Impact of Probiotics and Prebiotics on Human Health and Disease

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Abstract

The profound impacts of probiotics, prebiotics, and their synergistic combinations (synbiotics) on human health emphasize their potential for managing and preventing various diseases. Probiotics, as live microorganisms, and prebiotics, as non-digestible dietary fibers, modulate gut microbiota, enhance immune function, and promote gut health through mechanisms such as competitive pathogen exclusion, immune response modulation, and production of beneficial metabolites like short-chain fatty acids (SCFAs). The clinical applications of these agents extend to managing gastrointestinal disorders, cardiovascular diseases, metabolic disorders, mental health conditions, and even anemia and cancer. Synbiotics further amplify health benefits by combining probiotics with prebiotics, fostering an optimal environment for gut microbiota. However, considerations of strain specificity, dosage, and individual variability are critical for maximizing efficacy and safety. Despite their potential, further research and precise clinical trials are needed to substantiate health claims and address possibility. This comprehensive study underscores the transformative potential of microbiome modulators in preventative and therapeutic healthcare strategies whereas advocating for regulatory oversight and evidence-based application.

Keywords: Probiotics, Prebiotics, Synbiotics, Synergetic effect, Clinical Applications

Cite this Article as: Fareed M, Anwar S, Khadim S, Jamil S, Qamar-Un-Nisa, Akram MA, Aslam M, Nighat F, Tahir S and Shehzad S, 2025. Impact of probiotics and prebiotics on human Health and disease. In: Aadil RM, Salman M, Mehmood K and Saeed Z (eds), Gut Microbiota and Holistic Health: The Role of Prebiotics and Probiotics. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 57-64. https://doi.org/10.47278/book.HH/2025.54

A Publication of Unique Scientific Publishers

Chapter No: 25-008

Received: 29-Jan-2025
Revised: 15-Feb-2025
Accepted: 13-March-2025

Introduction

In recent years, one of the major issues is to feed the over-growing population with high-nutritional foods in order to improve human health that depends mainly on immune system. To maintain or improve the immunity there are trillions of microorganisms including fungi, bacteria and viruses known as gut microbiome. Scientists are focusing on developing new strategies to shape healthier gut micro flora. The gut microbiomes have been evolving in response to diet, environment, or host body characteristics (Kim & Mills, 2024). This imbalanced condition known as dysbiosis may cause various health ailments including inflammatory bowel disease, cancer, diabetes, obesity, and hypertension (Goyat & Bhatnagar, 2024). The gut microbiomes in the form of probiotics, prebiotics, and synbiotics have significant potential to prevent disease occurrence while distinguishing the balance between good and bad bacteria for human health (Olvera-Rosales et al., 2021).

Probiotics are microorganisms that impart health benefits to the host when administered in suitable amounts. Mostly these are found in certain dairy products, fermented foods, and dietary supplements. The most common genera of these beneficial bacteria include *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces* that can promotes human health by regaining gut balance and modifying the immune responses (Wang et al., 2021). The necessary probiotic consumption is beneficial for diminishing the signs of IBS (irritable bowel syndrome) and minimising lactose intolerance symptoms. Additionally, probiotics itself contain various properties such as antiviral, anti-inflammatory and anti-carcinogenic effects (Youssef et al., 2021).

Unlike the probiotics, prebiotics utilized by the gut microbiome in order to provide them nutritional values. Prebiotics are commonly defined as the non-digestible carbohydrates including fructans, fructooligosaccharides, galactooligosaccharides, and resistant starch which improve the activity and growth of gut bacteria. Microbes like *Lactobacillus* and *Bifidobacterium* are the preferable targets for prebiotics. Studies have shown that prebiotics also improve the gut health of host by producing short-chain fatty acids (SCFAs) which reduce the gut pH and prevent pathogen growth (Yoo et al., 2024).

