Synergistic Efficacy and Mechanism of Probiotics and Prebiotics in Enhancing Health Impact

Sultan Ayesh Mohammed Saghir [1*], Fouad Saleh Al Suede [1]

Abstract

The potential benefits of probiotics and prebiotics for enhancing human health are increasingly recognized. This review aims to investigate their effectiveness and underlying mechanisms in improving the gut microbiome and overall well-being. Probiotics are live bacteria that offer health advantages when consumed in adequate amounts, typically found in fermented foods or supplements. They help restore and maintain a healthy gut microbiome by regulating the immune system, promoting microbial diversity, and inhibiting harmful microorganisms. Clinical studies have shown their efficacy in treating gastrointestinal conditions like irritable bowel syndrome, as well as non-gastrointestinal issues such as allergies and immune function. Prebiotics, on the other hand, are indigestible substances, primarily dietary fibers, that serve as food for beneficial gut bacteria. By providing essential nutrition, prebiotics create an environment conducive to the growth and activity of these microorganisms, benefiting overall gut health. They have shown promise in managing conditions like type 2 diabetes and obesity by altering the gut flora composition. Understanding how probiotics and prebiotics work together, known as synbiotics, can enhance their efficacy in improving gut health and well-being. Ongoing research into their mechanisms of action enables personalized healthcare approaches. However, individual factors like genetics and baseline gut microbiota composition may influence their effectiveness. By modulating the gut flora, probiotics and prebiotics offer exciting opportunities for health improvement. Their actions include microbiological balance, immune regulation, and metabolic effects. This comprehensive understanding provides a solid foundation for leveraging their therapeutic potential and advancing contemporary healthcare.

Keywords: Microbiome, Human Health, Dysbiosis, Metabolism

Significance | Understanding the role of prebiotics and probiotics in health management can enhance immunity, gastrointestinal health, and production efficiency.

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Introduction

The term "prebiotics" was first coined by Gibson and Roberfroid in 1995 and was later defined by the Food and Agriculture Organization (FAO) in 2007 as "a non-viable food component that confers a health benefit on the host associated with modulation of the microbes." Popular prebiotics include fructo-oligosaccharides (FOS), mannan-oligosaccharides (MOS), inulin, clavulase, and xylo-oligosaccharides (XOS), often utilized in symbiotic relationships combining probiotic and prebiotic properties. Initially proposed by Gibson et al. (2004), prebiotics, also referred to as "bifidogenic factors," are substances believed to be selectively fermented, altering the composition and activity of beneficial intestinal flora in humans. In 2016, the International Scientific Association for Probiotics and Prebiotics classified prebiotics as chemicals that the host intestinal flora can utilize and modify

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selectively, broadening the definition to encompass non-carbohydrates, and extending their mode of action beyond the gastrointestinal system and specific foods (Hutkins et al., 2017).

Prebiotics play a significant role in enhancing animal health by mitigating the risk of food-borne infections through the augmentation of host mucosal immunity and fortification against the colonization of pathogenic bacteria (Choct, 2009). These prebiotics are essentially indigestible food substances that, when consumed in appropriate quantities, selectively foster the growth and activity of specific gut microorganisms, thereby potentially improving host health. They are characterized as food ingredients carefully fermented to target naturally occurring components deemed beneficial, ultimately enhancing host health (Walton et al., 2013). Dietary fibers and oligosaccharides commonly constitute prebiotics.

In recent times, the utilization of prebiotic supplements to bolster the immune and gastrointestinal systems of livestock has surged in popularity. Research indicates that prebiotic supplementation is particularly advantageous during periods of stress or heightened exposure to pathogens throughout an animal's lifespan (Morrison et al., 2010).

The digestive system plays a vital role in maintaining good health, often likened to the human body's "second brain." Through interactions between the human body and intestinal flora, essential substances such as amino acids, vitamins, and short-chain fatty acids (SCFAs) are produced, aiding in the metabolism of toxic waste and facilitating the digestion and absorption of nutrients from food (Zhou et al., 2022). Maintaining a balanced intestinal flora is crucial as disruptions can negatively impact human health, potentially leading to disorders like obesity, diabetes, irritable bowel syndrome, and colon cancer (Huang et al., 2022). Therefore, external interventions are necessary to regulate the levels of probiotics to uphold a healthy intestinal flora state.

Probiotics, live bacteria administered in adequate doses, play a pivotal role in enhancing host health by colonizing the body. They can alter the composition of intestinal microbes, preventing harmful bacteria from colonizing the intestines. Moreover, probiotics contribute to the development of a robust protective layer in the intestinal mucosa, strengthening the intestinal barrier and bolstering immunity (Wang et al., 2021). Understanding the distinctive features of probiotics is essential to promote their growth and reproduction within the human body.

While earlier research has predominantly focused on the health benefits of prebiotics and probiotics (Liu et al., 2022), comprehensive studies on the various types of prebiotics and probiotics, their mechanisms, and interactions are limited. Therefore, this work provides a detailed exploration of prevalent prebiotic types, the functional origins of newly discovered ones, and their roles in gut function. Additionally, it delves into probiotic varieties, functions, and applications, elucidating the mechanisms underlying probiotic effects on the human body. Emphasis is placed on the promotional relationship between probiotics and prebiotics in this review. It is aimed to enhance understanding of the connection between prebiotics and probiotics and offer insights for improving human health, particularly in maintaining intestinal flora harmony.

