



**INTERNATIONAL JOURNAL OF  
PHARMACEUTICAL SCIENCES**  
[ISSN: 0975-4725; CODEN(USA): IJPS00]  
Journal Homepage: <https://www.ijpsjournal.com>



## Review Paper

## Review Article on Probiotics

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### ARTICLE INFO

Published: 10 Sept 2026

**Keywords:**

Probiotics, live  
microorganisms, biological  
research

**DOI:**

10.5281/zenodo.22688447

### ABSTRACT

Probiotics, which are live microorganisms, are good for the host's health when taken in large enough amounts. Probiotics have changed from being just dietary supplements to a major area of biological research over the last few decades because they are important for maintaining gut microbial balance and affecting overall health. The gut microbiome is a large and varied group of microbes that live in the human gastrointestinal system. It is important for the immune system, metabolism, digestion, and even brain function. Dysbiosis, or the disruption of this microbial balance, has been associated with various illnesses, including metabolic syndromes, autoimmune diseases, mental health disorders, and gastrointestinal conditions. Probiotics have positive effects in many ways, such as by fighting off pathogens, making antimicrobial compounds, strengthening the intestinal barrier, changing immune responses, and interacting with the gut-brain axis. In addition to gut health, they are used to keep the heart healthy, prevent cancer, control allergies, and regulate metabolism.

### INTRODUCTION

The human gut microbiota is a complicated ecosystem made up of trillions of bacteria, viruses, fungi, and other types of microbes. Humans and this diverse microbiome have coevolved, affecting and being affected by our diet, lifestyle, and physiology.[1] The homeostasis of this vast microbial population is a crucial aspect of human health, fulfilling various functions within our

digestive systems. Recent scientific studies show that gut microbiota homeostasis is important for controlling inflammation in the gut, keeping the body's metabolism in balance, and helping the immune system grow and change.[2] For instance, type 2 diabetes, obesity, inflammatory bowel disease (IBD), and even systemic conditions such as heart disease, certain cancers, and neurological disorders.[3,4] Also, research on

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**Relevant conflicts of interest/financial disclosures:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



the gut-brain axis says that dysbiosis can change neurochemical pathways that make mental health problems like anxiety and depression worse.[5] In conclusion, the balance of the bacteria in our gut is very important for keeping us healthy and stopping us from getting sick. For the illnesses that come from an imbalance in the gut

Choosing the right treatments and therapies to restore and keep the balance of gut microbiota is the key to getting better health and treating related diseases. Synthetic drugs are now the most important part of modern medicine, and they can help with a wide range of health problems.[6] Synthetic drugs can target abnormal pathways with great accuracy by using the subtleties of molecular biology and chemistry. This shows that they are very effective and predictable in treating many diseases.[7] Synthetic drugs have changed the way we treat illnesses by giving us options when traditional treatments didn't work very well.

[8] However, as we learn more about human health, it is becoming clearer that diseases are rarely caused by single molecular malfunctions.[9,10] are specifically diseases caused by changes in the gut microbiota.[11] In the realm of synthetic medicine treatments, this finding presents a conundrum. These medications are effective at targeting specific molecules or pathways; however, they often neglect the intricate and dynamic equilibrium of the gut microbiota in relation to disease etiology.[12] Treatments for diseases resulting from disturbances in the gut microbiota often require a comprehensive and multidimensional approach.

Synthetic drugs may help with symptoms, but they may not be able to fully restore microbial balance or fix the root of the problem.[13]. Also, synthetic drugs can cause or make health problems linked to gut dysbiosis worse, especially broad-spectrum antibiotics that attack a wide range of bacteria.[14]. So, even though synthetic drugs are

a big step forward in treating illness, their effect on the gut flora is a big problem that needs a more complete solution.

The importance of probiotics, prebiotics, and postbiotics in the medical field has grown as more and more evidence shows that the gut microbiota is very important for health and disease. This is because probiotics can change the gut microbiota to treat illness and make health better.[15,16] Prebiotics are substances (usually dietary fibers) that don't break down in the body but help good gut bacteria grow and work. Postbiotics are the active substances that probiotics make while they grow and help gut health. Probiotics are live microorganisms that are good for your health when you eat enough of them.[17] Probiotics are live helpful microorganisms that eat prebiotics. Postbiotics are the healthy things that probiotics make. Each one plays a big role in keeping the body in balance and has its own job in the symbiotic relationship with the human host.[18] Probiotics are often present in fermented foods and dietary supplements, and studies indicate that they may improve immune function, gastrointestinal health, and various other health parameters.[19] Prebiotics help the host by encouraging the growth and activity of one or more types of bacteria in the colon.[20]. In short, they feed the good bacteria in the gut, which helps them grow and makes the microbiome better.[21] Postbiotics is the newest area of research of the three. They are the health-promoting compounds that probiotics make when they break down food, and they are a return to the beginning of probiotic research.[17,22]

### **Classifications of probiotics**

1. Conceptual / vitality- based classification
  - True probiotics (TP) – viable, active cells.
  - Pseudo-probiotics (PP) – viable but inactive cells (vegetative or spore forms).
  - Ghost probiotics (GP) – dead/non-viable cells, intact or ruptured.[23]



## 2. Strain based classification ;

Common probiotic genera include *Lactobacillus* (*sensu lato*), *Bifidobacterium*, *Saccharomyces*, *Enterococcus*, *Streptococcus*, *Pediococcus*, *Leuconostoc*, *Bacillus*, *Escherichia coli*[24]. Lactic acid bacteria dominate food applications[25,26,24]

Holzappel et al. emphasize phenotypic vs molecular classification and the need for 16S rRNA and genotyping methods to distinguish closely related groups (e.g., *L. acidophilus* group, *L. Casei/paracasei*, *bifidobacteria*)[26].

