metchnikoff, who hypothesized that Bulgarian peasants' long lives were because of the use of fermented milk products. Stillwell and Lilly used the word "probiotic" in 1965 to mention chemicals generated by one organism promoting the growth of another. They were designated as "microbial components of microbial cells that have a beneficial effect on health and well-being" (Gareau et al., 2010).

Numerous microorganisms that are present in the gastrointestinal tract, in the mouth, and on the skin, coincide closely with humans. With a surface area of around 400m^2, the GI tract has the largest concentration of commensal microorganisms. This constitutes the body's second largest surface area, behind the respiratory tract. More than 500 different bacterial species are found in the rich flora of the gastrointestinal tract (GIT), and some of them offer substantial health benefits such as improving the immune system, shielding the host from invasive viruses and bacteria, and facilitating the digestion. The gut microbiota is critical to maintaining human homeostasis, and is acquired quickly after birth, and stays mostly constant throughout life. An individual and distinct intestinal immune system evolves as a result of connections between the developing intestinal microbiota and the host. The task of the host mucosal immune system is to differentiate between benign and infectious species by inducing protective immunity while evading an overabundance of inflammation that could compromise the integrity of the gastrointestinal mucosa. (Tsilingiri and Rescigno 2013).

Among other forms of treatment, the usage of immunosuppressive medication, antibiotics, and radiation may change the composition and impact of the flora. Therefore, recreating the microbial equilibrium and preventing disease may be made easier by the introduction of beneficial bacterial species into the GIT (Marteau et al., 2002).

The Greek word "for life" is where the term "probiotics" originated. The probiotics are "live micro-organisms," which, when given in sufficient proportions, impose health advantage on the host, according to an expert panel that was commissioned by the Food and Agriculture Organization (FAO) and World Health Organization (WHO). The bacterial genera Enterococcus, *Streptococcus, Bifidobacterium, Bacillus, Escherichia*, and *Lactobacillus* are most frequently utilized in the formulations of probiotics. Moreover, a few Saccharomyces fungal strains have also been employed (Di Lena et al., 2015).

The first probiotic, *Lactobacillus rhamnosus* GG (LGG), has gotten the most medicinal interest thus far. Since the *Lactobacillus* strain that dairy companies had previously employed for fermentation could not colonize the gut, *Lactobacillus rhamnosus* strain GG was identified in 1985 through the creation of a list of optimal characteristics for probiotics. It has been demonstrated that *Lactobacillus rhamnosus* strain GG improves gut immunity. Payer's patches experience an increase in antigen uptake due to the increased number of IgA and other immunoglobulin-secreting cells in the intestinal mucosa, localized release of interferons, and facilitated antigen transport to core lymphoid cells (Zendeboodi et al., 2020).

Prebiotics are indigestible food elements that work to improve the health of the host by favourably provoking the development of a specific bacterium or a group of related microbes in the colon. Prebiotics are dietary carbohydrates, such as inulin, gluco-oligosaccharides, and fructo-oligosaccharides circumventing the digestion in the upper gastrointestinal tract and alter the type of substrate that is available to the gut's resident bacteria population. This leads to changes in the bacterial composition of the gut. Probiotics as well as prebiotics are examples of synbiotics. They raise the likelihood that bacteria will survive in the gastrointestinal tract, which increases their beneficial effects (Gupta and Garg 2009).

Selection Criteria of Probiotic Strain

A methodical approach is necessary for the selection of probiotic bacteria, employing a procedure similar to the one illustrated in Fig. 1. Most of the time, a "step-by-step approach" involving a series of tests to gradually narrow down a pool of potential probiotic candidates is necessary due to the high number of isolated strains. The strains exhibiting the greatest number of efficient qualities and, consequently, no unfavorable features are chosen after this process.

- Microorganisms should be capable to communicate or send messages to immune cells linked with the stomach.
- The capacity to endure in the intestine even if the probiotic strain is unable to colonize the stomach
- Should be nonpathogenic
- Resistance to processing

