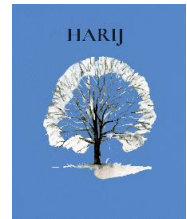




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## Probiotic Bacteria and Their Impacts on Gut Microbiota and Digestive Health: Mechanisms and Applications

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**Abstract:** The human gut microbiota, a complex and dynamic microbial community dominated by Bacteroidetes and Firmicutes, plays a fundamental role in maintaining host health through metabolic, protective, and immunological functions. Probiotic bacteria, particularly *Lactobacillus* and *Bifidobacterium* species, have emerged as critical modulators of gut homeostasis, exerting beneficial effects through multiple mechanisms, including pathogen inhibition, immune system regulation, and enhancement of intestinal barrier integrity. Beyond their biological significance, probiotics have found extensive applications in food biotechnology for fermentation and preservation, as well as in clinical settings for managing gastrointestinal disorders, including antibiotic-associated diarrhea, irritable bowel syndrome, and lactose intolerance. This review synthesizes current knowledge on the mechanistic basis of probiotic action, evaluates evidence for their health benefits, and discusses their industrial and therapeutic applications. Key findings highlight strain-specific effects, the importance of viability and dosage, and the need for personalized approaches due to inter-individual microbiota variability. Despite promising outcomes, challenges remain in standardization, safety assessment, and the development of next-generation probiotics. The present review concludes by emphasizing the potential of probiotics as versatile bio-therapeutic agents while underscoring the necessity for further research to optimize their efficacy and expand their applications in precision medicine.

**Keywords:** probiotics, gut microbiota, microbial therapeutics, fermented foods, personalized nutrition

### 1. Introduction

The term probiotics derives from two Greek words, pro(for), and bios(life) (Santacroce et al., 2019). It refers to microorganisms that provide health benefits to their host (Sánchez et al., 2017). The concept of probiotics was first introduced in 1907 by Élie Metchnikoff, who proposed that certain microorganisms within the human microbiota could exert positive effects on general health (Metchnikoff, 1907). According to the joint definition by the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) in 2014, probiotics are described as “live microorganisms which administered in adequate amounts, confer a health benefit on the host” (FAO, 2014; WHO, 2014). Probiotics are defined as viable microorganisms (bacteria or yeasts) that, when ingested in an appropriate concentration, exert various beneficial effects on the host (Govender et al., 2014). Among the known probiotic microorganisms, species of lactic acid bacteria (LAB) (e.g., *Lactococcus*, *Lactobacillus*, *Streptococcus*, and *Enterococcus*) and *Bifidobacterium* have a long history of safe use (Doron and Snyderman, 2015; Prado et al., 2015; Socol et al., 2015). This definition applies specifically to the beneficial forms of these bacteria, whether delivered via food, pharmaceutical products, or other preparations (Fenster et al., 2019). However, in individuals with weakened immune systems, the use of live probiotic bacteria can sometimes lead to severe inflammatory reactions (Ashraf et al. 2014). In such cases, the application of non-viable or inactivated bacterial cells referred to as paraprobiotics has been shown to provide health benefits without the risks associated with live microorganisms (Taverniti & Guglielmetti, 2011).

Probiotic microorganisms support host health through various mechanisms (Sánchez et al., 2017). One of the primary mechanisms is competitive adhesion to the intestinal epithelial cells, which prevents pathogenic microorganisms from

attaching to the intestinal lining and forming colonies. Species such as *Lactobacillus* and *Bifidobacterium* are particularly effective in this regard (Monteagudo-Mera et al., 2019). Another key mechanism involves the production of antimicrobial substances, including bacteriocins, active proteins, and other compounds that exhibit antibacterial activity and contribute to the destruction of pathogenic cells (Kumariya et al., 2019).

Lactic acid bacteria, for example, secrete compounds such as hydrogen peroxide, diacetyl, and short-chain fatty acids, all of which play essential roles in maintaining host health (Saha et al., 2022). Furthermore, probiotic microorganisms have been shown to modulate and stimulate the immune system (Rashidinejad et al., 2023).

