Review Article

Use of Probiotics in Gut Health and Immunity: Mechanisms, Clinical Evidence and Future Perspectives

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Abstract: Probiotics are defined as live microorganisms that confer health benefits to the host when administered in adequate amounts [(1)]. In recent decades, the study of probiotics has gained considerable attention because of their ability to regulate gut microbiota composition and improve immune function [(2)]. The human gastrointestinal tract contains a complex microbial ecosystem that plays a critical role in nutrient metabolism, barrier protection, and immune regulation [(3)]. Disturbance of this microbial balance, referred to as dysbiosis, has been associated with numerous diseases including inflammatory bowel disease, metabolic disorders, allergies, and infections [(4)]. Probiotics help restore microbial equilibrium and enhance intestinal barrier integrity while modulating host immune responses [(5)]. Several clinical trials have demonstrated the beneficial effects of probiotics in gastrointestinal disorders such as irritable bowel syndrome, antibiotic-associated diarrhea, and inflammatory bowel disease [(6)]. This review discusses the mechanisms by which probiotics influence gut health and immunity, summarizes clinical evidence supporting their therapeutic potential, and highlights future research directions in probiotic therapy.

Keywords: Probiotics; Gut microbiota; Gut health; Immunity; Dysbiosis; Intestinal barrier; Immunomodulation; Short-chain fatty acids; Gastrointestinal disorders; Microbiome; Probiotic therapy; Gut–brain axis.

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1. Introduction

The human gastrointestinal tract hosts trillions of microorganisms collectively known as the gut microbiota [(3)]. These microbes include bacteria, viruses, fungi, and archaea that coexist in a complex ecological network [(7)]. The gut microbiota plays a crucial role in maintaining host health through nutrient metabolism, vitamin synthesis, and protection against pathogenic organisms [(8)].

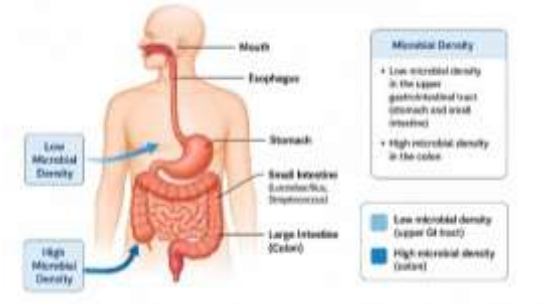

Figure 1. Structure of the Human Gut Microbiota

Probiotics are beneficial microorganisms that promote health when consumed in adequate quantities [(1)]. Early research on probiotics was inspired by observations that fermented foods containing beneficial bacteria were associated with improved health and longevity [(9)]. The most commonly used probiotic microorganisms belong to the genera *Lactobacillus* and *Bifidobacterium*, although yeast such as *Saccharomyces boulardii* is also widely used [(10)].

The gut microbiota interacts closely with the host immune system. Approximately 70% of the body's immune cells are located in the gastrointestinal tract, highlighting the importance of the gut as an immune organ [(11)]. Through interactions with immune cells and intestinal epithelial cells, gut microorganisms influence both innate and adaptive immunity [(12)].

Disruption of gut microbiota balance, referred to as dysbiosis, can lead to increased intestinal permeability, inflammation, and susceptibility to disease [(5)]. Dysbiosis has been linked to conditions such as inflammatory bowel disease, obesity, diabetes, allergies, and autoimmune disorders [(13)].

Probiotics have been proposed as a promising strategy to restore microbial balance and improve immune function [(5)]. These beneficial microbes exert their effects through several mechanisms including competitive exclusion of pathogens, production of antimicrobial compounds, and modulation of immune responses [(14)].

Recent advances in microbiome research have revealed that probiotic therapy may provide significant health benefits in both gastrointestinal and systemic diseases [(15)]. Therefore, understanding the mechanisms and clinical applications of probiotics has become an important area of research in biotechnology and medicine.

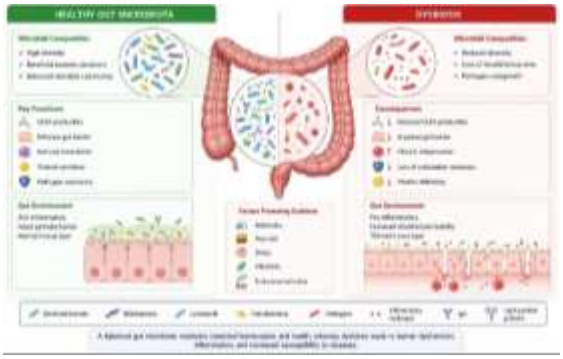

Figure 2. Composition of healthy gut microbiota and dysbiosis-associated alterations in the gastrointestinal tract.