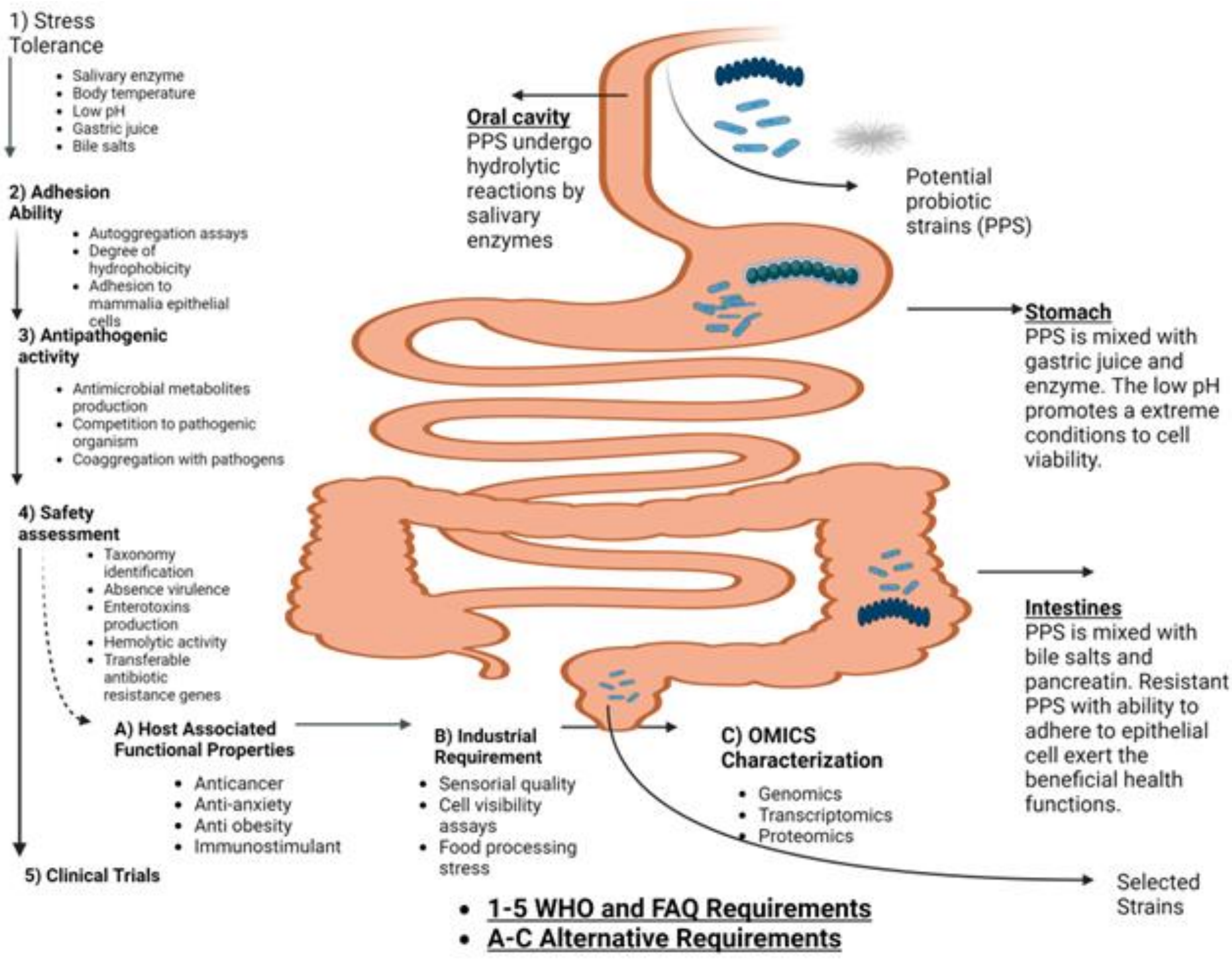

Fig. 1: Depicts the screening methods used for characterizing probiotic strains. According to studies by (Chang et al., 2001; Divya et al., 2012; Fiorda et al., 2016; Luna and Foster, 2015; Maragkoudakis et al., 2006; Ooi and Liong, 2010; Persichetti et al., 2014; WHO/FAO).

Table 1: Micro-organisms used as Probiotics (Jin et al., 2000)

Lactobacillus Spps.	*Bifidobacterium* Spps.	*Streptococcs* Spps.	*Saccharomyces* Spps.	Others
L.paracasei *L.plantarum* *L.reuteri* *L.salivarius* *L.bulgaricus* *L. johnsonii*	*B. adolescentis* *B. infantis* *B. longum* *B. lactis*	*S. thermophiles* *S.salivarius subsp thermophilus*	*S. boulardii*	*Bacillus cereus* *Escherichia coli* *Propionibacterium*

Mechanism of Action

Probiotics can be categorized according to how the bacteria specifically affect the immune system, allergy disorders, microbial milieu, cancer, intestinal epithelium, and distant mucosal locations.