This review aims to synthesise current understanding of probiotic mechanisms while addressing these unresolved challenges to guide future therapeutic development and clinical implementation.

## 2. Materials and Methods

This review was prepared by consulting recent and relevant scientific literature on probiotics, gut microbiota, and digestive health. Information was gathered from peer-reviewed articles, books, and reports available through databases such as PubMed, Scopus, Web of Science, and Google Scholar. Preference was given to publications from 2012 to 2025, while classical studies and key definitions from WHO/FAO were also included. Articles discussing mechanisms of action, clinical applications, safety considerations, and emerging concepts such as synbiotics and postbiotics were considered most relevant. The selected literature was synthesised to provide an overview of current knowledge and highlight future perspectives.

## 3. Results

### 3. Probiotic Bacteria in Gut Microbiota and Digestive Health

Probiotic bacteria play a crucial role in restoring and maintaining the gut microbiota, contributing significantly to the alleviation of digestive system disorders (Azad et al., 2018). In addition to their benefits for the gastrointestinal tract, these microorganisms promote overall health and the proper functioning of various organs (Dieterich et al., 2018). They have been associated with lowering blood cholesterol levels, strengthening the immune system, regulating nervous system activity, and enhancing bone strength by increasing intestinal calcium absorption (D'Amelio et al., 2018).

These beneficial microorganisms are collectively known as probiotic bacteria. Our understanding of the human gastric microbiota is continually advancing (Yang et al., 2013). The gastrointestinal tract hosts trillions of microorganisms collectively referred to as the microbiota, which are present in all humans regardless of age (Yatsunenko et al., 2012). The gut microbiota is primarily composed of two major phyla: Bacteroidetes and Firmicutes, with smaller proportions of Proteobacteria, Verrucomicrobia, Actinobacteria, and Fusobacteria. These microorganisms are distributed throughout the digestive system and maintain a symbiotic relationship with the host (Human Microbiome Project Consortium, 2012).

However, they are most abundant in the large intestine and colon. Diet directly influences gut microbiota composition (Bibbo et al., 2016). For example, individuals who consume a high-fibre diet tend to have higher levels of *Prevotella*, while those who consume a diet rich in protein and fat exhibit higher levels of *Bacteroides* (Ortega-Santos et al., 2019). Both of these genera belong to the Bacteroidetes phylum (Karlsson et al., 2011). When a person's diet returns to a balanced state, the microbiota also tends to revert to its normal composition. Two dietary components significantly influence the microbiome: probiotics and prebiotics (Piccioni et al., 2023).

Probiotics are beneficial microorganisms; *Lactobacillus* (belonging to the Firmicutes phylum) and *Bifidobacterium* (belonging to the Actinobacteria phylum) are among the most extensively studied groups. Prebiotics, on the other hand, refer to dietary substances that serve as nutrients for probiotic bacteria, supporting their growth and activity (Tsai et al., 2019).

## 4. Mechanisms of Action

### 4.1 Colonisation resistance and ecological interactions

Probiotics can inhibit pathogen expansion via niche competition, bacteriocin production, and pH modulation, thereby contributing to colonisation resistance. Although durable colonisation is often limited and host-specific, transient passage may still modulate community function and resist overgrowth of opportunists during ecological disturbances such as antibiotics. Contemporary work emphasizes inter-individual variability in colonization and responsiveness (Woelfel et al., 2024).

#### 4.2 Metabolite-mediated effects: SCFAs and bile acids

Probiotic activity intersects with broader microbiome metabolism, including short-chain fatty acids (SCFAs) that support epithelial energy and anti-inflammatory signalling, and the transformation of primary to secondary bile acids that modulate pathogen fitness and host receptors (FXR, TGR5). Mechanistic syntheses highlight these axes in AAD prevention and barrier support (Iyer et al., 2021).

#### 4.3 Epithelial barrier and mucosal immune modulation

Strains can enhance tight-junction integrity, increase mucin expression, and modify pattern-recognition receptor signalling, shifting mucosal cytokine profiles. Human studies increasingly show responder–nonresponder patterns linked to baseline microbiome and host features, reinforcing the importance of personalisation (Di Sabatino, A et al., 2023).