Currently, the interest of researchers has heaved towards the combined impact of probiotics and prebiotics. The combined effect of probiotics and prebiotics on the gut microbiota is known as synbiotics. The term 'synbiotics' as first coined at the meeting of International Scientific Association for Probiotics and Prebiotics (ISAPP). Synbiotics are the dietary products which contain the live bacteria (probiotics) with their specific growth-prompting substrates (prebiotics). This beneficial combination not only maintain the health of living bacteria, but

also improve their effectiveness on the gut (Dahiya & Nigam, 2022). Regardless of the promising, accessible and safe usage of these for modulating gut microbiota, certain precautionary measures need to be taken as this is not the solution of every health condition. However, with the efficient therapeutic potential, probiotics, prebiotics and synbiotics, get the major attention of researchers for maintaining the human health. In this chapter, we will discuss the latest research on probiotics and prebiotics with the focus on their mechanisms of action, human health benefits, clinical applications, synergetic effects, and potential risks on human health and diseases.

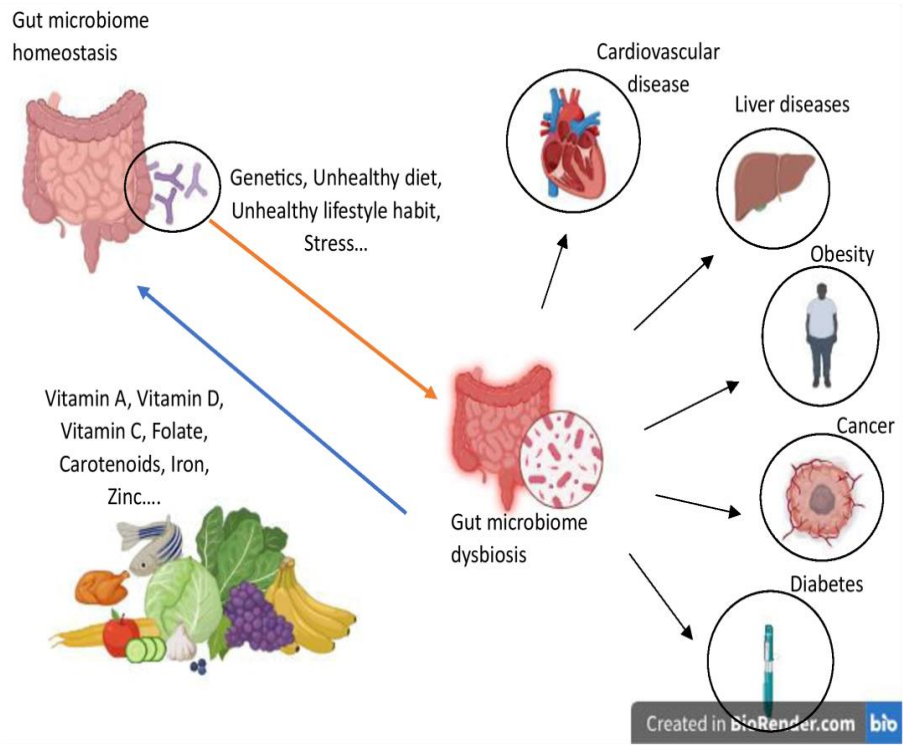

Fig. 1: Impact of Gut Microbes on health and disease (Retrieved from BioRender)

Probiotics

Since centuries probiotics have always been a vital and commercially target element due to their significant health improving effects. Probiotics are showing the promising effect on modulating the gut microbiota either are using as the nutrient supplements or complementary therapy. The effects of probiotics are not only limited to improving the composition of gut microbiota but also extended towards treating the various chronic health conditions. Different bacteria that are under the genera of *Lactococcus*, *Propionibacterium*, *Pediococcus*, *Enterococcus*, *Bacillus*, and *Streptococcus* are considered as probiotic strains. But the most common strains are under the *Bifidobacterium* and *Lactobacillus*. Although the probiotics are safe to use but some considerable properties still need to be considered. It should be survivable during the process such as production, delivery, storage and usage while maintaining their capability. They should be stable in acidic and bile conditions and capable of colonizing and adhering to the GI tract. Each strain must have a unique identification code and a human origin. Additionally, they should be resilient to various production processes and undergo thorough safety evaluations to ensure they are non-pathogenic, non-toxic, non-allergenic, and non-mutagenic (Ibrahim et al., 2023).