Types of prebiotics

Previous studies have classified prebiotics as oligosaccharide carbohydrates, predominantly including xylooligosaccharides (XOS), galacto-oligosaccharides (GOS), lactulose, inulin, and fructose-oligosaccharides (FOS) and their derivatives (Yin et al., 2022). However, recent research has expanded this definition, suggesting that prebiotics encompass not only carbohydrates but also other non-carbohydrate substances meeting the prebiotic criteria. For instance, polyphenols extracted from fruits such as blueberries and black raspberries have been identified as fitting the prebiotic profile (Gu et al., 2019). Continuous advancements in prebiotic synthesis processes have led to the emergence of new prebiotic species, predominantly comprising polysaccharides, polyphenols, and polypeptide polymers, offering promising avenues for future research.

Galacto-oligosaccharides

GOS (galacto-oligosaccharides) is a novel functional material with inherent qualities that pose challenges for the body's absorption and digestion. Comprising two to eight sugar units, GOS consists of a terminal glucose unit alongside galactose and disaccharides, each containing two galactose units (Delgado-Fernandez et al., 2021). The hybrid structure of GOS, characterized by distinct glycosidic connections between glucose and galactose or between the degree of polymerization (DP) and galactose molecules, is a crucial feature (Torres et al., 2010). A schematic model depicting enzyme-driven lactose hydrolysis and glucose-galactose synthesis is illustrated in Figure 1.

Extensive studies assessing toxicity and genotoxicity have deemed GOS a safe food additive (Torres et al., 2010). Official approval from various countries, including the US, Japan, and the EU, further supports its safety (Slavin, 2013). As one of the most popular and widely used prebiotics, GOS offers several beneficial qualities, such as balancing the microbiota in the human colon and promoting the growth of Bifidobacterium in the gut (Slavin, 2013). In a study involving thirty-five healthy full-term newborns, the supplementation of GOS to infant formula led to a significant increase in Bifidobacterium abundance, albeit with a noticeable decrease in microbiota alpha-diversity (OM55N). Additionally, their fecal pH and short-chain fatty acid (SCFA) patterns mirrored those of control infants, indicating that GOS facilitates the proliferation of native Bifidobacterium and establishes a microbiota akin to breastfed infants (Matsuki et al., 2016). These findings align with previous studies by Fanaro et al. (2005), encompassing over 400 preterm and term infants, which demonstrated the effectiveness of probiotic mixtures (long-chain FOS and short-chain GOS) in stimulating the growth of lactic acid bacteria (LAB) and Bifidobacterium, reducing pathogen growth, and improving stool characteristics in infants consuming formula enriched with GOS.

Inulin-type fructans

Prebiotics encompass not only GOS but also common carbohydrates like inulin-type fructans. Inulin-type fructans are polymers consisting of fructose with β-2,1 bonds connecting it to terminal α-linked glucose. Inulin, with a longer chain (DP 2–60), and oligofructose/FOS, with a shorter chain (DP 2–8), are both categorized under this type (Wilson & Whelan, 2017). Research indicates that inulin-type fructans have the ability to stimulate the growth of LAB, Anthobacteria, and Bifidobacteria (Moens et al., 2017).

Inulin, a non-digestible carbohydrate of the fructan type, serves as a water-soluble storage polysaccharide (Martínez et al., 2022) and has been a part of the human diet for generations. Chicory root stands out as the most abundant source, with inulin present in approximately 36,000 plant species (Giri et al., 2021). Structurally, inulin comprises a linear chain of β-2,1-linked d-fructofuranose molecules, with a glucose residue forming a sucrose-type connection at the reducing end. While challenging for the human small intestine to absorb and digest due to the β-()-D-frutosyl fructose bonds, inulin can be fermented by the intestinal flora in the human large intestine (Apolinário et al., 2014).

Inulin serves various purposes in food processing, including its use as a fat or carbohydrate substitute to enhance flavor without significantly increasing energy intake, its role in mineral absorption, particularly calcium, magnesium, and iron, its potential to alleviate constipation, prevent gastrointestinal disorders, and enhance the immune system (Le Bastard et al., 2020). As a prebiotic with bifidogenic effects, inulin effectively stimulates the growth and metabolism of Bifidobacterium and Lactobacillus in the colon, while also altering the relative abundance of certain intestinal microorganisms (Le Bastard et al., 2020).

Additionally, fructans of sulfur (FOS), another type of inulin, are found in many common plants like wheat, onions, bananas, and garlic. These non-digestible, low-calorie carbohydrates, with a DP of less than 10, are frequently utilized by the food industry as prebiotics (Sunu et al., 2019). Fructans offer numerous physiological benefits, including reduced carcinogenicity, improved intestinal mineral absorption, and lowered levels of triacylglycerols, phospholipids, and serum cholesterol (Rahim et al., 2021).