2. Mechanisms of Probiotics in Gut Health and Immunity

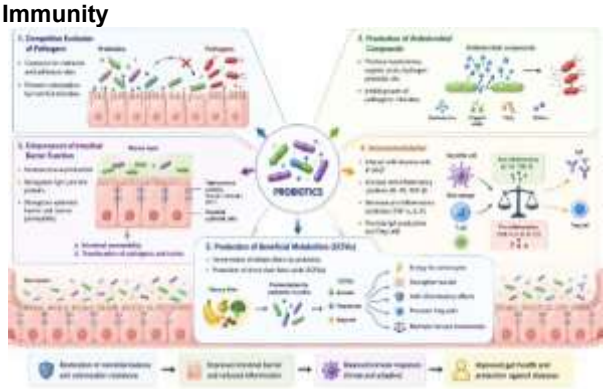

Figure 3. Major mechanisms of probiotic action in maintaining gut health and immune regulation.

2.1 Regulation of Gut Microbiota Composition

One of the primary functions of probiotics is the regulation of gut microbiota composition (2). Probiotics can compete with pathogenic microorganisms for nutrients and adhesion sites on intestinal epithelial cells [16]. This competitive exclusion prevents colonization by harmful bacteria and promotes the growth of beneficial microbial communities [17].

Probiotic bacteria also produce antimicrobial compounds such as bacteriocins, hydrogen peroxide, and organic acids that inhibit pathogenic microbes [18]. These compounds create an unfavorable environment for pathogenic bacteria while supporting beneficial microbial populations [19].

2.2 Enhancement of Intestinal Barrier Function

The intestinal epithelial barrier is a crucial defense mechanism that protects the host from harmful microorganisms and toxins [20]. Tight junction proteins between epithelial cells regulate intestinal permeability and maintain barrier integrity [21].

Probiotics strengthen the intestinal barrier by stimulating mucus production and increasing the expression of tight junction proteins [22]. This helps prevent the translocation of pathogens and toxins across the intestinal epithelium [23]. Additionally, probiotics promote epithelial cell proliferation and repair of damaged intestinal tissues [24].

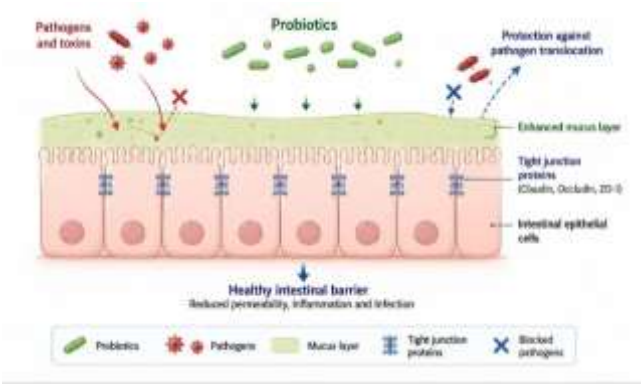

Figure 4. Role of probiotics in strengthening intestinal barrier integrity and preventing pathogen invasion.

2.3 Immunomodulatory Effects

Probiotics influence both innate and adaptive immune responses [25]. They interact with immune cells such as dendritic cells, macrophages, and T lymphocytes present in the gut-associated lymphoid tissue (GALT) [26].

Probiotic microorganisms can stimulate the production of immunoglobulin A (IgA), which plays a key role in mucosal immunity [27]. They also modulate cytokine production, balancing pro-inflammatory and anti-inflammatory immune responses [28]. This immune regulation helps reduce chronic inflammation and maintain immune homeostasis [29].

2.4 Production of Beneficial Metabolites

Probiotic microorganisms contribute to host health by producing beneficial metabolites such as short-chain fatty acids (SCFAs) including acetate, propionate, and butyrate [30]. These metabolites are produced through fermentation of dietary fibers in the colon [31]. Short-chain fatty acids serve as energy sources for intestinal epithelial cells and play a critical role in regulating immune responses and inflammation [32]. SCFAs also promote the differentiation of regulatory T cells, which help maintain immune tolerance [33].