Mechanisms Action of Probiotics

With the introduction of the significant potential of probiotics for maintaining health, a considerable progress has been made in studying the efficacy of probiotics. Despite detailed studies on probiotics, a breakthrough in documenting their mechanism action has yet to be achieved. The possible mechanism actions of probiotics can be defined in various ways for treating the different types of health conditions as it has ability to colonize in the GI tract in customised manner depending on the type of microbiota and strain (Maftei et al., 2024). A mechanism involves the occupation of the binding sites as well as the nutrients by the probiotics in order to reduce the colonization of pathogens in the gut. By maintaining the balanced population in the gut, probiotics contribute to keep the balanced microbial environment (Mazziotta et al., 2023). Another mechanism involves growth encouragement of beneficial bacteria while decreasing the growth of harmful bacteria which plays a key role in gut homeostasis. Probiotic strains have ability to produce short-chain fatty acids including bacteriocin, which shows the inhibitory efficacy against wide variety of both bacteria (Gram-positive and Gram-negative), resulting an improved immune system of host (Ahire et al., 2021). Through another type of mechanism probiotics strengthen the intestinal barrier. The improved and strong intestinal barrier plays a vital role to stop the leakage of harmful substances into the bloodstream. Gut or intestinal barrier integrity enhanced by the probiotics through different ways including the regulation of tight junction protein expression (e.g. occludin and claudins), production of mucins, and controlling the immune response (Bu et al., 2022). Moreover, some probiotics have ability to modify the dendritic cells, macrophages, B & T lymphocytes to control the innate and adaptive immune system. Probiotics stimulates the production of anti-inflammatory cytokines when interact with intestinal epithelial cells while drawing the mononuclear cells and macrophages to regulate immune responses (Petruzziello et al., 2023). Probiotics strains that specifically regulate the production of neurotransmitters including

gamma-aminobutyric acid (GABA), serotonin and dopamine level can affect the different health conditions such as behaviour, mood and stress-related conditions (Sajedi et al., 2021).

Health Benefits of Probiotics

Nutritional Enrichment

Probiotics have been recognized for their health benefits for centuries, particularly in improving nutritional health. Initially linked to disease control, they are now incorporated into fermented and nutrient-rich foods to aid digestion. Common foods, such as yogurt and fortified milk, provide probiotics like *Lactobacillus* and *Bifidobacterium*. Studies suggest that fermented dairy products containing various probiotic strains can help reduce cardiovascular disease, metabolic syndrome, and obesity risks. Probiotics are also valuable for type 2 diabetes patients, with evidence showing that probiotic yogurt consumption may improve HbA1c and total cholesterol levels, aiding glycemic control and managing dyslipidemia (Mirjalili et al., 2023).

Immune System Modulation

Probiotics play a significant role in supporting immune health by prompting cellular metabolism and epithelial barrier functions through different mechanisms that involves enhanced mucus secretion, strengthened tight junctions, reduced bacterial adhesion, increased cell viability, and stimulation of defensins or immunoglobulin A (IgA) production. They can release anti-inflammatory cytokines within the gut with potential of impacting the various immune cells such as dendritic cells, cells in the epithelial lining, monocytes, macrophages, and lymphocytes (Mazziotta et al., 2023).

Intestinal Health Maintenance

The role of probiotics in maintaining intestinal health is well established. Probiotics contribute to the preservation of the epithelial barrier, stimulate cell survival, and help producing protective compounds including antimicrobial molecules and mucin and tight junction proteins. For maintaining the overall gut homeostasis, intestinal barrier plays a vital role by implementing the various barrier functions (chemical, immune and microbial). For example, *Lactobacillus acidophilus (LA) 1* can enhance the integrity of the intestinal barrier by reducing TNF-α-induced increases in epithelial tight junction permeability (Haque et al., 2024).

Clinical Application of Probiotics

Probiotics have gained great attention for their clinical applications in managing and preventing various health conditions. These medical conditions include diarrhea, constipation, cancer, inflammatory bowel disease, diabetes and many other. Before initiating clinical trials, various in vitro tests are used to evaluate the efficacy of probiotics. These methods include agar spot test, cross streak method, antimicrobial gradient diffusion, TLC-bioautography, and resazurin assay (Hossain, 2024). Current clinical trials of probiotics for different medical conditions are summarized in the Table 1.