Antimicrobial Effects on Microflora

Probiotics have long been thought to work by altering the microbiota in the body. A number of studies indicate that eating specific species of lactobacilli can raise endogenous levels of these bacteria and decrease concentrations of E. coli and Bacteroides clostridium in feces. However, the most significant effect is on the flora's metabolic activities, as these bacteria have been shown to reduce the production of substances that cause cancer, like fecal azoreductase, β-glucoronidase and nitroreductase (Wollowski et al., 2001). It's still unclear if colonization is necessary for probiotics to work.

Neonatal reaction to preparations of probiotics depends on gestational age, postnatal age, weight, and previous exposure to antibiotics. A study on infants, found that colonization with Lactobacillus GG happened in 21% of infants weighing less than 1500g compared to 47% of bigger infants. The antibiotic's usage interfered with the probiotic's capability to colonize (Shi and Walker 2004).

Production of Antimicrobial Factors

Short-chain fatty acids, which probiotics produce, can decrease the pH of the colon and promote the growth of less harmful microorganisms. Antimicrobial proteins, called bacteriocins, are produced by probiotic organisms and particularly are potent against Gram-Positive Bacteria. Moreover, lactobacilli generate chemicals that render virus particles inactive (Cadieux et al., 2002). Within minutes, soluble compounds generated by *Lactobacillus fermentum* RC-14 and *Lactobacillus rhamnosus* GR-1 render vesicular stomatitis virus and adenovirus inactive. Lactobacillus GG is a producer of antimicrobial chemicals like lactic acid, hydrogen peroxide, and pyroglutamate, which hinder the growth of several gram-negative and gram-positive bacteria. Furthermore, *Lactobacillus acidophilus* strain LA1 generates an antibacterial agent that is not lactic acid nor bacteriocin and that is effective against a range of gram-negative and gram-positive bacteria (Lievin et al., 2000).

Competition for Nutrients

Probiotics can also compete with pathogenic organisms for the nutrients that they would then absorb. For instance, a probiotic that consumes monosaccharides may inhibit the growth of Clostridium difficile, a bacterium that needs monosaccharides to flourish.

Probiotics as Immune Modification Vehicles

It is possible to genetically modify probiotics like lactobacilli to emit chemicals like IL-10 that have an anti-inflammatory impact. The gastrointestinal tract's inflamed parts may locally release anti-inflammatory cytokines when the host consumes these genetically modified probiotics. (Steidler et al., 2000).

Effect on Humoral Immunity

Numerous studies show that a wide range of probiotics can reliably and powerfully induce a certain type of antibody response. IgA antibody responses specific to the rotavirus are induced by the viable *L. casei* strain GG. Furthermore, by influencing the generation of virus-neutralizing antibodies, the two strains of probiotics—*Lactobacillus acidophilus* CRL431 and *Lactobacillus rhamnosus* GG induced an immunologic reaction against the poliomyelitis vaccine virus. Additionally, in an animal model, eaten *B. bifidum* markedly augmented the amount of immunoglobulin (IgA, IgG, and IgM) secreting cells in the spleen and mesenteric lymph nodes. (Saikali et al., 2004).

Anti-proliferative Effect of Probiotics

Probiotics have the ability to affect several intestinal processes, including immunological status, transit, detoxification, and colonic fermentation. These effects may be linked to the emergence of colon cancer. Probiotic use has been shown to have direct antiproliferative effects on immunological and malignant cells. It has been demonstrated that modulating gut and systemic immunity in rats and specifically reducing carcinogenic bacterial enzymes have the potential to have major antiproliferative effects against colon cancer. The indication is still growing, and additional study is needed, but data point to a favorable role for probiotics in preventing colon cancer (Marotta et al., 2003).

Functional Properties

Growth Promotion in Farm Animals

Probiotic bacteria break down hydrocarbons, which implies food is being broken down into its utmost basic components. This permits nearly complete absorption via the gastrointestinal tract. Probiotics, therefore, significantly improve overall nutrition and promote cellular development and growth at a rapid pace. For example, in young pigs, Bifidobacteria and Lactobacillus boosted weight gain and decreased mortality. Additionally, pigs fed *Bacillus coagulans* performed better than pigs treated with sub-therapeutic antibiotics, with reduced mortality, improved feed conversion, and weight gain compared to un-supplemented piglets.

