**Literature review: Differentiating Probiotics and Prebiotics in Terms of Mechanism of Action and Clinical Application**

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**Abstract**

This systematic review explores the key differences between probiotics and prebiotics in terms of their mechanisms of action and clinical applications. Probiotics are live microorganisms that confer health benefits when consumed in adequate amounts, whereas prebiotics are non-digestible food ingredients that promote the growth of beneficial gut bacteria. The review highlights how these two categories of microbiota-targeted interventions work independently and synergistically to maintain and improve human health. A detailed examination of their impact on gastrointestinal health, metabolic disorders, immune function, neurological health, and more is provided [1]. The clinical efficacy of specific probiotic strains and prebiotic compounds is also evaluated. This comprehensive overview aims to inform both clinical practice and future research on microbiota modulation strategies.[13,25]

# IntroductionThe human gut microbiota plays a fundamental role in maintaining homeostasis and modulating various physiological processes. Recent advances in microbiome research have underscored the importance of dietary and microbial interventions in promoting health and preventing disease. Among such interventions, probiotics and prebiotics are frequently used—both in clinical practice and as over-the-counter supplements. Although they are often mentioned together, they differ significantly in their composition, mode of action, and therapeutic use. This systematic review aims to comprehensively compare and contrast probiotics and prebiotics, focusing on their biological functions, clinical efficacy, and applications in human health.[1,18]

**Aim of the study**

The aim of this systematic review is to provide a comprehensive comparison of probiotics and prebiotics, with a focus on their distinct mechanisms of action, clinical applications, and contributions to human health. This review seeks to elucidate how these two types of microbiota-targeted interventions operate independently and synergistically to support gastrointestinal health, metabolic function, immune modulation, and neurological well-being. Additionally, it aims to evaluate the clinical efficacy of specific probiotic strains and prebiotic compounds, while identifying key areas for future research in microbiome modulation and the potential for personalized therapeutic approaches.

**Materials and Methods**

This review follows PRISMA guidelines. A literature search was conducted using PubMed, Scopus, and Web of Science up to March 2024. Keywords included 'probiotics', 'prebiotics', 'mechanism of action', 'clinical application', and 'gut microbiota'. We included review articles, randomized controlled trials, and meta-analyses published in English. Inclusion criteria required a clear focus on the differentiation between probiotics and prebiotics with respect to mechanisms and applications.
**Conclusion**

Probiotics and prebiotics have distinct yet complementary roles in supporting gut health. Probiotics are live microorganisms—commonly from the genera Lactobacillus, Bifidobacterium, and Saccharomyces—that must survive gastrointestinal conditions and positively affect the host’s microbiome [1]. Their health effects are strain-specific, underscoring the importance of targeted clinical research.

Prebiotics, on the other hand, are non-digestible substrates like inulin, FOS, and GOS, which selectively stimulate beneficial gut bacteria [11]. Their fermentation by gut microbes produces SCFAs, which help maintain gut barrier function and modulate immunity and metabolism.[4] While probiotics provide microbial supplementation, prebiotics nourish the host’s existing microbiota. Used together in synbiotics, they can enhance each other’s effectiveness, offering a promising approach for future personalized therapies.

**Keywords**

Probiotics, prebiotics, gut microbiota, clinical applications, microbiome, gastrointestinal health, immune modulation, synbiotics.

# 1. Definitions and Characteristics

Probiotics are defined by the World Health Organization (WHO) and the International Scientific Association for Probiotics and Prebiotics (ISAPP) as “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host” [1]. The most widely studied and utilized probiotics include strains from the genera *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces*, especially *Saccharomyces boulardii* [2,3]. These microorganisms are commonly found in fermented foods such as yogurt, kefir, kimchi, sauerkraut, and dietary supplements. To be classified as a true probiotic, a microorganism must fulfill specific criteria: it should be safe for human consumption, able to survive passage through the gastrointestinal tract, and demonstrate documented health effects in controlled clinical trials [1,4].

Each probiotic strain may differ significantly in its physiological properties and health outcomes. For instance, *Lactobacillus rhamnosus* GG has been associated with prevention of antibiotic-associated diarrhea, while *Bifidobacterium infantis* 35624 has demonstrated efficacy in alleviating symptoms of irritable bowel syndrome (IBS) [5]. Hence, clinical effectiveness is highly strain-specific, emphasizing the importance of precise characterization and targeted application.

Prebiotics, on the other hand, are defined as “substrates that are selectively utilized by host microorganisms conferring a health benefit” [6]. Most prebiotics are non-digestible carbohydrates, primarily oligosaccharides such as inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS). These compounds are resistant to digestion in the upper gastrointestinal tract and are fermented by beneficial bacteria—mainly *Bifidobacteria* and *Lactobacilli*—in the colon. This fermentation process results in the production of short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate, which are crucial for maintaining intestinal barrier integrity, modulating immune responses, and supporting metabolic health [7,8].