Emerging prebiotics

Advancements in technology have led to enhanced techniques for preparing prebiotics. Moreover, numerous novel prebiotic species have been developed, with polysaccharides, polyphenols, and polypeptide polymers emerging as the most noteworthy (Rezende et al., 2021). Algae, fruit juices, fruits and their by-products, herbal remedies, and various microorganisms serve as the primary sources of these emerging prebiotics. Although our understanding of these prebiotics is not as extensive as that of FOS and GOS, their potential merits further investigation and holds promise for the future. Table 1 provides a summary of the roles played by polysaccharides, polyphenols, and peptide polymers in the development of prebiotics in recent years.

Mechanism of action of prebiotics

Prebiotics typically resist digestion in the small intestine, as the human gut lacks enzymes to break down their polymer bonds, allowing them to remain in the gastrointestinal system. These intact prebiotics are then transported to the large intestine, where intestinal flora ferment them selectively, producing specific secondary metabolites. These metabolites can positively impact host physiological processes, including regulation of immunity, resistance to pathogens, enhancement of intestinal barrier function, increased mineral absorption, and reduced blood lipid levels (Slavin, 2013).

Beneficial bacteria, such as acetate, butyrate, and propionate, metabolize the most prevalent short-chain fatty acids (SCFAs) in the colon, contributing to the preservation of intestinal and systemic health (Ríos-Covián et al., 2016). Moreover, prebiotics support the growth of target bacteria, fostering the proliferation of beneficial flora by safeguarding or promoting the production of advantageous fermentation products. This mechanism can occur following the consumption of specific prebiotics such as inulin, FOS, and GOS (Ashaolu, 2020). Figure 2 illustrates potential mechanisms through which prebiotics may enhance human health.

Probiotics

The concept of traditional probiotics traces back to Elie Metchnikoff's 1907 discovery, linking the longevity and well-being of elderly Bulgarians to their regular consumption of fermented dairy products rich in lactobacilli (LAB), such as yogurt. Metchnikoff proposed that the presence of bacteria could benefit the natural gut microbiota, thus laying the foundation for the understanding of probiotics. Over time, the definition of probiotics has evolved significantly (Martín & Langella, 2019).

Probiotics are defined as live strains of microorganisms that undergo rigorous screening and, when consumed appropriately, can exert positive effects on an individual's health, as recognized by the Food and Agriculture Organization of the United Nations and the World Health Organization (Markowiak & Śliżewska,

Table 1. Different kinds of emerging prebiotics.

Prebiotic	Component	Source	Function
Polyphenol	Blueberry polyphenol extract	Blueberry	Reduce weight and normalize lipid metabolism
	Wine grape seed flour	Grape seed	Intestinal permeability is enhanced, and adipocyte gene expression is altered to inhibit high-fat-induced obesity and inflammation.
	Orange albedo	Orange	Stimulates the growth, reproduction, and metabolism of Lactobacillus acidophilus and Lactobacillus animalis
	Catechin and punicalagin	Fermented pomegranate juice	Increases antioxidant capacity and improves survival of lactic acid bacteria
Polypeptide polymers	Poly-gamma-glutamate (PGA)	Bacillus fermentation	Increases abundance of Lactobacillus and reduces abundance of Clostridium, helping to regulate the intestinal microbiota.
Polysaccharides	Algae polysaccharides	Algae	Improves the activity of some beneficial flora and stimulates the production of functional metabolites in the intestinal microbiota.
	Lotus seed resistant starch (LRS3-20%)	Lotus seeds	Shows high probiotic activity against Bifidobacterium and Lactobacillus acidophilus.
	Longan pulp polysaccharides	Longan	Promotes the growth of Lactobacillus plantarum, Lactobacillus bulgaricus and Lactobacillus fermentum