Defense against Intestinal Infections in the Host

Probiotics help to cleanse the gastrointestinal tract. They penetrate the intestinal walls' layer of filth, attach themselves, and lift the buildup of deterioration. After that, this waste naturally disappears. Probiotic supplements help avoid and occasionally treat fungal and yeast infections. By the production of antimicrobial compounds competing with the pathogens for nutrients, encouraging the intestinal immune system, and adhering to the intestinal mucosa, probiotic bacteria added to feed may defend piglets against pathogens of the intestine through a diversity of potential mechanisms (Ellin, 2001).

Relief of Constipation

Probiotics rapidly alleviate constipation and restore regular bowel motions. You can take lactobacillus both during and after an antibiotic course of therapy. This lessens the symptoms of antibiotic-induced diarrhea, which is brought on by the gastrointestinal tract's "bad" and "good" bacteria dying off randomly.

Anti-carcinogenic Effect

Carcinogenic intestinal beta-glucouronidase and nitroreductase are rendered inactive by Lactobacillus. Research conducted at the University of Nebraska and Sloan Kettering Institute for Cancer Research demonstrated that Lactobacillus inhibits the growth of tumors and has a clear anti-tumor effect. Further research is necessary; however, animal studies have indicated that some lactic acid bacteria may aid prevent colon cancer (Walker and Duffy, 1998; Zabala et al., 2001).

Nutrient Synthesis and Bioavailability

Probiotic strains of Lactobacillus plantarum produce lysine, one of the amino acids that are immediately digested by the body. They generate B vitamins, which function as biocatalysts in the metabolism of food and combat stress. These include pantothenic acid, B6, niacin, folic acid, B12, and riboflavin (Koop-Hoolihan, 2001).

Diseases Treated by Probiotics

- Treating atopy
- Irritable bowel syndrome
- Antibiotic-associated diarrhea
- Traveler’s diarrhea
- Infectious diarrhea
- Necrotizing enterocdiarrheaolitis

Prebiotic Introduction

One may quite readily impact nutrition, which is continuously recognized as one of the most important environmental elements influencing human health, both individually and as a whole in the population. Functional meals have gained popularity recently among lay people who are attempting to live better lives as a result of education and training, as well as among professionals. Food that offers additional health advantages from nutrients whose nutritional value improves the consumer's physical and mental well-being in addition to traditional elements is referred to as functional food. Particularly useful ingredients in nutritious foods are minerals, vitamins, prebiotics, and probiotics. The notion of prebiotics and probiotics is often regarded as the most noteworthy development in the realm of intestinal microbiota support and nutrition. (Hijová et al*.,* 2019)

Prebiotics are beneficial food ingredients, produced artificially by converting carbohydrates through an enzyme process or naturally occurring in foods derived from plants. These substances are often soluble dietary fibers or carbohydrate structures that are preferentially digested by bacteria both within and outside the body. Thus, this activity promotes the growth of particular microorganisms and benefits the host's health. (Gibson et al*.,* 2010). A fresh definition that defies the notion that prebiotic effects must be specific/selective has recently been put out in light of the rapidly expanding field of diet-gut microbiota interactions (Bindels et al*.,* 2015). For generations, people have been consuming foods high in prebiotics; estimates place daily consumption for hunter-gatherer populations as high as 135g (Leach et al*.,* 2010). Banana, sugar beet, beans, human breast milk, artichokes, rye, barley, cow's milk, onion, garlic, tomato, and asparagus are natural sources of prebiotics (Cooper et al*.,* 2022).

Professors Roberfroid and Gibson coined the term "prebiotics" in 1995. Prebiotics were part of the functional food concept that was prepared by both of them. In general, prebiotics are described as "nondigestible food components that pass into the colon in their undamaged state, are resistant to the action of hydrolytic enzymes at the top of the GIT, and beneficially affect the microflora of the host organism by selectively stimulating the growth and/or activity of one or limited number of bacteria in the colon and thus improving the host's health" (Gibson and Roberfroid 1995). The term "selectively fermented ingredients that allow specific changes, both in the composition and/or activity in the gastrointestinal microflora that confer benefits upon the host well-being and health" was added to prebiotics definition in 2004 (Gibson et al., 2004). Prebiotics are now defined to include non-carbohydrates and their mode of act is no longer restricted to the gastrointestinal system or to specific foods (Gibson et al., 2017).

Substances used as Prebiotics

According to earlier research, prebiotics are oligosaccharide carbohydrates, primarily xylooligosaccharides (XOS), lactulose, inulin, and the fructose-oligosaccharides (FOS) that are generated from them (Yin et al., 2022; Zhao et al., 2021). Recent research, however, has shown that prebiotics also include other non-carbohydrate substances that satisfy the prebiotic requirements, such as polyphenols that have been extracted from fruits like black raspberries (Gu et al., 2019) and blueberries (Jiao et al., 2019).