Table 1: Clinical trials of probiotics for various medical conditions

Probiotic Strain	Clinical Application	Findings	References
Bifidobacterium bifidum	Immune modulation in respiratory infections	Reduces respiratory tract infection rates and enhances immune response	(Wu et al., 2024)
Lactobacillus casei	Oral mucositis in cancer therapy	Reduces severity and incidence of oral mucositis in chemotherapy patients	(Yang et al., 2024)
Streptococcus salivarius K12	Cancer-related oral mucositis	Decreases incidence of oral mucositis in cancer therapy patients	(Peng et al., 2024)
Lactiplantibacillus plantarum	COVID-19 management	Reduces nasopharyngeal viral load and shortens respiratory symptoms	(de Oliveira, 2024)
Bifidobacterium longum & *Lactobacillus plantarum*	Skin health	Alleviates symptoms of Allergic Rhinitis in children	(Jeong et al., 2024)

Probiotics for Gastrointestinal Disease Treatment

According to literature, probiotics exerts beneficial impacts on treating the diarrhea (traveler's diarrhea and acute diarrhea). During the acute diarrhea, probiotic strains help by inducing effect on immune signalling pathways, generating anti-pathogenic compounds, and prompting the host's own secretion of these factors to fight off intestinal infections. A study conducted by Haidry and collaborators, aimed to gauge the probiotic strain effect on children of age group of 6 months to 5 yrs (Haidry et al., 2024).

Probiotics for Heart Disease Treatments

With the promising impacts on human health, probiotic strains, especially *Bacteroides* are offering a natural approach for managing hypercholesterolemia and lowering cardiovascular disease risk by providing a safe alternative to conventional treatments. These strains have showed significant bile salt deconjugation property and upregulation of the *BT_416* gene, indicating a possible molecular mechanism for cholesterol reduction (He et al., 2023).

Probiotics for Controlling Obesity

The clinical applications of probiotics regarding to control the obesity, showing beneficial outcomes for not only controlling the obesity

but also other conditions such as type 2 diabetes and hypertension. In another clinical study, encompassing the consumption of probiotic capsules by obese people, concluding a significant reduction of insulin, weight, waist circumference and BMI along with decrement in cholesterol, and triglycerides (Hasani-Ranjbar et al., 2024).

Probiotics for Oral Diseases Treatment

Probiotics can reduce inflammation in the oral cavity, promoting gum and tooth health by countering harmful microorganisms. The *L. acidophilus* and *B. lactis* are considered natural, low-risk therapeutic options against oral fungal infections though effective strains should colonize the entire oral cavity without significantly altering pH. A meta-analysis of nine randomized trials concluded that probiotics may reduce caries frequency in preschool children (Panchbhai et al., 2024).

Probiotics for Urogenital Infections Treatment

Various urogenital infections, such as yeast vaginitis, urinary tract infections (UTIs), and bacterial vaginosis, are common in women. In premenopausal women, *Lactobacillus* species usually dominate the vaginal microbiota, supported by glycogen, pH, and high estrogen levels. In a recent placebo-controlled trial, 174 premenopausal women received either a vaginal probiotic, an oral probiotic, or both, resulting in significantly reduced UTI recurrences. This suggests that vaginal or combined probiotic supplements may serve as a non-antibiotic approach for recurrent UTI prevention (Gupta et al., 2024).

Probiotics in the Treatment of Anemia

Recent studies suggest that probiotics probiotics can play a supportive role in managing anemia, particularly iron-deficiency anemia, by enhancing iron absorption in the gut. Probiotics have been shown to improve iron absorption. A randomised control trial report that probiotic supplementation (especially *Lp299v*) in women of reproductive age and children can improve the iron absorption in both groups as well as enhance ferritin levels in women (Apte et al., 2024).

Prebiotics

Prebiotics are non-digestible dietary compounds that support the growth of gut beneficial microbiota, improving overall host health. Unlike probiotics, prebiotics were only defined as substrates selectively used by host microorganisms to confer health benefits (Han et al., 2023). Currently, prebiotics are exerting their various health benefits not only on GI tract but also on mental and cardiovascular systems. Prebiotics primarily are derived from non-digestible carbohydrates or fermentable dietary fibres, such as inulin and fructooligosaccharides (FOS). Other types of prebiotics consist of carbohydrate-based oligosaccharides (OSCs) with famous types including fructans, galacto-oligosaccharides (GOS), resistant starch (RS), and pectic oligosaccharides (POS), having specific structure and microbial effects. For instance, fructans like inulin support various bacteria depending on their chain length, especially in infants. All types of prebiotics are easily accessible through consumption of natural products. The prebiotics must be able to be fermented by microbes in order to stimulate their growth (Jenkins & Mason, 2022).

