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Review on Synergistic Effects of Probiotics, Prebiotics, and Synbiotics on Gut Microbiota Homeostasis

Ghulam Murtaza[1], Zaighum Abbas[2], Sabeen Gul[3], Asfa Karam[4], Nadia Cheema[2], Maham Zahra[4], Sarwat Abbas[5], Fazil Ali[6], Abdul Kabir[7], Muhammad Kamal Shah[8], Muhammad Sajid[9]

[1]Department of Anatomy, University of Agriculture, Faisalabad, Punjab, Pakistan.
[2]Department of Biotechnology, University of Sialkot, Punjab, Pakistan.
[3]Department: Microbiology, Abasyn University, Islamabad campus, Pakistan.
[4]Department of Food Science and Human Nutrition, University of Veterinary and Animal Sciences, Lahore, Punjab, Pakistan.
[5]Institute of Industrial Biotechnology, Government College University, Lahore, Punjab, Pakistan.
[6]Bachelor of Science in Microbiology and Biotechnology, University of Lahore, Punjab, Pakistan.
[7]Department of Veterinary Microbiology, Sindh Agriculture University, Tando Jam, Sindh, Pakistan.
[8]Faculty of Veterinary Sciences, Gomal University, Dera Ismail Khan, KP, Pakistan.
[9]Faculty of Veterinary Sciences, University of Agriculture, Faisalabad, Punjab, Pakistan.

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Corresponding Author: Muhammad Kamal Shah
Faculty of Veterinary Sciences, Gomal University, Dera Ismail Khan, KP, Pakistan .
Email: kamaluaf560@gmail.com

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ABSTRACT

Functional foods are an essential part of the contemporary diets, and it is evident that these foods contain the health benefits in addition to the familiar nutritional effects. Probiotics and prebiotics together is referred to as synbiotics and are presently the most popular functional food ingredients. The most commonly used probiotic strains are Lactobacilli, Bifidobacterium, S. boulardii and B. coagulans. Some of the most used fibers are galacto-oligosaccharides (GOS), fructo-oligosaccharides (FOS), xylose-oligosaccharide (XOS), inulin, and fructans when blended with probiotics are referred to as synbiotics and are efficient in provoking the growth of the bacteria.

INTRODUCTION

Probiotics are live microbes that, when ingested in an inadequate amount, have been reported to benefit the host's health (FAO/WHO, 2002). On the other hand, probiotics have been defined as live microbial feed additives that modify the intestinal microbiota of the host animal (Thilagavathi, 2020). Probiotics were initially utilized to improve the health of the intestinal tract of microorganisms. The manipulation of the gut microbiota affects both animals and humans, and the various recognized strains of bacteria, which is used for the following reasons, such as humans utilize *lactobacilli* and *bifidobacteria* to prevent, and treat

gastrointestinal (GI) illnesses (Kim *et al.*, 2019). The benefits of using probiotics may include the following such as probiotics have a number of health advantages, such as: probiotics help maintain intestinal health by controlling microbiota, boosting and strengthening the immune system, facilitating nutrient synthesis and bioavailability, lessening the signs and symptoms of lactose intolerance, and lowering the risk of a number of other illnesses. Probiotics have mostly been utilized to prevent and cure gastrointestinal infections and illnesses (Maldonado Galdeano *et al.*, 2019). In this review, it is worth noting that changes in gut microbiota have been associated to greater vulnerability to specific diseases; thus, the concept of probiotic therapy involves attempting to rectify an unhealthy indigenous microbiota (Gomaa, 2020). Furthermore, the use of alternative or adjuvants therapies, such as, bacterial replacement therapy, is emerging as a significant factor due to the rapid generation of antibiotic-resistant pathogenic strains and the side effects of antibiotics beneficial microorganisms, which in turn heightens the risk of infection (Terreni *et al.*, 2021). However, prior to probiotic consumption, more in-depth research on the benefits and pitfalls of probiotics is required.