Fructans

The most varied class of prebiotics that are commercially accessible are called fructans, and they comprise fructose polymers that are not digested. A review of their impacts on bone mineral density and calcium absorption has been conducted (Roberfroid et al., 2010). The bulk of glycosidic links in every chain of these molecules is beta (b) (2–1) fructosyl–fructose connections, which is one of their defining characteristics. In addition to being naturally occurring in plant-based foods including asparagus, bananas, artichokes, onions, and wheat, these chemicals can also be produced synthetically (Sabater-Molina et al., 2009).

Galactooligosaccharide

Oligosaccharides galacturonic GOS is a novel functional material with inherent qualities that the body finds difficult to absorb and digest. GOS are made up of two to eight sugar units, of which two are galactose and disaccharides (which contain two galactose units) and one is terminal glucose (Delgado-Fernandez et al., 2021).

A combination of galactose-based oligosaccharides with variable DP and connections to various monomers of sugar, such as lactose, and glucose, results in GOS, a well-known prebiotic component. The various health benefits of GOS are explained by their unique oligosaccharide composition. Research has demonstrated that GOS promotes the development of useful gut flora like lactobacillus, and bifidobacteria in early life stages because these substances resemble human milk oligosaccharides which support immunity and gut health in nurturing newborns (Fanaro et al., 2005).

Research on animals has shown that the ingestion of GOS in postmenopausal rat models led to a noteworthy elevation in the calcium content of the skeleton in ovariectomized rats (Chonan et al., 1995) and mineralization of bone in male rats (Weaver et al., 2011). It has also been shown that dietary GOS increases postmenopausal women's absorption of calcium (van den Heuvel et al., 2000).

Lactose Derivatives

The main disaccharide included in dairy products is lactose. It is a combination of galactose and glucose sugar monomers linked by glycosidic bonds. It has been demonstrated that rats fed a diet high in lactose and calcium had stronger and more mineralized bones (Schaafsma et al., 1987). Lactase's enzyme activity diminishes with age in humans, which may permit microbes to break down this sugar when it enters the lower gastrointestinal tract (Misselwitz et al., 2013). Since people with lactose intolerance absorb more calcium from milk containing lactose than people with usual lactase action, this could lead to a larger absorption of minerals (Griessen et al., 1989). Some examples of prebiotics production are given in Fig. 2.

Functional Properties of Prebiotics

When consumed in suitable amounts, probiotic-living microorganisms benefit the health of the host by colonizing the body. Probiotics have the capability to transform the human intestinal microbes' composition and prevent harmful bacteria from colonizing the intestines. Additionally, probiotics have been shown to have the capacity to support the body's development of a robust intestinal mucosa layer, strengthening the function of the intestinal barrier and boosting immunity (Wang et al., 2021). The promotion of prebiotics is necessary for the growth and replication of probiotics. Prebiotics are substances—mostly polysaccharides—that the body is unable to process and absorb. They can aid in the development or propagation of live microorganisms within the host (Li et al., 2021).

Prebiotics influence metabolism, strengthen immune regulation, fend off infections, improve mineral absorption, and generally improve health (Peredo-Lovillo et al., 2020) (Fig. 3). Prebiotics come from a diversity of sources and are typically defined as certain microalgae, oligosaccharides, polysaccharides, and natural plants. The main sources of emerging prebiotics include seeds, peels, fruit juice, algae, polysaccharide- and polyphenol-containing microorganisms, and traditional Chinese medicine (Quigley 2019).