Mechanisms Action of Prebiotics

By considering getting the full advantages of health benefits from prebiotics, it is necessary to understand the mechanism of action of prebiotics. According to studies, prebiotics shows the complex mechanisms to affect the human health, specifically gastrointestinal health. Through these mechanism prebiotics can influence the composition of gut microorganisms, metabolic processes, immune responses, and the gut's barrier function. Prebiotics are the substrates that can be fermented by beneficial bacteria. As a result of this fermentation, the metabolites including short-chain fatty acids are produced to preserve the homeostasis in gut. Prebiotics, commonly including fibers such as inulin and fructooligosaccharides (FOS), are resistant to digestion in the upper digestive tract and reach the colon mostly unchanged. In the colon, they serve as a substrate for fermentation by specific bacteria, aiding to maintain microbial balance (Kumari et al., 2024). The produced SCFAs also decrease the colonic pH, maintaining the acidic environment in the colon that is favourable for beneficial bacteria (*Bifidobacterium spp*.) and inhibiting the pathogenic (*Bacteroides spp*) growth, resulting in improved gut health (Roupar et al., 2023).

Prebiotics can also influence immune function by promoting the growth of bacteria in order to maintain the immune system and reduce inflammation (Zhou et al., 2024). Additionally, prebiotics also improve the activity of immunes system cells (phagocytes and lymphocytes), resulting in inhibition of pathogenic bacteria and preserving the gut health (Rousseaux et al., 2023).

Health Benefits of Prebiotics

According to recent study, prebiotics offers wide range of health benefits that are not limited to digestive health but also extends towards the metabolic and mental health. The functional foods, particularly prebiotics and probiotics, have offered significant additional health benefits beyond basic nutrition (Obayomi et al., 2024).

Gut Health Maintenance

One of the major health benefit of prebiotics is it have ability to support gut health. This activity is achieved by promoting the growth of beneficial bacteria (*Bifidobacteria* and *Lactobacilli*) while inhibiting potentially pathogenic bacteria. Studies have shown that prebiotics like inulin and fructooligosaccharides (FOS) increase *Bifidobacterium* which are associated with reduced gut inflammation and enhanced gut barrier function (Dou et al., 2022).

Enhancement of Immune Function

The prebiotic fermentation generates SCFAs that interact with immune cells to promote anti-inflammatory cytokines and reduce

inflammatory responses. This immunomodulatory effect is particularly beneficial for individuals with autoimmune disorders or allergies (Seethaler et al., 2022).

Mental Health Benefits

The SCFAs produced from prebiotic fermentation are known to influence the central nervous system by crossing the blood-brain barrier or by signalling through the vagus nerve. The supplementation with GOS can reduce symptoms of anxiety in individuals with mild anxiety due to changes in gut microbiota composition and SCFA levels. This ability of prebiotics makes them a non-pharmacological option to support mental health (Facchin et al., 2024).

Clinical Applications of Prebiotics

The potential therapeutic uses of prebiotics have gained a lot of attention in the healthcare profession. Recent clinical studies demonstrate that prebiotics can affect the health of host and are beneficial therapeutic agents against various diseases ranging from gastrointestinal disorders to psychological conditions. Current clinical trials of prebiotics for different medical conditions are summarized in the Table 2.

Table 2: Clinical trials of prebiotics for various medical conditions.

Prebiotics	Clinical Application	Findings	References
FOS and GOS	Gastrointestinal Disorders	Improves symptoms of IBS and promotes gut barrier integrity.	(Gąsiorowska et al., 2022)
Insulin	Diabetes Management	Improves gut microbial proportion.	(Dixon et al., 2023)
Resistant Dextrin	Metabolic Health	improves sleep in women with obesity and type 2 diabetes.	(Saleh-Ghadimi et al., 2023)
FOS & GOS	Mental Health	Alleviates stress in adults	(Mysonhimer et al., 2023)

Prebiotics for Gastrointestinal Disorders treatment

Prebiotics like inulin and fructo-oligosaccharides (FOS) have a long history to shown to alleviate symptoms of irritable bowel syndrome (IBS) by reducing bloating and pain while improving stool consistency. In recent clinical study, embracing the oral consumption of GOS) supplementation by ulcerative colitis (UC) patients, concluding stool stabilization and improved number of *Bifidobacterium* and *Christensenellaceae,* but only for individuals with less active UC (Wilson et al., 2021).