METHODS

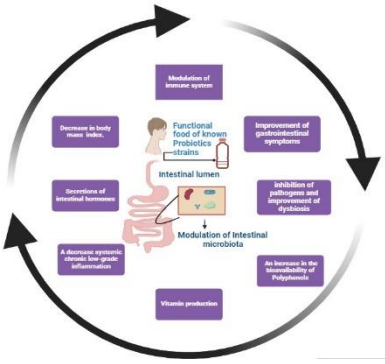
The current review was designed using an exhaustive and systematic search of the literature about various medicinal and health benefits of probiotic and prebiotics between 2010 and 2024. The explorations were performed using databanks, including Google Scholar (http://www.scholar.google.com/ (accessed on 18 June 2024), Science Direct (http://www.sciencedirect.com/ (accessed on 19 June 2024) Scirus (http://www.scirus.com/ (accessed on 20 June 2024) and PubMed (http://www.ncbi.nlm.nih.gov/pubmed (accessed on 21 June 2024). In our literature review, we concentrated on the latest research papers using the keywords: " probiotic," " prebiotics," " Synbiotics," "bioactive compounds," and " their medicinal properties".

Functional Foods

Foods in which ingredients have been added or modified during manufacturing and are then sold for the benefits, they will provide to customers/consumers. Sometime other relevant nutrients are added to prepared functional food, such as vitamin D supplementation in milk. Functional foods are traditional foods with ingredients or components that provide a particular therapeutic or physiological benefit in addition to nourishment as shown in Fig.1. All functional foods must satisfy three consecutive sets of requirements, such as it should be in the form of food, it will not a pill, tablet, or powder, and it can be consumed every day and should have a function in the body to prevent or control a disease (Granato *et al.*, 2020).

Figure 1

Functional Food of Known Probiotics, and their Significant Applications



Functional Foods as Immune Function

Nutrition can impact immunological function at any stage in the human life cycle. The potential ingredients that could be used for the production of functional foods, would enhance the immune response are consist of trace elements such as manganese, zinc, copper, n-3 and n-6 PUFAs, nucleotides, l-arginine, prebiotics, probiotics and synbiotic (Kim *et al.*, 2019).

Functional Foods as Gut Health

The gastrointestinal system is a natural focus for the production of functional foods since it links dietary intake to all other stages of metabolism. the GI system requires an optimum balance of beneficial bacteria, to avoid the invasion of harmful bacteria. Using ingredients to alter gut microbiota composition and metabolic activity is a promising field for functional food development, such as prebiotics, probiotics, and synbiotics (probiotic and prebiotic combinations) (Wan *et al.*, 2019).

Functional Food Classification

Functional foods are mainly categorized in three classes, such as Prebiotic, Probiotic, and Synbiotics (Gomaa, 2020).

Probiotic

The term "probiotic," derived from the Greek phrase "for life," is commonly used to describe microorganisms that have a favorable impact on both humans and animals. When administered in adequate quantities, living microbes provide the host with health benefits. When taken in sufficient numbers, living bacteria known as probiotics can give health benefits that go beyond simple nutrition. Probiotics are a microbial dietary supplement that boosts the host's health.

Probiotics are living microorganisms such as yeasts, Bifidobacterium, and Lactobacillus. These chemicals have a positive impact on human health by improving the balance of the intestinal microbiota when ingested in specific amounts (Anadón *et al.*, 2021). In fact, the fermentation process carried out by microbes was one of the oldest ways to produce and preserve food. The soured milk and cultured dairy products were widely used in medicine. These common beliefs are confirmed by current, well-conducted scientific research, which shows that probiotics are a vital component of a healthy diet. The stomach produces chyme when food and gastric fluids containing hydrochloric acid and digestive enzymes interact. The breakdown of food proteins, lipids, and carbohydrates is completed in the small intestine, where extra enzymes and bile are mixed. After the small intestine has received the majority of the nutrients, the colon, or large intestine, receives the remaining nutrients. Water and electrolytes are absorbed here, while wastes are expelled via the rectum. The gut is a complex ecosystem in which the host and intestinal microbes are in delicate balance (Mani, 2018). Microbes complete the digestion of any meal components left undigested in the small intestine in the large intestine. Lactose, which is intolerant to lactose, and certain fibers that are resistant to the enzymes of the small intestine are two examples of these components. The gut microbiota is critical for maintaining a regulated inflammatory response, developing adequate intestinal architecture, and maturing the immune system. However, the microflora strengthens the gut mucosa's barrier function, preventing allergens from penetrating and dangerous microorganisms from attaching. Furthermore, some microorganisms may assist the body satisfy its vitamin requirements. Probiotics include *Lactobacillus, Bifidobacterium* (commonly known as lactic acid bacteria or LAB), *Enterococcus*, *Streptococcus thermiphilus*, *Lactococcus, and Saccharomyces*. Although bacteria account for the vast majority of probiotics on the market today, one form is a yeast known as *Saccharomyces boulardii* (Thilagavathi, 2020). When it pertains to probiotics' impacts on the health of humans, it's crucial to take into account that various strains of bacteria, might have differed benefits. As a result, the health benefits of a given probiotic may differ depending on the testing conditions. Nonetheless, a lot of studies suggest that some strains, when taken in adequate proportions, have a positive influence on human health, particularly with regard to diarrhea, antibiotics, irritable bowel syndrome, inflammatory bowel disease, lactose intolerance, hepatic encephalopathy, immune system, vaginal infections, *Helicobacter pylori*, kidney stones, cholesterol, allergies and eczema (Sanders *et al.*, 2018). Some of the health attributes of probiotics are discussed in Tab.1.