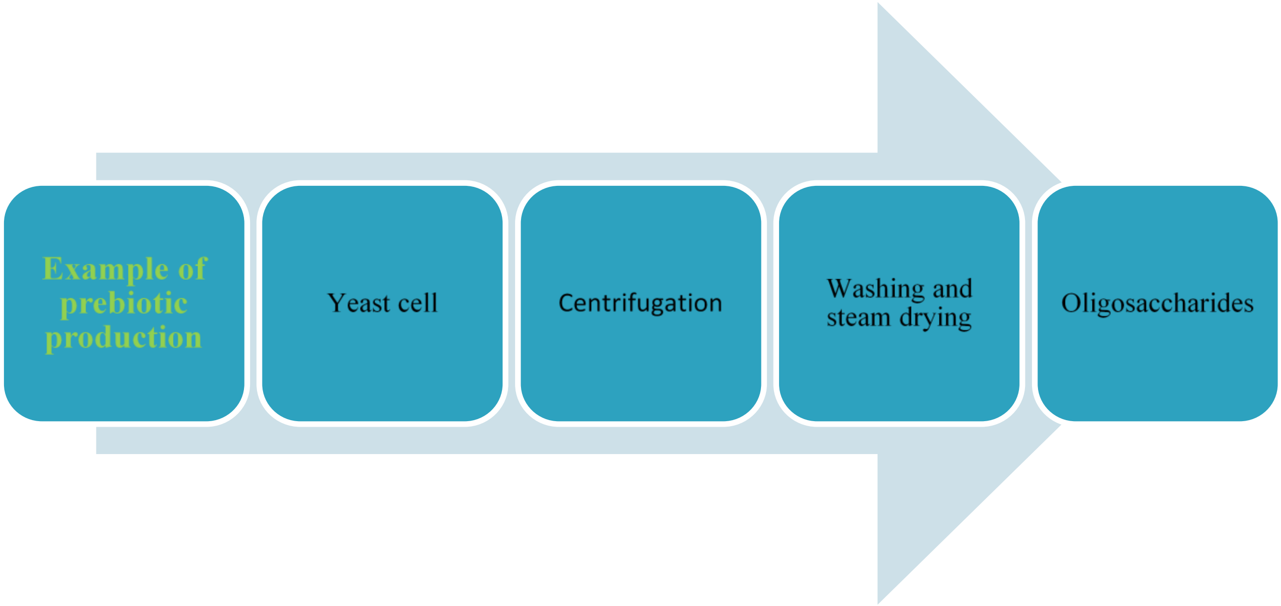

Fig. 2: Example of prebiotic production

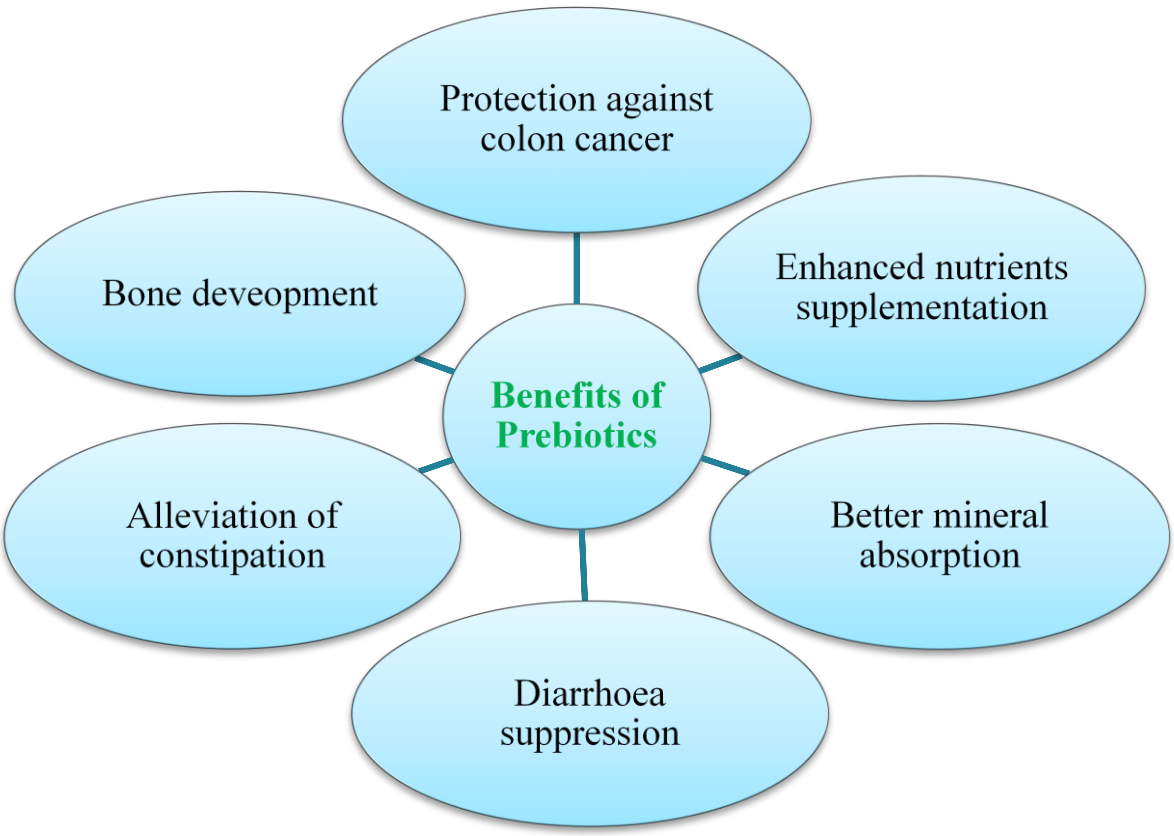

Fig. 3: Benefits of Prebiotics

Mode of Action

Prebiotics can generally withstand digestion in the small intestine by remaining in the gastrointestinal system because of absence of enzymes in the human gut that break down their polymeric bonds. Prebiotics are subsequently supported by the body intact to large intestine, where intestinal flora breaks them down and selectively ferments them to produce definite secondary metabolites. These types of metabolites are then engrossed by intestinal epithelium or go to the liver via the portal vein. These metabolites have positive impacts on the physiological processes of the host, including pathogen resistance, immunity regulation, and increased absorption of minerals, decreased blood lipid, and improved intestinal barrier function (Guarino et al., 2020).

Beneficial bacteria in the gut metabolize the most prevalent SCFAs, such as propionate, butyrate, and acetate, which are good for preserving systemic and intestinal health (Baert et al., 2020) (Fig. 4). Additionally, one particular benefit of prebiotics is that they support the growth of the target bacteria. By safeguarding or encouraging the creation of advantageous fermentation products, they might encourage the proliferation of useful flora to contend with other species following the consumption of particular prebiotics (FOS, inulin, and GOS) (Ashaolu 2020).