While probiotics introduce beneficial microorganisms directly into the gut, prebiotics function by nourishing and enhancing the growth of beneficial bacteria already present. Together, they form the basis of microbiota-directed therapies and may act synergistically when combined in synbiotic formulations [9].

# 2. Mechanisms of Action

Probiotics exert their health-promoting effects primarily through several interrelated mechanisms. One of the key pathways involves colonization of the intestinal mucosa, where they can compete with pathogenic microbes for adhesion sites and nutrients, thereby reducing the risk of infections [10]. In addition, many probiotic strains produce antimicrobial substances such as bacteriocins, organic acids (e.g., lactic acid), and hydrogen peroxide, which directly inhibit pathogenic bacteria [11]. Another important function of probiotics is their ability to modulate the host immune system. Certain strains can stimulate the production of anti-inflammatory cytokines, regulate the activity of dendritic cells, and enhance the production of secretory IgA, thereby promoting mucosal immunity [13].

A growing body of evidence also indicates that probiotics may reinforce the integrity of the intestinal epithelial barrier by upregulating tight junction proteins such as occludin and claudin, which are critical for preventing the translocation of bacteria and toxins into the bloodstream [14]. This is particularly relevant in the context of conditions like inflammatory bowel disease (IBD), leaky gut syndrome, and irritable bowel syndrome (IBS), where barrier dysfunction is a common feature. However, it is important to note that these beneficial effects are strain-specific; not all probiotics confer the same health benefits, even within the same species [15].

In contrast, prebiotics function as non-digestible substrates that selectively promote the growth and activity of beneficial commensal bacteria in the colon, especially *Bifidobacterium* and *Lactobacillus* species [16]. Unlike probiotics, prebiotics do not contain live microorganisms or exert direct biological activity on the host. Instead, their effects are mediated through microbial fermentation in the large intestine, which produces short-chain fatty acids (SCFAs), notably acetate, propionate, and butyrate [17].

These SCFAs play critical roles in maintaining host health. Butyrate, for instance, serves as the primary energy source for colonocytes and is involved in regulating gene expression, inflammation, and oxidative stress [18]. Propionate and acetate, on the other hand, can enter systemic circulation, influencing metabolic processes such as gluconeogenesis, lipid metabolism, and appetite regulation [19]. Furthermore, SCFAs exhibit anti-inflammatory properties and contribute to maintaining intestinal pH, which inhibits the growth of pathogenic bacteria.

Taken together, while probiotics act directly on the host and its immune system, prebiotics work indirectly by enriching beneficial bacterial populations and promoting the production of health-supporting metabolites. Their complementary mechanisms of action provide a strong rationale for their combined use in synbiotic formulations.

# 5. Clinical Applications

Probiotics and prebiotics have demonstrated promising clinical efficacy in a broad spectrum of health conditions. Their roles extend from gastrointestinal support to systemic effects such as immune modulation and mental health enhancement. Below, key therapeutic areas are described for both categories.

**6. Probiotics**

**a. Infectious Diarrhea**

Probiotics, particularly strains such as *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*, have been extensively studied in the context of acute infectious diarrhea in children. Meta-analyses confirm that probiotics significantly reduce the duration and severity of diarrhea, especially when administered early in the course of illness [1,2].

**b. Antibiotic-Associated Diarrhea (AAD)**

AAD is a common complication of antibiotic therapy. Clinical trials show that certain probiotic strains can restore microbial balance disrupted by antibiotics and reduce the incidence of AAD by up to 60% [3]. The most effective strains include *S. boulardii* and *L. rhamnosus* GG [4].

**c. Irritable Bowel Syndrome (IBS)**

IBS is a functional gastrointestinal disorder characterized by abdominal pain, bloating, and altered bowel habits. Several probiotic strains, including *Bifidobacterium infantis* 35624 and *Lactobacillus plantarum* 299v, have been shown to alleviate symptoms by reducing intestinal inflammation, regulating gut motility, and modulating visceral hypersensitivity [5,6].

**d. Inflammatory Bowel Disease (IBD)**

Though evidence is still emerging, probiotics have shown some benefit in maintaining remission in ulcerative colitis and pouchitis. For example, the multi-strain preparation VSL#3 has demonstrated efficacy in reducing inflammation and preventing relapse in patients with ulcerative colitis [7]. The role of probiotics in Crohn’s disease remains less clear and warrants further investigation [8].

**e. Mental Health and the Gut-Brain Axis**

The term "psychobiotics" refers to probiotic strains that have a positive impact on mental health. These probiotics may influence the central nervous system via modulation of the vagus nerve, immune signaling, and production of neuroactive compounds such as GABA and serotonin. Clinical studies suggest improvements in mood, anxiety, and stress levels after probiotic supplementation [9,10].