#### 4.4 Neuro gut and systemic crosstalk

Beyond local effects, probiotics can alter host immune–metabolic tone and, in some cohorts, stress-linked behaviours relevant in functional GI conditions such as IBS. A 2023 randomised study found distinct microbiome shifts and biomarker changes among “responders,” illustrating mechanistic heterogeneity (Montagnani et al., 2023).

### 5. Delivery Formats and Related Categories

Fermented foods (e.g., yoghurt, kefir, kimchi) may deliver live microbes but are not necessarily “probiotics” unless they contain defined strains with demonstrated health effects. ISAPP consensus clarifies these boundaries. Prebiotics are substrates selectively utilised by host microbes to confer health benefits. Synbiotics combine live microbes with such substrates; ISAPP updated the synbiotic definition in 2020 (including complementary vs. synergistic types). Postbiotics encompass inanimate microorganisms and/or their components that confer health benefits (Marco et al., 2021).

Live biotherapeutic products (LBPs) are drug-class products regulated under pathways distinct from those for supplements, with increasing relevance as next-generation strains move into trials; current guidance continues to evolve across agencies (not comprehensively reviewed here) (Elkrief et al., 2025).

### 6. Clinical Evidence by Indication

#### 6.1 Antibiotic-Associated Diarrhoea (AAD)

Systematic reviews (adults and children) generally show a protective effect of selected probiotics against AAD, though results depend on strains, dose, and trial quality. A 2021 adult meta-analysis reported risk reduction, and overviews in 2023 reaffirm efficacy in pediatric AAD while noting methodological limitations. Recent RCTs and overviews suggest that the benefit remains context-dependent, with some large, high-quality trials showing no effect (Mitra et al., 2023).

Practice note: Choose evidence-based strains/doses (e.g., *Lactobacillus/Lactocaseibacillus rhamnosus* GG, *Saccharomyces boulardii*, or specific multi-strain mixes) initiated early with antibiotics; counsel that benefit is probabilistic and not universal. (Strain-specifics vary across trials; see AAD meta-analyses above.)

#### 6.2 Prevention of *Clostridioides difficile* Infection (CDI)

Evidence is mixed. Earlier, Cochrane (2017) suggested that probiotics given alongside antibiotics reduced CDI risk, particularly in high-risk populations. However, subsequent US and gastroenterology society guidance (IDSA/SHEA updates; ACG) has recommended against routine probiotic use for primary or secondary CDI prevention due to inconsistent benefit and concerns about evidence quality and applicability to modern care pathways. Recent narrative/systematic reviews continue to report heterogeneity, with possible benefits in select older or high-risk cohorts (Kelly et al., 2021).

Practice note: If considered, reserve for carefully selected patients after weighing local CDI epidemiology, individual risk, and prevailing guidelines.

#### 6.3 Irritable Bowel Syndrome (IBS)

Multiple meta-analyses and RCTs support modest symptom improvement (overall and abdominal pain) with certain probiotic regimens; effect sizes are generally small to moderate and strain-specific. Recent RCTs (including 2024) continue to report benefits in subsets (e.g., IBS-mixed/diarrhoea-predominant) and suggest that some products have

psychobiotic effects on quality-of-life domains. Still, heterogeneity is high, and personalisation is emerging as key (Hajela et al., 2015).

Personalisation: Baseline microbiome features may predict response and colonisation, implying that stool profiling (research use) and clinical phenotyping (bowel habit, diet) could guide choice (Kok et al., 2023).

#### **6.4 Inflammatory Bowel Disease (IBD) and Pouchitis**

Data support certain high-potency multi-strain products as adjuncts for maintaining remission in pouchitis; evidence for ulcerative colitis (UC) induction/maintenance and Crohn's disease is mixed and strain-dependent (e.g., findings on *E. coli* Nissle 1917 vary across eras and formulations). Professional guidelines generally favour standard medical therapy first, with probiotics as optional adjuncts in narrow contexts (Akiyama et al., 2021).