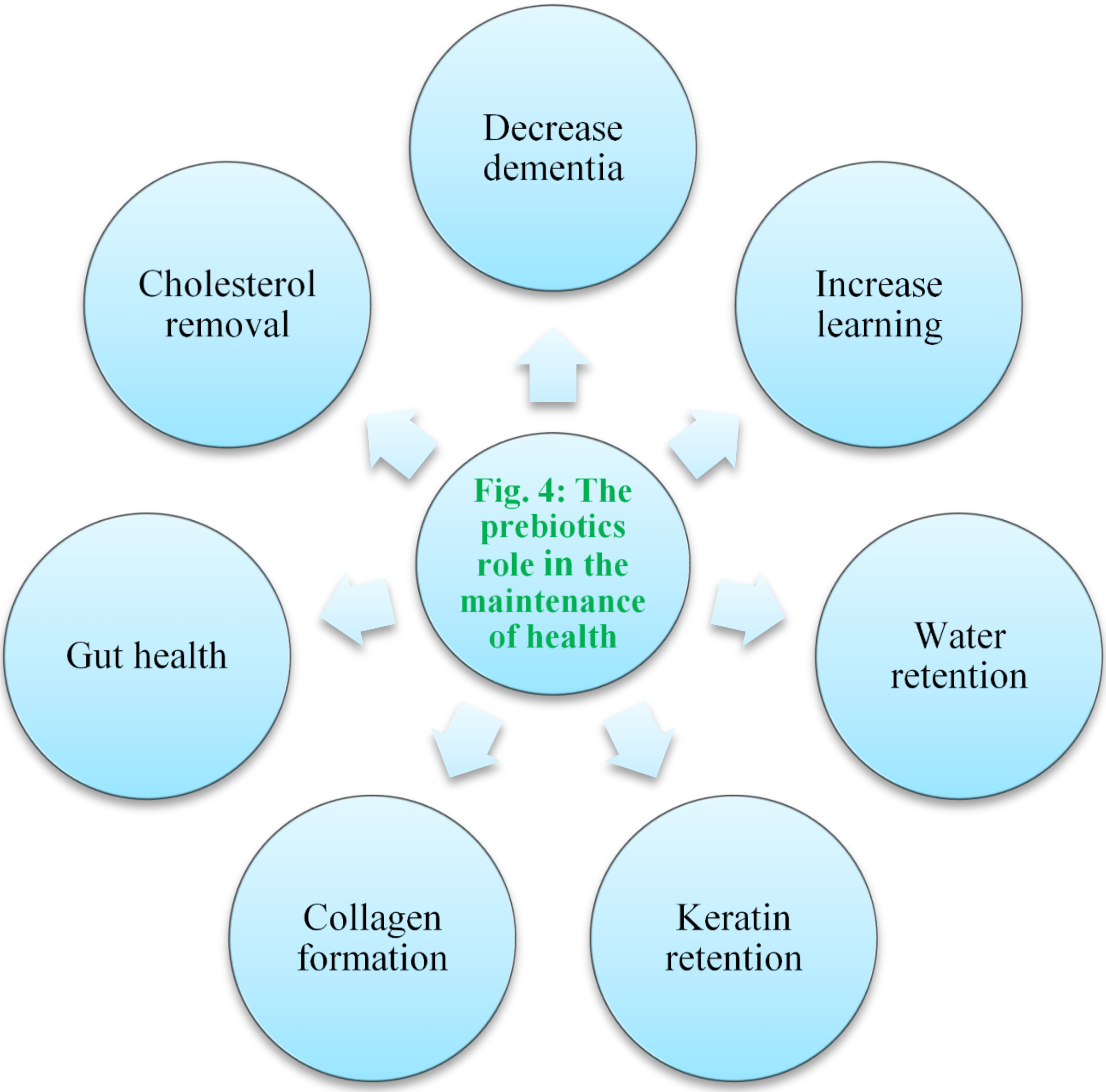

Fig. 4: The prebiotics role in the maintenance of health

Synbiotics and their Importance for Animals

The word "synbiotic" has historically been used to describe a mixture of probiotics and prebiotics increasing the survivability of probiotics that are eaten (Pandey et al., 2015). Combining prebiotics with different chain lengths and monomer connections is one way to use synbiotics; this has been demonstrated to extend the prebiotic impact over a wider GI tract (Coxam 2005). The criterion that each independently delivers a health benefit and that each dose be sufficient to independently accomplish those benefit(s) is shared by definitions of prebiotics and probiotics (Gibson et al., 2017). Long-chain prebiotics such as inulin may be digested more distally or beside a prolonged stretch of the gut, but short-chain prebiotics like oligofructose are thought to be processed in the proximal colon. Often referred to as ITF-mix, this most frequently reported prebiotic mixture has variable chain lengths and is made up of inulin-type fructans. It has been proved that this combination improves bone health outcomes and the absorption of magnesium and calcium in both postmenopausal ladies and adolescents (Abrams et al., 2007).

Prebiotics and plant polyphenols work synergistically, and this has extensive implications for bone health as well (Devareddy et al., 2006). Research on synbiotics—which assesses how well prebiotics work in conjunction with probiotics—is expanding quickly. At the moment, Bifidobacterium species are the most researched in synbiotic applications concerning the health of bones. According to a study, adding GOS to two species of Bifidobacterium—Bifidobacterium bifidum and longum—markedly improved the bioavailability of calcium, magnesium, and phosphorus as well as the mineral content of the hind limbs (Pérez-Conesa et al., 2007).