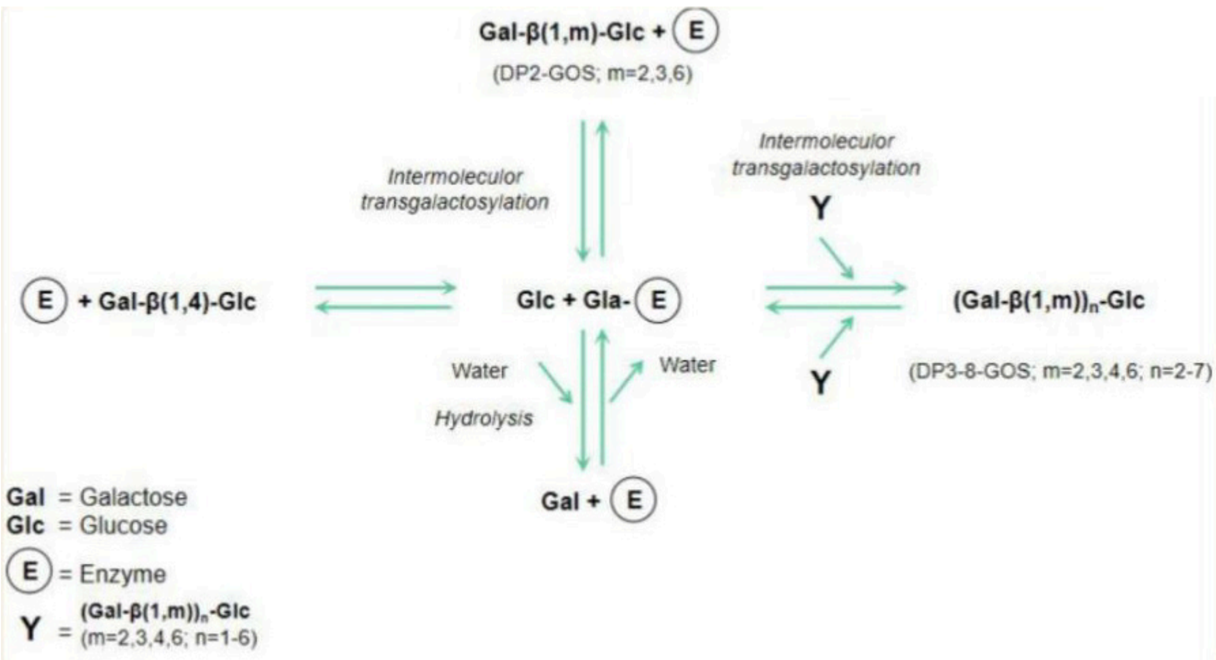

Figure 1. Schematic model of lactose hydrolysis and GOS synthesis (Delgado-Fernandez,2021)

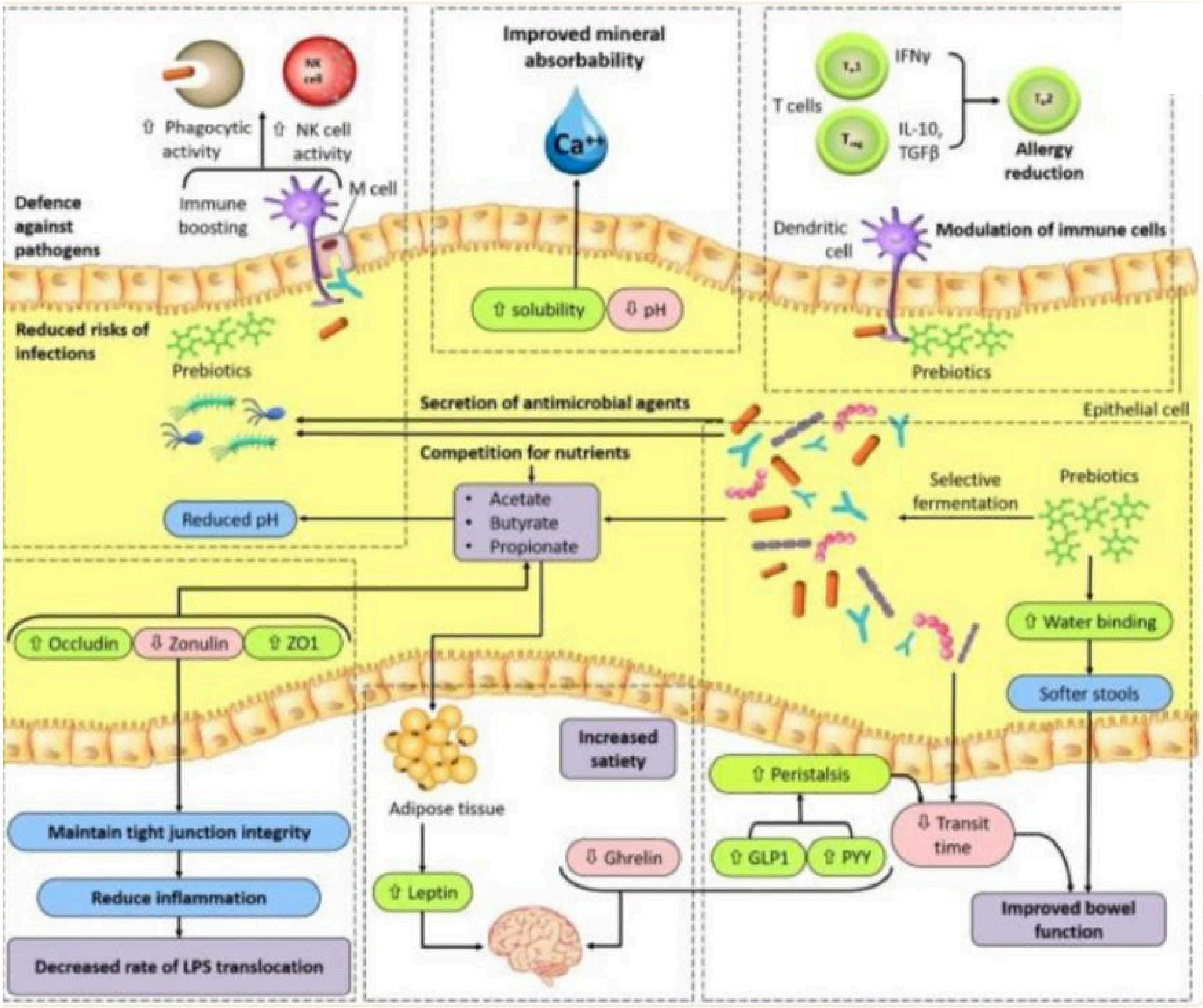

Figure 2. A model for possible mechanisms of prebiotic benefits to human health. GLP1, glucagon like peptide1; M cell, microfold cell; NK, natural killer; PYY, peptide YY; TGFβ, transforming growth factor-β; TH1, TH2, type 1 T helper, type 2 T helper; Treg, regulatory T; ZO1, zonula occludens 1.