Table 1
Health Attributes of Probiotics

Attribute	Description	Example Strains/Sources	References
Microbial Balance	Maintains gut bacteria balance.	Lactobacillus acidophilus, Bifidobacterium bifidum	(Kim et al., 2019)
Digestive Health	Supports digestion and relieves issues.	Lactobacillus rhamnosus, Saccharomyces boulardii	(Wan et al., 2019)
Immune Support	Boosts immune system.	Lactobacillus casei, Bifidobacterium lactis	(Terreni et al., 2021).
Anti-inflammatory	Reduces inflammation.	Lactobacillus reuteri, Bifidobacterium longum	(Anadón et al., 2021)
Nutrient Absorption	Enhances nutrient absorption.	Lactobacillus plantarum, Bifidobacterium breve	(Quintieri et al., 2024)
Mental Health	Improves mood and mental health.	Lactobacillus helveticus, Bifidobacterium longum	(Maftei et al., 2024)
Skin Health	Improves skin conditions.	Lactobacillus rhamnosus GG, Bifidobacterium lactis	(Kushwaha and Maurya, 2024)
Metabolic Health	Regulates metabolism.	Lactobacillus gasseri, Bifidobacterium breve	(Ansari et al., 2023)
Antimicrobial Properties	Inhibits harmful bacteria.	Lactobacillus salivarius, Lactobacillus reuteri	(Bilal et al., 2024)
Lactose Intolerance Relief	Helps digest lactose.	Lactobacillus bulgaricus, Streptococcus thermophilus	(Wang and Zhong, 2024)

Probiotic Foods for Improved Gastrointestinal Health

Probiotics, which target gastrointestinal microbes, have been found to help prevent and treat illnesses. Probiotic bacteria, such as *Bifidobacteria, and Lactobacilli* can assist the gastrointestinal tract become more metabolically active. Clinical trials have confirmed their therapeutic capabilities, and they have been successfully integrated into functional and nutritious food formulations. Probiotics help the immune system by improving antimicrobial activity, increasing immunological defense cells, regulating metabolic enzymes, and preventing degenerative processes. Probiotic advantages differ according to the target group

and microorganisms. Colonic foods, such as probiotics, prebiotics, and synbiotics, can assist enhance digestive health (Wang and Zhong, 2024). Some of the benefits of probiotic foods are discussed below, Lactic acid production lowers intestinal pH and inhibits pathogens such as *Salmonella, E. coli, Shigella*, and *Clostridium*. Reduce the generation of hazardous or carcinogenic metabolites, Improves mineral absorption, particularly calcium, by increased intestinal acidity, produce β-D galactosidase enzymes to break down lactose, Produce antimicrobial compounds like acidophilin and bacitracin to combat harmful microorganisms, and Produce vitamins, including K and B, and act as barriers: prevent hazardous microorganisms from invading the intestines (Maftei *et al.*, 2024). In addition to their nutritional value, probiotics have numerous health benefits. Probiotics have been used in fermented foods for many years. Probiotics may have health benefits in addition to their primary function. Supplementing fermented foods with Lactobacillus and Bifidobacterium species can increase their health advantages (Kushwaha and Maurya, 2024). Probiotic cultures that have been shown to promote human health in dairy products include *L. acidophilus*, *Bifidobacterium spp*., and *L. casei*, as well as yeast and *Bacillus* species (Maftei *et al.*, 2024; Quintieri *et al.*, 2024).