Up until now, prebiotics and probiotics have had an excellent safety record (Van den Nieuwboer and Claassen 2019), and synbiotics made with them may likewise be considered safe for the same purposes. Nonetheless, new formulations need to be properly evaluated for safety (Ioannidis et al., 2004).

Future Prospects of both Probiotics and Prebiotic

Research on the impact of probiotics on cardiovascular conditions, such as atherosclerosis and myocardial infarction, is being focused on a large scale (Loscalzo et al., 2011). According to neuro-gastroenterologist Dr. Gershon's working hypothesis, there is an enteric nervous system that plays a part in gut physiology and other related gut illnesses (Gershon, 1998). By comprehending the function of BMicrobials endocrinology, the study of the ability of microorganisms to produce and respond to neurochemicals that originate either within the microorganisms themselves or within the host they inhabit, the aforementioned notion can be addressed. Probiotics both produce and react to neuroactive substances (Roshchina 2010).

Conclusion

It is commonly well-known that intestinal flora plays a substantial part in both maintaining health and also preventing disease. Its constant "communication" or interaction with the immune system, endocrine system, central nervous system, and environment reveals the intricate underlying systems. If this delicate equilibrium is upset, it can cause various problems and make it easier for a disease to spread. In particular, it has been proposed that microbiologists ought to be heavily involved in strain isolation, mechanism of action testing, and "packaging these into steadfast products for usage of humans (Potera, 1999). Probiotics and prebiotics most likely have distinct "target" areas. Important information is still required despite the surge in papers on probiotic organisms published in recent years by microbiologists, nutritionists, food scientists, and doctors. More cutting-edge techniques should be created to track modifications in gut flora's makeup and how they interact with the host's metabolism and immune system.

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