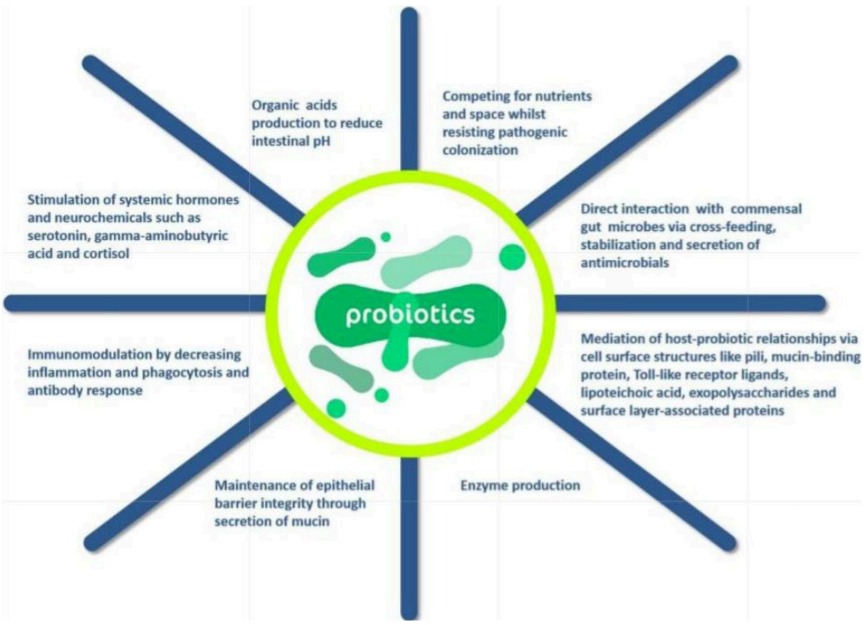

Figure 3. Action mechanisms of probiotics

2018). These microorganisms offer a myriad of health benefits, including regulation of intestinal health, immune function, blood lipid and sugar metabolism, improved food digestion and absorption, and treatment of lactose intolerance, collectively contributing to overall well-being (Cho & Kim, 2015).

For probiotics to exert their positive health effects, they must proliferate in the food product and survive in sufficient quantities until they reach the gut, their ultimate destination. Therefore, the ability of probiotics to adhere to intestinal mucosa and epithelial cells is crucial in selecting effective probiotics (Shewale et al., 2014).

Probiotics operate through four primary mechanisms to benefit the body: they prevent and reduce the growth of potential infections, enhance the gut's barrier function, modulate the body's immune system, and produce neurotransmitters that can influence the host (Sánchez et al., 2017). Moreover, probiotics can directly influence immune cells, other host cells, or food ingredients through immune system modulation, according to Oelschlaeger (2010). Complete components like peptidoglycan and DNA are essential for the effectiveness of probiotics. It is important to note that no single strain of probiotics possesses all probiotic qualities.

Probiotics can enhance host immunity through various mechanisms, directly affecting immune and other host cells, as depicted in Figure 3. Often, probiotics are formulated by combining the actions of multiple bacteria, facilitating the creation of antibiotic component compounds and cross-feeding processes.

Types of probiotics

Lactobacillus

Probiotics encompass a wide array of species and can be broadly classified into three main groups: Bifidobacteria, Lactobacilli, and others. Among these, Lactobacilli, within the LAB (lactic acid bacteria) group, dominate current probiotic research due to their prevalence and significance in human intestinal microorganisms, closely tied to human health. Lactobacillus, a notable probiotic, not only synthesizes essential vitamins and amino acids and facilitates mineral absorption but also plays a crucial role in improving intestinal microecology by inhibiting the growth of pathogenic microorganisms (La Fata & Mohajeri, 2018).

Additionally, short-chain fatty acids (SCFAs), a significant metabolite of Lactobacillus, support the growth and proliferation of Lactobacillus itself. This, in turn, reduces the presence of Escherichia coli in the intestine, thereby maintaining normal physiological function of the colon and the morphology of the colonic epithelium (Ding et al., 2019). Lactobacillus intervenes microbially to prevent pathogen invasion and uphold or restore microbial balance in the host environment. Synergistic interactions between LAB and endogenous commensal flora are vital for restoring microbial homeostasis (Zhang et al., 2018).

In practical applications, LAB from sourdough, for example, can be combined with plant or animal-derived substances to enhance functional qualities, flavor, and nutritional value. This combination benefits from various modes of action and perfect symbiotic activities (Bartkiene et al., 2022). By strengthening the intestinal epithelial barrier function and producing chemicals with antimicrobial properties, LAB contribute to defense against pathogens, complementing their synergistic effects with commensal flora (Rajoka et al., 2021).

Bifdobacterium

The name "Bifidobacterium" derives from the genus of specialized anaerobic Gram-positive bacteria known for their characteristic bifurcated ends (Henrick et al., 2018). This genus encompasses physiological bacteria crucial for human health and is abundant in probiotic foods. Bifidobacterium thrives and metabolizes in both the middle and end sections of the small intestine, as well as the large intestine. It adapts to anaerobic intestinal conditions by secreting bifidogenic substances with probiotic effects, contributing to intestinal health regulation (Bested et al., 2013).