**f. Allergic Disorders**

Probiotics have also been investigated for their role in preventing and alleviating allergic diseases, such as atopic dermatitis and allergic rhinitis. Early-life administration of probiotics may influence immune development and reduce the risk of eczema in infants [11].

**7. Prebiotics**

**a. Constipation Relief**

Prebiotics like inulin and FOS increase stool frequency and improve stool consistency by enhancing microbial fermentation and stimulating colonic motility. Their osmotic effect and ability to increase fecal biomass also contribute to bowel regularity, especially in elderly populations and children [12].

**b. Mineral Absorption**

Inulin-type prebiotics improve the bioavailability of minerals such as calcium and magnesium by lowering intestinal pH through SCFA production. This promotes greater solubility and passive diffusion of these minerals, which is particularly beneficial during adolescence and menopause [13,14].

**c. Immune Modulation**

Prebiotics have immunomodulatory effects by promoting the growth of beneficial bacteria that regulate host immune responses. GOS and FOS supplementation in infants has been associated with a reduced incidence of infections and allergy-like symptoms [15]. In adults, prebiotics may reduce inflammatory markers and improve resistance to upper respiratory infections [16].

**d. Metabolic Health and Weight Management**

Prebiotics modulate the composition of the gut microbiota, particularly increasing populations of *Bifidobacteria* and *Akkermansia muciniphila*, which are associated with improved glucose and lipid metabolism. SCFAs produced by fermentation enhance satiety hormones (GLP-1, PYY), reduce low-grade inflammation, and improve insulin sensitivity [17,18].

**e. Neurocognitive Function**

Emerging evidence suggests that prebiotics may influence brain function via the gut-brain axis. In one study, healthy volunteers who consumed GOS experienced reduced cortisol levels and improved emotional processing, indicating potential stress-reducing effects [19].

**8. Synbiotic Approaches**

Combining probiotics and prebiotics in synbiotic formulations has been proposed to enhance the survival, implantation, and efficacy of probiotic strains. Clinical studies using synbiotics have reported improved outcomes in liver disease, obesity, and even cancer patients undergoing chemotherapy by mitigating gut dysbiosis and reducing systemic inflammation [20].

# 9. Clinical Distinctions and Synergism

While both agents influence the gut microbiota, probiotics act through direct microbial intervention, while prebiotics function indirectly via nutrient provision. The choice between them depends on the desired therapeutic effect. An emerging trend involves the use of synbiotics—formulations combining both probiotics and prebiotics—which aim to maximize benefits by supporting both the introduction and sustenance of beneficial microbes. Research supports that synbiotics may be more effective than either component alone in certain clinical conditions[26].

# 10. Challenges and Limitations

Despite growing interest, there remain limitations in standardizing probiotic strains, dosages, and treatment durations. Inter-individual variation in gut microbiota composition further complicates treatment outcomes. Similarly, prebiotics may cause gastrointestinal side effects in some individuals, and their benefits are often dose-dependent. More robust clinical trials are needed to validate specific indications and to establish personalized microbiota-based therapies[11].

# 11. Conclusion

Probiotics and prebiotics play distinct but complementary roles in maintaining and restoring gut health. While probiotics provide live microbial support, prebiotics nourish the microbiota already present. Understanding their mechanisms and applications is key to integrating them effectively in personalized medicine. Future studies should focus on strain-specific actions, host-microbiota interactions, and the development of synbiotic formulations with demonstrated clinical efficacy.Probiotics are defined by the World Health Organization as “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host”.[1] These microorganisms are most commonly derived from the genera Lactobacillus, Bifidobacterium, and Saccharomyces, and are frequently included in fermented foods such as yogurt, kefir, and dietary supplements. A critical criterion for any microorganism to be classified as a probiotic is its ability to survive gastric acidity and bile exposure, adhere to the intestinal mucosa, and positively modulate the gut microbiome[3]. Probiotic strains may differ substantially in their health effects, highlighting the importance of strain specificity in clinical research and applications.
In contrast, prebiotics are selectively fermented dietary substrates that result in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefits to the host[2]. They are typically composed of non-digestible carbohydrates such as inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS). These compounds escape digestion in the upper gastrointestinal tract and are fermented by commensal bacteria—primarily Bifidobacteria and Lactobacilli—in the colon. This fermentation process produces short-chain fatty acids (SCFAs), such as acetate, propionate, and butyrate, which play a key role in maintaining gut barrier integrity, modulating the immune system, and even influencing host metabolism and inflammation[4].
While probiotics exert a direct effect by introducing beneficial microbes, prebiotics support endogenous beneficial bacteria already residing in the host’s gut. Importantly, their roles are complementary rather than interchangeable. When used in combination, as in synbiotic formulations, they may exert synergistic effects by improving survival and activity of the introduced probiotic strains.

**Authors' Contributions Statement:**

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