Prebiotics for Psychological and Neurological Conditions

The gut-brain axis highlights the bidirectional communication between the gut microbiota and the central nervous system. SCFAs (propionate, acetate and butyrate) have been shown to exert beneficial affect for modulating the brain functions by directly influence the immune cells (endocrine and vagal neuronal) (Ashique et al., 2024). Recently, the effect of Galacto-oligosaccharides has been studied on the children with autism. Research findings showed that GOS positively impact the behaviour by modulating the *Bifidobacterium* level (Palmer et al., 2024).

Prebiotics for Bone Health

Prebiotics also play a critical role in calcium absorption hence contributing to bone health. Several Studies indicate that prebiotics such FOS and GOS enhance mineral bioavailability by lowering gut pH and facilitating calcium absorption in the colon (Peredo-Lovillo et al., 2020). A double-blind, RCT approach conducted to examine the effect of SCF in Malaysian children of age 9-11. Results showed a significant improvement in TBBMD by regulating the microbiome (Arasu et al., 2023).

Prebiotics for Anemia Treatment

The iron-deficiency anemia remains a global health challenge particularly in developing countries. Prebiotics promote the growth of iron-transporting gut bacteria, improving iron absorption in children from dietary sources. Currently, a randomized controlled trial performed on the Kenyan anemic infants with GOS supplementation, resulting in improved anemia along with mitigating the negative effects associated with iron supplementation (Mikulic et al., 2024).

Potential Risks and Considerations of Probiotics and Prebiotics

Some side effects including skin irritations, intestinal infections, migraine, and headache can be caused by ingesting the probiotics, especially for People with underlying treatments like chemotherapy (Liu et al., 2024). However, prebiotics showed minor side effect in case of high dosage. Moreover, some probiotic strains are genetically modified for increasing their beneficial aspects. To overcome the potential risks of consuming next-generation probiotics, some considerations must be kept in mind. Firstly, a thorough evaluation of probiotic strains such as safe usage, necessity dose, processing method is needed. Secondly, quality control in manufacturing is vital for ensuring product safety and proper practices are needed to avoid contamination and maintain consistency in probiotic potency. There is also need of proper labelling of probiotic-based product (dietary and drug) that will further ensure the safe consumption of these products (Roe et al., 2022).

Synergetic Affect

The health benefits of probiotics and prebiotics have led to the emergence of a new field known as synbiotics. In this synergetic combination, prebiotic is particularly selected by desired live probiotic bacteria for fermentation, promoting the microbial growth. The main purpose of this synergistic effect is to provide a favourable *in vivo* environment for probiotics and enhance beneficial characteristics of both (probiotics and prebiotics) (Roy & Dhaneshwar, 2023). Additionally, an easily fermentable substrate enhances probiotic survival, as the

prebiotic have ability to protect these live organisms from gastric acidity and proteolytic enzymes. To get the greater benefits than using probiotics or prebiotics alone, a great consideration is needed in selection of substrate as well as the microorganism in synbiotic combination. A recent study found synbiotic combinations safe and effective for improving anemia in haemodialysis patients (Kooshki et al., 2023). Such clinical studies highlight the growing importance of synbiotics in addressing specific health challenges and enhancing overall well-being.