Currently, there are 32 species and 9 subspecies of Bifidobacterium, with 14 of these species isolated from humans. Bifidobacterium plays several physiological roles:

(i) Similar to other LAB (lactic acid bacteria), Bifidobacterium has the ability to inhibit pro-inflammatory cytokines and maintain the balance of normal intestinal bacterial flora by restricting the growth of pathogenic bacteria (Klaassens et al., 2009). Studies indicate that Bifidobacterium can provide in vivo and in vitro protection against gut barrier disruption, linked to enhanced intestinal tight junction integrity, suppression of pro-inflammatory cytokine secretion, and vimentin release (Krumbeck et al., 2018).

(ii) Bifidobacterium bifidum is believed to promote bone health by enhancing calcium bioavailability and synthesizing vitamins and amino acids in the colon (Dubey & Patel, 2018).

(iii) Bifidobacterium bifidum exhibits anti-tumor properties. Shimizu et al. successfully generated a strain of Bifidobacterium longum secreting C-CPE-PE23, capable of selectively locating and multiplying within tumors. Their study suggests that Bifidobacteria could serve as unique carriers of anti-cancer proteins against malignant tumors. The isolated Bifidobacteria specifically targeted the tumors of mice with breast cancer and significantly inhibited tumor growth without causing adverse effects such as weight loss or liver and kidney damage (Shimizu et al., 2020).

Other bacteria species

In modern food production, Gram-positive parthenococci like Enterococcus are commonly used alongside Lactobacillus and Bifidobacterium in probiotic formulations. Enterococcus strains possess notable probiotic characteristics, including the ability to

Table 2. The functions and uses of a few typical probiotics based on recently published research.

Strain	Function	Application
Bifidobacteria	The exopolysaccharides produced have antioxidant, anticancer, antibacterial, and immunological activities	Used as a starter culture for fermented foods
Lactobacillus casei	Prevention or treatment of diseases that disrupt the intestinal microbiota	Dairy fermentation
Bifidobacterium adolescentis	It reduces the inflammation of spleen and brain, and changes the microbiota of cecum and colon	Medicine and clinic
Lactobacillus acidophilus	Reduces cytokines to relieve inflammatory bowel disease, alleviate cancer, modulate immunity, lower cholesterol and relieve diarrhea	Medicine and clinic
Bacillus coagulans	It can regulate the balance of intestinal microbiota, promote the metabolism and utilization of nutrients, improve immunity, and has the characteristics of high temperature resistance, acid resistance, and bile resistance	Medicine and animal husbandry
Bacillus subtilis	Improved growth, nutrition, immunity and disease resistance of aquatic species	Aquaculture

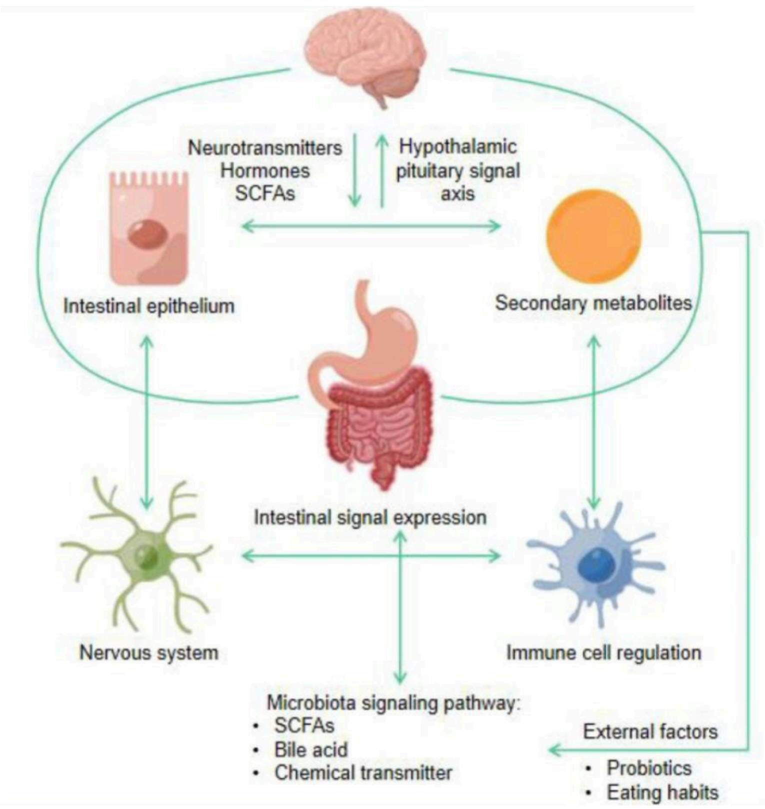

Figure 4. Schematic diagram of microbiota gut-brain axis bidirectional signal pathway.

coexist, compete, and adhere to host cells in the colon. Additionally, Enterococcus demonstrates significant bacteriocin production, serving as a natural antibacterial agent applicable in the food industry. Moreover, Enterococcus exhibits high resistance to a wide range of pH and temperature fluctuations (Shimizu et al., 2020).

Another probiotic commonly utilized in modern food production is Saccharomyces cerevisiae, a well-known non-pathogenic and selective probiotic. Specifically, Saccharomyces boulardii has garnered significant attention for its probiotic properties and is frequently employed in treating digestive disorders, particularly diarrhea symptoms often associated with antibiotic therapy. Notably, Saccharomyces boulardii demonstrates superior survival rates in the digestive tract compared to other probiotics, contributing to the preservation of natural microflora equilibrium in the intestinal tract. Additionally, it possesses immunomodulatory properties beneficial for regulating immune pathways, particularly in chronic illnesses or pathogenic infections (Czerucka & Rampal, 2019).