2.5 Advanced Role of Microbial Metabolites in Host Immunity

Microbial metabolites derived from probiotic activity play a crucial role in maintaining host physiological and immunological balance. Among these, short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate have been extensively studied for their systemic effects beyond the gut environment [34]. These metabolites not only serve as energy sources for colonocytes but also act as signaling molecules that influence host cellular pathways [35].

SCFAs regulate immune function through interaction with G-protein-coupled receptors (GPCRs) such as GPR41 and GPR43, which are expressed on immune cells including neutrophils, macrophages, and dendritic cells [36]. Activation of these receptors leads to modulation of inflammatory responses and maintenance of immune homeostasis. Additionally, SCFAs have been shown to inhibit histone deacetylases (HDACs), thereby influencing gene expression related to immune regulation and inflammation [37].

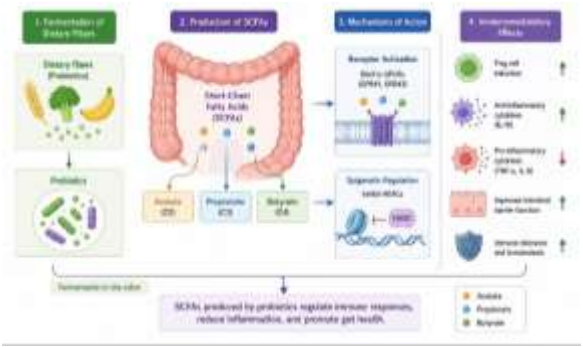

Figure 5. Production of short-chain fatty acids by probiotics and their immunomodulatory effects.

Recent studies have also demonstrated that microbial metabolites play a role in the gut–brain axis, highlighting the connection between gut microbiota and neurological function [38]. SCFAs can cross the blood–brain barrier and influence neuroinflammatory pathways, suggesting their potential role in neurodegenerative and psychiatric disorders [39]. This expands the functional relevance of probiotics beyond gastrointestinal health to systemic and neurological effects.

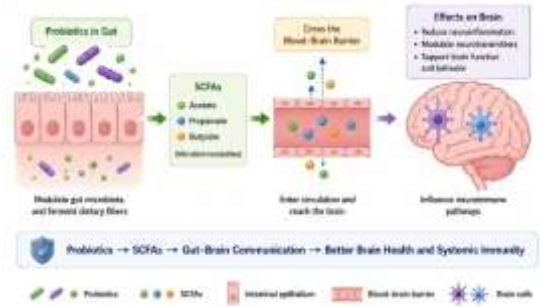

Figure 6. Role of probiotic-derived metabolites in gut–brain axis communication and systemic immunity.

Furthermore, SCFAs contribute to metabolic regulation by influencing lipid metabolism, glucose homeostasis, and energy balance [40]. These findings suggest that probiotic-mediated production of microbial metabolites has far-reaching implications in preventing metabolic disorders such as obesity and type 2 diabetes.

3. Clinical Evidence of Probiotics in Gut Health and Immunity

3.1 Probiotics in Irritable Bowel Syndrome (IBS)

Irritable bowel syndrome (IBS) is a common gastrointestinal disorder characterized by abdominal pain, bloating, and altered bowel habits [41]. Increasing evidence suggests that disturbances in gut microbiota composition contribute to the pathogenesis of IBS [42]. Probiotic therapy has emerged as a promising approach to restore microbial balance and improve symptoms in IBS patients [43].

Clinical trials have shown that probiotic strains such as *Lactobacillus* and *Bifidobacterium* can reduce abdominal pain, bloating, and intestinal discomfort [44]. These probiotics improve gut motility, regulate intestinal permeability, and modulate inflammatory responses in the gut [45]. Some studies also indicate that probiotics may improve quality of life in IBS patients [46].

3.2 Probiotics in Antibiotic-Associated Diarrhea

Antibiotic-associated diarrhea (AAD) occurs due to disruption of normal gut microbiota following antibiotic therapy [47]. This condition is frequently associated with the overgrowth of opportunistic pathogens such as *Clostridioides difficile* [48].

Several clinical trials have demonstrated that probiotic supplementation can significantly reduce the incidence of antibiotic-associated diarrhoea [49]. Strains such as *Saccharomyces boulardii* and Lactobacillus rhamnosus have shown protective effects by restoring microbial balance and inhibiting pathogenic bacteria [50]. Probiotics also enhance intestinal barrier function and reduce intestinal inflammation during antibiotic treatment [51].

3.3 Probiotics in Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) includes chronic inflammatory conditions such as Crohn's disease and ulcerative colitis [52]. Dysbiosis of the gut microbiota plays a major role in the development and progression of IBD [53].