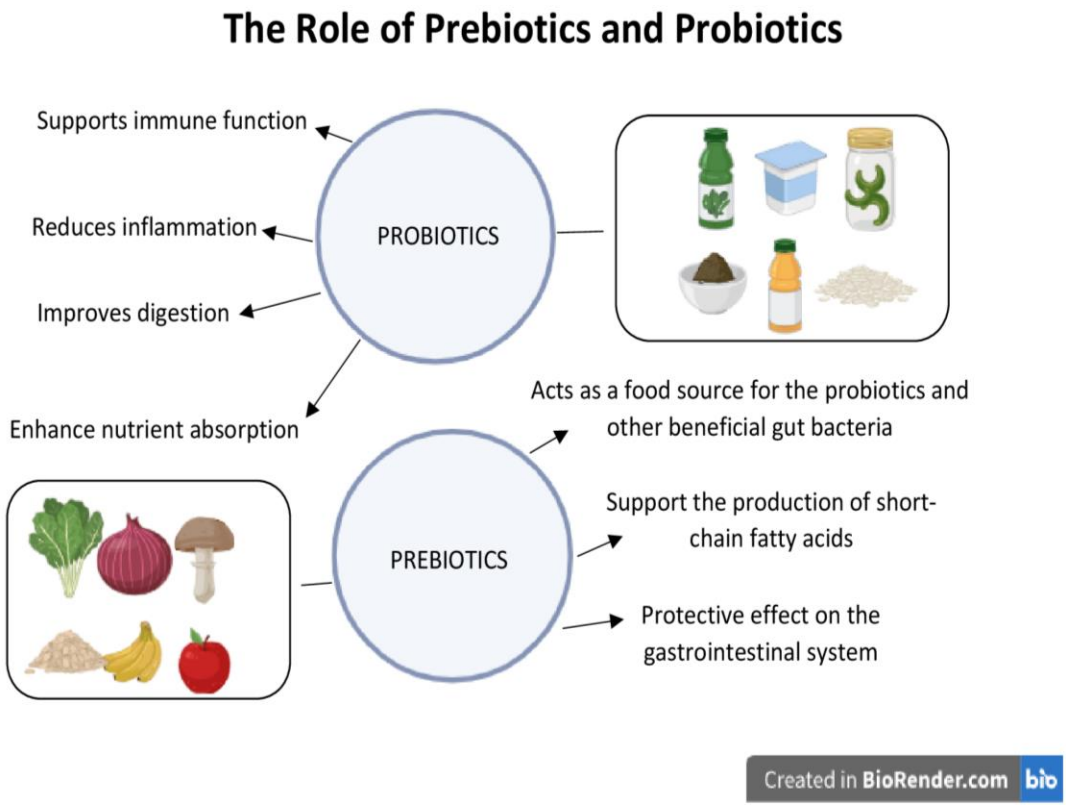

Figure 2: Health Benefits of Prebiotics and Probiotics (Retrieved from BioRender)

Future Consideration

Probiotics and prebiotics have great potential for treating diseases and improving host's health. The personalized application of these agents can optimize the human health in various ways, depending on the composition of host microbiota. With the incorporation of bioinformatics, genetic engineering, the development of next-generation probiotics, including engineered strains with enhanced efficacy, can offer significant potential for targeted treatment of complex diseases (Abouelela & Helmy, 2024). *In silico* approaches can also be implemented for gauging the effects of prebiotic's mechanism of action before testing on animal or human. The field of prebiotics can be extended by adding some novel non-digestible compounds beyond traditional oligosaccharides, such as polyphenols and certain fatty acids. These compounds can be explored for their potential in modulating microbiota to address specific health issues. Additionally, the role of synbiotics is being investigated for synergistic effects to enhance therapeutic outcomes. However, regulatory frameworks must evolve to ensure safety, efficacy, and quality control of probiotic and prebiotic products as their use come to mainstream. In addition to these, education and awareness campaigns are essential to promote evidence-based usage. Continued research into mechanisms of action, optimal dosages, and long-term impacts will strengthen their place in healthcare approaches. Utilizing these microbiome modulators could revolutionize preventative medicine and treatment strategies for various health conditions.

Conclusion

This chapter thoroughly explore the beneficial impacts of probiotics and prebiotics in health and disease management. Collectively these elements exert the systematic effects on immune systems and host health. By understanding the underlying mechanism of actions of probiotics and prebiotics in disease and health management, new dietary foods and supplements can be crafted for improving human health. Modulating the gut microbiota with prebiotics and probiotics offers a promising approach to managing major health conditions. Despite of extensive research, the effect of these components for various health conditions is still limited. Additionally, health claims need to be supported by rigorous clinical trials on an advanced level. The potential of these microorganisms and substrates to target specific microorganisms in the colon is significant, but a careful attention must be paid to potential risks like overuse, unintended microbial interactions, and individual variability.

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