Probiotics Preventing and Treating Various Diseases

The current review has provided evidence that the use of probiotics can help infants with atopic eczema. It has also been proven that consuming of probiotics by expecting mothers and to the new born immediately after birth may decrease the rate of allergy incidences in infants who are allergin prone by fifty percent. It has been believed that the taking of probiotics assists in the development of healthier immune system that results to less allergies. (Xue *et al.*, 2023). Helicobacter pylori is pathogenic bacterium that causes peptic ulcers, gastritis, gastric ulcer and gastroesophageal reflux disease; probiotics and antibiotics are known to be safe and effective for this infection. These include the use of antibiotics to treat Helicobacter pylori, although this remedy like most treatments involving the use of antibiotics is costly and is associated with quite uncomfortable side effects. (Wang *et al.*, 2023). According to research, probiotic bacteria contained in food can help treat and prevent children's diarrhea. *Rotavirus* infections are a common cause of childhood diarrhea. In study trials, children with the virus who drank probiotic-fermented milk saw fewer episodes of diarrhea. Probiotic therapy has been used successfully to treat antibiotic-associated diarrhea (Săsăran *et al.*, 2023). Bacteria ferment milk, causing the protein to degrade into smaller peptides. The small intestine is where peptides are absorbed. Clinical research has shown that ingesting these peptides in milk and yogurt can lower blood pressure in certain people (Althnaibat *et al.*, 2023). Probiotic consumption facilitates waste passage through the intestines more quickly. Constipation is lessened, and colon cancer may be avoided. Prebiotics are a kind of fiber that can speed up the intestines' transit time (Xue *et al.*, 2023). Probiotics and prebiotics can aid in the prevention of infections in sick and post-operative patients. Antibiotics destroy gut flora, thus eating probiotics and prebiotics to replenish the digestive tract can help prevent infection (Aljaberi *et al.*, 2023). Lactose intolerance is caused by an absence of the digestive enzyme lactase (Maftei *et al.*, 2024). Lactase, an enzyme produced by probiotic bacteria, aids in the digestion of lactose. Probiotics can help with natural immune functions (Xue *et al.*, 2023). Probiotics can prevent cancer by reducing DNA damage produced by carcinogens, as shown in both in vitro and animal studies (Kim et al. 2019). LAB can degrade bile in the gut and prevent it from being reabsorbed as cholesterol in the circulation (Maftei *et al.*, 2024). Some the health benefits, sources of probiotics are discussed in Tab.2.

Table 2
Health Benefits of Probiotics

Health Benefit	Description	Example Strains/Sources	References
Improved Digestion	Aids food breakdown and absorption.	Lactobacillus acidophilus, Bifidobacterium longum	(Anadón et al., 2021)
Reduced Risk of Diarrhea	Prevents and treats diarrhea.	Saccharomyces boulardii, Lactobacillus rhamnosus	Quintieri et al., 2024)
Enhanced Immune Function	Strengthens immune response.	Lactobacillus casei, Bifidobacterium lactis	(Terreni et al., 2021).
Alleviation of IBS Symptoms	Reduces IBS symptoms.	Bifidobacterium infantis, Lactobacillus plantarum	(Wan et al., 2019)
Lowered Cholesterol Levels	Lowers LDL cholesterol.	Lactobacillus reuteri, Bifidobacterium longum	(Kim et al., 2019)
Blood Pressure Regulation	Helps reduce blood pressure.	Lactobacillus helveticus, Bifidobacterium lactis	(Wang and Zhong, 2024)
Prevention of Allergies and Eczema	Reduces allergies	Lactobacillus rhamnosus GG,	(Wang and Zhong, 2024)

	and eczema risk.	Bifidobacterium breve	
Weight Management	Aids in weight loss and belly fat.	Lactobacillus gasseri, Bifidobacterium breve	(Ansari et al., 2023)
Mental Health Support	Improves mental health conditions.	Lactobacillus helveticus, Bifidobacterium longum	(Terreni et al., 2021).
Enhanced Oral Health	Improves oral health.	Streptococcus salivarius, Lactobacillus reuteri	(Inchingolo et al., 2023)