In addition to enterococci and yeasts, other widely available probiotic categories include Streptococcus species, E. coli, and Bacillus species. Table 2 provides a summary of the functions and uses of several typical probiotics, as per recent research findings.

Mechanism of action of probiotics

Enhancement of barrier function for intestinal mucosa

The gut, as the largest immunological organ in the human body, plays a vital role in overall health. It comprises a heterogeneous structure consisting of the mucus layer, cellular layer, and lamina propria of the intestinal epithelium, collectively forming the intestinal barrier (Wang et al., 2021).

Within this barrier, the intestinal epithelium and mucus layer possess distinct cell types that function as physical barriers against intestinal microbes. Enterocytes facilitate the uptake of molecules from the intestinal lumen, while paneth cells produce and release antimicrobial peptides upon contact with intestinal bacteria. The mucus layer, secreted by cells like Saccharomyces cerevisiae, serves essential functions including preventing pathogen adherence, facilitating food flow, and creating a protective barrier against the luminal environment (Burgueño & Abreu, 2020; Patel & Cormick, 2014).

Upon entering the intestine, probiotics interact with intestinal bacteria, with the intestinal mucosa acting as the initial physical barrier. This interaction protects the intestine from potentially harmful compounds in the luminal environment. As probiotics reach the colon, they further interact with bacteria to reinforce chemical, mechanical, biological, and immunological barriers. Their actions in the colon include preserving mucosal barrier integrity, enhancing mechanical barrier function, promoting mucus production, facilitating mucosal regeneration, and restoring intestinal permeability (Mennigen et al., 2009; Toumi et al., 2013).

Enhancement of the immune response of the system

Certain probiotics in the gut possess immunostimulatory properties, meaning they act as immune regulators and control inflammation by directly or indirectly influencing various immune cells in the body, including monocytes, macrophages, T cells, B cells, and natural killer (NK) cells (Shida et al., 2011). These probiotics enhance non-specific cellular immune responses, combating cancer cells, inducing IL-12 production to activate NK cells and promote Th1 cell development, and releasing cytokines in a dose-dependent and strain-specific manner. They also maintain a balance between Th1 and Th2 cells, offering protection against allergies (Azad et al., 2012).

Consuming yogurt, for example, can supply necessary probiotics to enhance the immune response and increase the number of IgA+ cells and cytokine-producing cells in intestinal effector sites, thus improving the intestinal mucosal immune system (Ashraf & Shah, 2014). Short-term use of probiotic supplements has been shown to enhance cellular immunity in the body. Elderly individuals taking probiotic supplements at appropriate doses experienced increased polymorphonuclear phagocytosis and tumor-killing activity of natural killer cells (Miller et al., 2019).

Probiotics often enhance gut immune cell function by directly or indirectly stimulating them. Certain probiotics, such as immunomodulatory probiotics, can also control enzyme activity by modifying microbial metabolism (Duary et al., 2012). The host intestinal mucosal immune system responds to foreign antigens through adaptive immune responses and inflammation to maintain homeostasis. Immunomodulatory probiotics induce IL-10 production and Treg cell generation, mitigating inflammation and allergy symptoms (Chiba et al., 2010).

Mechanism of action between probiotics and gut-brain axis

The gut-brain axis represents a crucial pathway in bidirectional communication between the gut and the brain, operating at neuronal, endocrine, and immunological levels to maintain overall bodily homeostasis (Lerner et al., 2017). Microbiota have emerged as key regulators of this system, with pathways such as the immune system, tryptophan metabolism, and the vagus and enteric nervous systems facilitating gut microbial signaling to the brain via microbial metabolites like short-chain fatty acids (SCFAs), branched-chain amino acids, and peptidoglycans (Doifode et al., 2021). Through the autonomic nervous system, the brain can influence microbial composition and behavior (Cryan et al., 2019).

The gut produces various hormones and neurotransmitters, including SCFAs, dopamine, and serotonin, through the fermentation of carbohydrates, which directly impact behavior and brain function (MacFabe, 2012). The gut microbiota exerts a profound influence on the gut-brain relationship, affecting mental health, mood regulation, neuromuscular function, hypothalamic-pituitary-adrenal (HPA) axis regulation, and emotional and cognitive centers of the brain, either directly or indirectly (Baji et al., 2019).

Increasingly, research has explored the association between intestinal flora and depression, implicating the gut microbiota in the pathophysiology of depression through mechanisms such as alterations in brain-derived neurotrophic factor (BDNF) expression, HPA axis activity, and monoamine neurotransmitter modulation (Baji et al., 2019). Probiotics have been found to modulate BDNF expression in the central nervous system and reduce depression incidence by promoting SCFA production, particularly butyric acid (Mörkl et al., 2019). Clinical studies have shown that probiotic supplementation can lead to significant reductions in depression scores and insulin levels among patients with major depressive disorder (Akkasheh et al., 2016; Kazemi et al., 2019).