#### **6.5 Functional Constipation**

Findings in adults are inconsistent across strains; some meta-analyses report increases in stool frequency and improvements in consistency with specific *Bifidobacterium* and *Lactobacillus* strains or synbiotics, while others show minimal effects. Overall, it is considered an adjunct to fibre, fluids, and behaviour therapy (Wojtyniak et al., 2017).

#### **6.6 Lactose Intolerance**

Fermented dairy products containing live cultures and some probiotic strains can improve lactose digestion and symptoms in many individuals, although effects are not universal and depend on the dose/product. (Broader mechanistic and older clinical evidence; contemporary head-to-head RCTs remain limited.)(Oak et al.,2019).

#### **6.7 Infant Colic**

Pediatric evidence, especially with *Lactobacillus reuteri* DSM 17938 in breast-fed infants, suggests reduced crying time; extrapolation to formula-fed infants is less consistent. (Recent pediatric AAD evidence overview also underscores pediatric strain- and dose-specificity (Ong et al., 2019).

#### **6.8 Helicobacter pylori (Adjuvant)**

Meta-analyses indicate that selected probiotics, including *S. boulardii* or *Lactobacillus* spp., added to standard eradication regimens can modestly increase eradication rates and reduce adverse effects (e.g., diarrhoea, nausea), without replacing antibiotics (Baryshnikova et al., 2023).

### **7. Criteria for the Selection of Probiotics**

Scientifically, probiotic products must have an adequate shelf life, contain a high number of viable cells at the time of consumption, and be safe from pathogenic and toxic factors. The most extensively studied probiotics are lactic acid-producing bacteria, such as *Lactobacillus* and *Bifidobacterium*, which never induce inflammation. The selection of an appropriate probiotic strain requires a systematic investigation and analysis based on specific mechanisms and criteria (Terpou et al., 2019).

The criteria set by the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) include essential parameters, while additional recommended criteria may be applied based on specific needs (Aidara-Kane et al., 2018).

#### **7.1 WHO Criteria for Probiotic Selection**

##### **Stress Tolerance**

Probiotics must remain viable under environmental stresses such as salivary enzymes, gastric enzymes, body temperature, low pH, gastric juice, and bile salts. These factors are encountered in the gastrointestinal tract and can adversely affect the survival of probiotics, as shown in Fig 1. Additionally, probiotics must resist enzymes present in the oral cavity during food intake, such as amylase and lysozyme. Thus, probiotics directly face these stressors in the digestive system and must demonstrate resilience (Vinícius et al., 2018).

##### **Adhesion Ability**

The second critical step for probiotic bacteria is their ability to adhere to the epithelial cells of the host's digestive tissues. This adhesion occurs between bacterial and epithelial cell membranes and is primarily mediated by electrostatic

interactions and van der Waals forces at specific surfaces. However, research has shown that the surface components of bacterial cells also significantly influence this adhesion process (Boonaert and Rouxhet, 2000; Duary et al., 2011). Probiotic adhesion to host cells occurs through mechanisms such as autoaggregation and hydrophobic interactions. Autoaggregation is the ability of probiotic bacteria to cluster together on the intestinal surface, thereby occupying available space and preventing pathogenic microorganisms from adhering to epithelial cells. The other important factor is the surface hydrophobicity of probiotic cells: the higher the hydrophobicity, the greater their tendency to form stable colonies on the mucosal surfaces (Vinícius et al., 2018).

### Anti-Pathogenic Activity

When probiotic bacteria enter the gastrointestinal tract, they produce extracellular compounds derived from carbohydrate metabolism, proteins, and other substances that contribute to their antimicrobial activity. These compounds can kill pathogenic microorganisms and include organic acids, enzymes, hydrogen peroxide, bacteriocins, and low-molecular-weight peptides. Additionally, probiotics compete with pathogens for nutrients and adhesion sites, further inhibiting their growth (Lebeer et al., 2008).

Another important mechanism is coaggregation, in which genetically related bacteria adhere to each other via interactions between surface molecules, forming aggregates that prevent pathogen colonisation. Probiotics also stimulate the host's immune system, enhancing its defensive response against harmful microbes (Vinícius et al., 2018).