Prebiotics

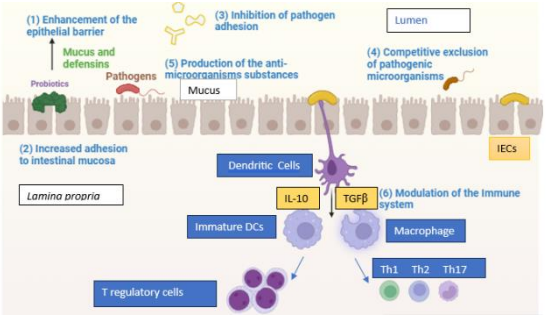
A prebiotic is an indigestible substance that confers health benefits to the host by selectively promoting the growth and/or activity of a single or small group of intestinal bacteria. Non-digestible food elements that may benefit the gut flora by improving its condition are referred to as prebiotics. Prebiotics, also known as bifidogenic factors, are mostly oligosaccharides that preferentially promote the growth of bifidobacteria (Roberfroid *et al.*, 2010). These include pyrodextrins, lactilol, lactosucrose, lactulose, fructooligosaccharides, isomalto-oligosaccharides, transgalactooligosaccharides, and xylo-oligosaccharides (Kumar and Sharma, 2024). Prebiotics offer antimicrobial, anticarcinogenic, hypolipidemic, glucose-modulatory, and antiosteoporotic effects. They can be used to treat inflammatory bowel diseases, constipation, and hepatic encephalopathy. They may provide some help in diabetes mellitus and be able to guard against some intestinal infections in addition to potentially having good lipid effects (Palai *et al.*, 2020). In addition, prebiotics are also involved in the process of mineral homeostasis and absorption; i. e they might enhance the intestinal absorption of certain minerals. Prebiotics are categorized as non-digestible substances which can selectively effect metabolic activity of certain bacterial species populating the intestine and/or stimulate their growth; therefore, prebiotics are supposed to enhance the state of the gut. Also under research is their capacity for minimizing the probabilities of colon cancer besides enhancing the immune system. Some of the minerals which are absorbed in the large extent, for instance calcium and magnesium, have been linked to enhanced synthesis of short chain fatty acids in the colon. Whole Wheat, Rye; Barley; Chicory Roots, Onions; Garlic; and Inulin (Mande *et al.*, 2023). It has been suggested that an increase in colonic *bifidobacteria* will benefit human health by lowering blood ammonia levels, producing vitamins and digestive enzymes, and generating compounds that combat potential infections (Kumar and Sharma, 2024).

Prebiotics Application

Prebiotic's chemical composition enables them to reach the colon without being broken down. A fraction of the material enters the large bowel after passing through the small and pancreatic intestines in the human body. Microorganisms with population densities and species distributions that are typical of specific gut areas can be found throughout the human gut. Adults have a shorter transit duration in the small intestines (4-6 hours) than in the large intestines (48-70 hours), hence the larger intestines have far more stable colonies. Large microbial colonization and growth are further fostered by the pH and the colon's relatively low absorptive state (Bedu-Ferrari *et al.*, 2022). This bacterium permits the colon to carry out complex hydrolytic digesting processes. This involves the breakdown of complex proteins, carbohydrates that are not absorbed or hydrolyzed in the upper gastrointestinal tract, and dietary components. The colonic microbiota feeds on nutrients such as dietary fiber, non-digested protein, and non-digestible oligosaccharides. They also get nourishment from mucin, the major glycoprotein component of mucus. As a result, prebiotics can be found in any undigested food that enters the colon, including nondigested carbs, certain proteins, and certain lipids. There have been several claims made regarding the health advantages of prebiotics for people. It serves as a substrate for the beneficial bacteria in the stomach (Rawi *et al.*, 2020). Functional foods and their role in gut microbiomes defense as shown in Fig.2.

Figure 2

Role of Functional Foods in Gut Microbiomes Defense



Synbiotics

The word "synbiotic" refers to food product that contain both probiotics and prebiotics, that benefit from both the inclusion, and stimulation of beneficial bacterial development. The most effective synbiotic combinations include *bifidobacteria* and fructo-oligosaccharides (FOS), *Lactobacillus* GG and inulins, and *bifidobacteria* and *lactobacilli* with FOS or inulins (Swanson *et al.*, 2020). Through the specific stimulation of one or a small number of health-promoting bacterial