Moreover, emerging research suggests a potential link between autism and gut flora dysbiosis, with autistic children exhibiting abnormal levels of SCFAs, lipopolysaccharides (LPS), and indoles in their urine, possibly indicating compromised gut barrier function (Srikantha & Mohajeri, 2019).

Promotion mechanism of prebiotics for probiotics

Promoting the growth and multiplication of probiotics: Previous research has demonstrated that prebiotics can enhance the diversity of gut microbes and facilitate the proliferation of probiotics in the human gut (Yadav et al., 2022). Probiotics, constituting a minor fraction of the natural intestinal flora, play a significant role in health by modulating the immune system and inhibiting the growth of pathogenic bacteria. Essential for the growth and metabolism of probiotics is the availability of carbon, primarily sourced from carbohydrates. Unlike human digestive fluids, prebiotics remain unaffected and unbroken down, with indigestible prebiotics being converted into the carbon sources necessary for probiotic growth within the gut. This process fosters the proliferation of beneficial bacteria and contributes to the regulation of probiotic composition.

Promoting the metabolism of probiotics: The metabolic byproducts of gut bacteria's fermentation of proteins and carbohydrates from dietary or endogenous sources are known as short-chain fatty acids (SCFAs). Comprising saturated fatty acids with chains of two to six carbons, SCFAs play crucial roles in gut health (Heng et al., 2022). The presence of probiotics and prebiotics is essential for the development of SCFAs. Prebiotics, in particular, foster the production of beneficial metabolites, primarily SCFAs, which modulate the gut pH and environment (Dai et al., 2021).

SCFAs are predominantly formed when anaerobic bacteria ferment undigested and unabsorbed carbohydrates in the colon. Probiotic strains such as Lactobacillus, Bifidobacterium, and Clostridium Butyricum contribute to SCFA production. The synthesis of SCFAs is significantly influenced by prebiotics, with studies indicating that the physical form of prebiotic substrates affects both SCFA synthesis and fermentation rates (Ashaolu et al., 2021).

Research by Fei et al. (2023) further highlights the fermentation of prebiotics into SCFAs, underscoring the benefits of SCFAs in strengthening tight junctions, promoting colon cell proliferation and mucus production, and reducing intestinal pH to create a favorable environment for probiotics. SCFAs can be viewed as nutrients that enhance probiotic performance (Markowiak & Śliżewska, 2020).

Moreover, probiotics can produce antimicrobial peptides, which exhibit antibacterial activity by competitively binding to receptors on epithelial cells along with prebiotics and pathogens. This interaction underscores the multifaceted role of probiotics and prebiotics in maintaining gut health.

Challenges and Future Recommendation

Current research into the effectiveness and mechanisms of action of probiotics and prebiotics faces several significant challenges alongside promising avenues for future exploration. One major issue is the lack of standardized research procedures and outcome measurements (Kothari et al., 2020). The use of different strains, doses, and study methodologies by researchers makes it challenging to evaluate and synthesize research findings. Establishing standardized research protocols encompassing strain identification and evaluation criteria is crucial to enhance the reproducibility and comparability of studies.

The diversity of the human gut microbiota poses another challenge, leading to considerable inter-individual heterogeneity in the absorption of probiotics and prebiotics (Lynch & Pedersen, 2016). Overcoming this challenge requires the promotion of personalized strategies investigating how an individual's gut microbiota composition influences their response to these dietary supplements.

Furthermore, most research primarily focuses on the immediate benefits of probiotics and prebiotics, with their long-term effects on health remaining largely unknown (Gibson et al., 2017). To assess the long-term impact and safety of these therapies, future research should prioritize long-term, longitudinal studies.

Pinpointing the exact mechanisms by which probiotics and prebiotics influence the gut microbiota and host health presents a challenging task (Flint et al., 2015). To address this, more research into the mechanisms of action of these supplements using advanced approaches such as metagenomics, metatranscriptomics, and metabolomics is needed to gain valuable insights into their effects on the gut microbiota and host physiology.

A comprehensive understanding of their benefits also requires expanding research beyond gastrointestinal health to explore their potential applications in other medical conditions, such as metabolic disorders, mental health issues, and immune-related diseases (Hill et al., 2014).

To protect consumers against deceptive or ineffective products, probiotic and prebiotic products must adhere to clear regulatory criteria ensuring safety, efficacy, and accurate labeling (Sanders et al., 2019).

Educating the public and healthcare professionals about the advantages and limitations of probiotics and prebiotics is essential to promote evidence-based decisions regarding health and nutrition (Davani-Davari et al., 2019).

Conclusion

In conclusion, research on probiotics and prebiotics has provided valuable insights into their effectiveness and mechanisms of action. Probiotics, with their live microorganisms, have been shown to enhance immune function, promote gut health, and even influence mental health. Conversely, prebiotics play a crucial role in supporting a healthy microbial community by providing essential nutrients for beneficial gut bacteria. While both probiotics and prebiotics have demonstrated promising results in various studies, further investigation is needed to fully understand their precise effects, optimal dosages, and long-term implications. The evolving understanding of this field presents exciting opportunities for improving human well-being through modification of the gut microbiome.

Author Contributions

S.U.A.S. drafted the manuscript and made substantial contributions to the design of the study. D.S.N. reviewed and drafted the paper.

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Competing financial interests

The author has no conflict of interest.

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