### Safety Assessment

The safety of probiotic strains is primarily determined by their history of safe use, which is the first criterion for their selection. Additionally, probiotics must be accurately identified taxonomically, be non-inflammatory, and should not produce enterotoxins. They must also possess intrinsic, nontransferable antibiotic resistance genes, ensuring they do not contribute to the spread of antibiotic resistance. Furthermore, industrial selection of probiotic strains follows specific criteria, as illustrated in Figure 1 (Vinícius et al., 2018).



Figure 1. Criteria for the Selection of Probiotics (Peivasteh Roudsari et al., 2019).

## 4. Discussion

Probiotic bacteria are important for digestive health, as shown in the studies reviewed here. They help balance gut microbes, support digestion, and improve gut health. Research shows that *Lactobacillus*, *Bifidobacterium*,

Saccharomyces, and other helpful microbes can restore balance, especially in people with gut issues caused by antibiotics, diet, or disease. This evidence supports the idea that probiotics can help prevent and treat digestive problems.

The review shows that probiotics work in many ways. They block harmful bacteria, produce antimicrobial substances, strengthen the gut barrier, modulate the immune system, and support nutrient use. Although these effects are proven, the extent to which each matters depends on the specific strain. This means it is important to choose probiotics based on their proven functions, not just their species.

People respond differently to probiotics. Results can change based on age, diet, genetics, and the gut microbes people already have. For example, one probiotic strain might help IBS symptoms in one group but not in another. This shows that probiotic treatments should be tailored to each person or condition, and that the relationship between people and microbes is complex.

Probiotics show promise for treating digestive problems, but the evidence is not always strong. They have been studied for diarrhoea, IBD, IBS, lactose intolerance, and constipation. The best results are for acute infectious diarrhoea and antibiotic-induced diarrhoea. More research is needed for conditions like ulcerative colitis, Crohn's disease, and colorectal cancer. Also, many probiotic products on the market lack standardised doses, proven strains, or strong clinical evidence, raising questions about their reliability.

Safety is very important when using probiotics. They are usually safe for healthy people, but new reports warn that they can be risky for people with weak immune systems or serious illnesses. These risks include infections or excessive immune response. Because of this, it is important to weigh the risks and benefits and to have clear rules for their use.

Future studies should focus on understanding what each probiotic strain does and how they work over time. It is also important to study how probiotics interact with diet, prebiotics, and the whole microbiome. New technologies such as metagenomics, metabolomics, and proteomics can help us better understand how probiotics work and develop more targeted products.

In summary, this review demonstrates that probiotics have significant therapeutic and preventive potential, but their full clinical value depends on evidence-based selection. In conclusion, this review shows that probiotics can help prevent and treat digestive problems, but their benefits depend on selecting the right strains, personalising treatments, and improving regulatory oversight. Progress will require teamwork between experts in microbiology, nutrition, immunology, and clinical research.

## 8. Conclusion

Probiotic bacteria contribute significantly to gut microbiota balance and digestive health by enhancing colonization resistance, producing antimicrobial metabolites, strengthening the intestinal barrier, and modulating immune responses. Clinical evidence strongly supports their use in the prevention of antibiotic-associated diarrhea, while findings in other gastrointestinal conditions such as *Clostridioides difficile* infection, irritable bowel syndrome, and inflammatory bowel disease remain promising but variable and strain-dependent. Selection of appropriate probiotic strains is crucial, as not all microorganisms exert the same effects, and factors such as viability, stress tolerance, and safety must be carefully evaluated. Although probiotics are generally safe for healthy individuals, their application in immunocompromised or critically ill patients requires caution. Advances in microbiome research, along with the development of synbiotics, postbiotics, and live biotherapeutic products, are paving the way for more effective and personalized therapeutic approaches. In summary, probiotics represent a valuable adjunct in maintaining digestive health and managing certain gastrointestinal disorders, but their clinical use should be guided by robust scientific evidence, strain specificity, and patient safety considerations.

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