Probiotics have been investigated as a therapeutic approach for maintaining remission in patients with ulcerative colitis [54]. Certain probiotic formulations have demonstrated anti-inflammatory effects and improved mucosal healing in clinical studies [55]. Probiotics can regulate immune responses by modulating cytokine production and reducing intestinal inflammation [56].

3.4 Probiotics in Immune System Enhancement

Probiotics play a significant role in enhancing immune function by stimulating both innate and adaptive immune responses [57]. Clinical studies suggest that probiotic supplementation can increase the production of immunoglobulin A (IgA), which provides protection against pathogens at mucosal surfaces [58].

Probiotics have also been shown to enhance natural killer (NK) cell activity and improve resistance to infections [59]. Some studies indicate that probiotic consumption may reduce the risk of respiratory infections and gastrointestinal infections [60].

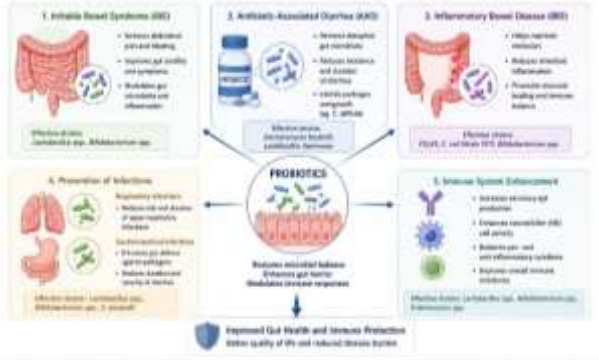

Figure 7. Clinical applications of probiotics in gastrointestinal and immune-related disorders.

4. Safety and Limitations of Probiotic Therapy

Although probiotics are generally considered safe, certain limitations and risks should be considered [61]. Most probiotic strains have been classified as safe for human consumption, particularly those belonging to lactic acid bacteria [62].

However, in rare cases, probiotic use may cause infections in immunocompromised individuals or critically ill patients [63]. Therefore, careful selection of probiotic strains and proper clinical evaluation are necessary before their therapeutic use [64].

Another limitation of probiotic therapy is the variability in strain-specific effects [65]. Different probiotic strains may produce different physiological outcomes, and not all strains provide the same health benefits [2]. Standardization of probiotic formulations and dosage remains an important challenge in clinical research [66].

5. Future Perspectives in Probiotic Research

The field of probiotic research is rapidly evolving with advances in microbiome science and biotechnology [67]. New technologies such as metagenomics and next-generation sequencing have improved our understanding of the human gut microbiome [68].

Future research may focus on the development of next-generation probiotics, which include beneficial microbial species that are naturally present in the human gut but have not yet been widely used as probiotics [69]. These microorganisms may offer more targeted therapeutic benefits for specific diseases [70].

Another promising area is personalized probiotic therapy, where probiotic treatments are tailored according to an individual's microbiome composition [71]. Such approaches may enhance treatment efficacy and reduce variability in clinical outcomes [73].

Additionally, the combination of probiotics with prebiotics, known as synbiotics, may further enhance gut microbial balance and improve health outcomes [73]. Continued research and large-scale clinical trials are essential to establish evidence-based guidelines for probiotic therapy in human health [74].

Figure 8. Future perspectives and emerging approaches in probiotic and microbiome-based therapy.

6. Conclusion

Probiotics represent a promising therapeutic strategy for maintaining gut health and regulating immune function. These beneficial microorganisms exert their effects through multiple mechanisms, including modulation of gut microbiota composition, enhancement of intestinal barrier integrity, production of beneficial metabolites, and regulation of immune responses.

Clinical evidence supports the use of probiotics in several gastrointestinal disorders such as irritable bowel syndrome, antibiotic-associated diarrhea, and inflammatory bowel disease. Furthermore, probiotics have shown potential in enhancing immune responses and reducing the risk of infections.

Despite these promising findings, further research is required to better understand strain-specific effects, optimal dosage, and long-term safety of probiotic therapy. Advances in microbiome research and biotechnology may lead to the development of next-generation probiotic therapies with improved clinical efficacy.

Ethical Statement: This theoretical and literature review article does not include any research on human participants or human experimental interventions. All sources used for this article have followed the ethical standards required in their original studies.

Conflict of Interest Statement: Authors have also declared that there are no conflicts of interest regarding this article.

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