growth and/or metabolism, a synbiotic product helps the host by enhancing the survival and implantation of live microbial dietary supplements in the gastrointestinal system. Given the reference to synergism in the name "synbiotics," products where the prebiotic compound(s) preferentially affect the probiotic organism(s) (Arruda *et al.*, 2022). Synbiotics were created to address potential survival challenges for probiotics. Synbiotics are believed to promote probiotic bacteria survival in the upper intestine. Ke et al. (2021) found that efficient colon implantation and the establishment of probiotics and bacteria promote intestinal homeostasis and overall health. Probiotic viability in dairy products, such as yogurts, can be affected by many parameters such as pH, H^2O^2, organic acids, oxygen, and moisture stress (Ke *et al.*, 2021) as shown in Tab.3. Synbiotic formulations use probiotic strains such as *Lacbobacilli*, *Bifidobacteria spp.*, *S. boulardii*, and *B. coagulans*, as well as prebiotics such as fructo-oligosaccharides (FOS), GOS, and xylose-oligosaccharides (XOS), inulin, and prebiotics from natural sources such as chicory and yacon roots. Synbiotics have been shown to improve human health by increasing lactobacilli and bifidobacteria, improving liver function in cirrhotic patients, improving immunomodulation, preventing bacterial translocation, and reducing nosocomial infections (Scorletti *et al.*, 2020).

Table 3
Probiotic Microorganisms and Foods

Probiotic Microorganisms	Probiotic Foods	Prebiotic Foods	References
Lactobacillus species	Yogurt (plain, no added sugar, active cultures)	Garlic	(Swanson et al., 2020)
Lactobacillus acidophilus	Buttermilk	Onions	(Scorletti et al., 2020)
Lactobacillus amylovorus	Acidophilus milk	Leeks	(Ke et al., 2021)
Lactobacillus brevis	Kefir	Asparagus	(Arruda et al., 2022
Lactobacillus casei	Tempeh	Bananas	(Rawi et al., 2020)
Lactobacillus rhamnosus	Kimchi	Barley	(Bedu-Ferrari et al., 2022).
Lactobacillus crispatus	Sauerkraut	Oats	(Roberfroid et al., 2010)
Lactobacillus delbrueckii subsp. Bulgaricus	Kombucha	Apples	(Wang and Zhong, 2024)
Lactobacillus fermentum	Pickles	Flaxseeds	Kumar and Sharma, 2024)
Lactobacillus gasseri	Miso	Wheat Bran	(Mande et al., 2023).
Lactobacillus helveticus	Dark chocolate	Artichokes	(Palai et al., 2020).
Lactobacillus johnsonii	Sourdough bread	Berries	(Wang et al., 2023)
Lactobacillus lactis	Cheese (aged)	Black beans	(Scorletti et al., 2020)
Lactobacillus paracasei	Cottage cheese	Cherries	Ke et al., 2021)
Lactobacillus plantarum	Fermented meats	Dandelion greens	(Kim et al. 2019).
Lactobacillus reuteri	Fermented vegetables	Chicory root	(Anadón et al., 2021)
Lactobacillus salivarius	Fermented grains	Chickpeas	(Mande et al., 2023).
Lactobacillus gallinarum	Kombucha	Eggplant	(Terreni et al., 2021).
	Kvass	Endive	(Wan et al., 2019)
Bifidobacterium species	Lassi	Honey	(Panesar et al., 2022)
Bifidobacterium adolescentis	Natto	Legumes	(Xue et al., 2023)
Bifidobacterium animalis	Raw vinegars	Lentils	Quintieri et al., 2024)
Bifidobacterium breve	Sour cream	Mangoes	Quintieri et al., 2024

Health Benefits of Probiotics, Probiotics and Synbiotics

Probiotics have demonstrated benefits such as preventing diarrhea and constipation, altering bile salt conjugation, improving antibacterial activity, and reducing inflammation. Probiotics boost nutrient synthesis and bioavailability, and some have anti-oxidative effects through intact cells or lysates. Probiotics help alleviate symptoms of allergies, cancer, AIDS, respiratory and urinary tract infections. Modern studies indicate that they can potentially aid in, autism, osteoporosis, fatigue, obesity, type 2 diabetes, and aging (Panesar *et al.*, 2022).

CONCLUSION

In conclusion, this review has examined probiotics, prebiotics, synbiotics and their systemic effects on the immune system, metabolism, and general health of the host. Probiotics must be used in conjunction with prebiotics in order to maintain a strong synergy between the them and improve their therapeutic benefits. Probiotics have several health advantages for human, plants, and animals. Probiotic applications present a number of challenges. Probiotics have proved exceptional health advantages to individuals in regards to how their use may reduce the use of antibiotics for the treatment of illnesses, such as traveler's diarrhea, reducing the likelihood of antimicrobial resistance and other health issues caused by microbiota imbalances.

Finally, it is critical to develop global standards for probiotics and prebiotics, as well as functional health claims on the label, to assure product efficacy and safety.

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