Sniffen/McFarland and colleagues highlight strain-specific designations (e.g., *L. rhamnosus* GG, *S. boulardii* CNCM I-745) and show that efficacy is both strain- and disease-specific[27,28].

## FUNCTION/ INDICATION BASED CLASSIFICATION :-

Gut and metabolic health: IBS, IBD, antibiotic-associated diarrhea, metabolic diseases, obesity, diabetes[25,27,29,30]

- \* Immune / anti-infective: respiratory infections, ventilator-associated pneumonia, necrotizing enterocolitis, *H. pylori*-related side-effects[25,29,27,30]
- \* System-specific "-biotics": psychobiotics (brain/mental health), cardiobiotics (cardiovascular), dermabiotics (skin), oralbiotics (oral cavity), urogeniobiotics (urogenital), gastrobiotics (GI tract), gerobiotics (aging)[31,32]

Large evidence syntheses for indication-based efficacy: Sniffen et al. practical guide[27] McFarland et al. meta-analysis[28] multiple meta-analyses summarized by Rondanelli et al [33] clinical focus reviews[29,30]

## 4. Regulatory / Product-Category Classification

From a regulatory lens, probiotic products are grouped as[31,34,35]

- Probiotic foods (fermented foods, functional foods).
- Dietary/nutritional supplements.
- Live biotherapeutic products (LBPs; medicinal use).

Different regions apply distinct rules for health vs nutrition claims, quality standards, and proof of efficacy[25,34,35].

## Sources of probiotics :-

- Main microbial sources: Lactic acid bacteria (*Lactobacillus sensu lato*, now split into multiple genera), *Bifidobacterium*, *Saccharomyces boulardii*, some *Enterococcus*, *Streptococcus*, *Lactococcus*, *Bacillus*, and select *E. coli* strains.[36,37]
- Food sources & products: Fermented milk/curd, yogurt cultures (*Streptococcus thermophilus*, *L. delbrueckii* subsp. *bulgaricus*), fermented foods and dietary supplements.[36,38]

## Mechanism of Probiotics :-

Probiotics act through multiple, overlapping mechanisms that are highly strain-specific and involve direct effects on microbes, the intestinal barrier, immune cells, and host metabolism. The papers below are strong starting points for a review, combining mechanistic depth with broad clinical relevance.

## Major Mechanistic Themes

### 1. Modulation of gut microbiota and pathogen interference:-

Microbiota reshaping & colonization: Probiotics normalize dysbiotic communities and restore intestinal homeostasis in children and adults[39,40].



**Competitive exclusion & antimicrobials:** They compete for adhesion sites and nutrients and produce bacteriocins, organic acids, and other antimicrobials that inhibit pathogens[40,41]

**Metabolite production:** Short-chain fatty acids and other metabolites influence local pH, pathogen growth, and systemic metabolism (e.g., insulin sensitivity)[42,39].

## 2. Strengthening of the intestinal barrier:-

**Epithelial adhesion & mucin:** Adhesion to epithelial cells and stimulation of mucin production help block pathogen access and enhance barrier integrity[40,41].

**Tight junctions & epithelial signaling:** Surface molecules and secreted factors interact with epithelial receptors to reduce apoptosis, promote repair, and tighten junctions[42,43].

## 3. Immunomodulation :-

**Pattern-recognition receptor signaling:** Cell wall and surface structures activate TLRs and NOD-like receptors, modulating NF- $\kappa$ B/MAPK pathways and antimicrobial responses with limited inflammation[40,44,45].

- **T cell and cytokine balance:** Probiotics promote Treg differentiation and increase anti-inflammatory cytokines (e.g., IL-10, TGF- $\beta$ ), while modulating Th1/Th2 responses[44,39].

## 4. Systemic metabolic and neuroimmune effects:-

- **Metabolic diseases:** Through microbiota and metabolite modulation, probiotics affect obesity, metabolic syndrome, NAFLD, and type 2 diabetes.[39,42].
- **Gut–brain and gut–lung axes:** Production of neurotransmitters and immune crosstalk influence CNS function and respiratory immunity[39,41].

## Health benefits of probiotics:-

Probiotics are live microorganisms that, in adequate amounts, can benefit human health, mainly by modulating the gut microbiota and immune system.

## Major Health Benefits :-

### Gastrointestinal and Metabolic Health :-

- Reduced risk or severity of infectious and antibiotic-associated diarrhea, IBS symptoms, and some inflammatory bowel conditions[46].
- Support for lactose intolerance, constipation, and general digestive comfort[47].
- Potential benefits for obesity, type 2 diabetes, lipid profile, and hypertension, although effects are often modest and strain-specific[48].

### Immune, Respiratory, and Infection-Related Outcomes:-

- **Immunomodulation:** enhanced barrier function, increased antibodies and immune cells, and modulation of inflammation[48].
- Prevention or mitigation of respiratory tract infections, with evidence strong enough to be considered "evidence-based" in meta-analyses.
- Adjunctive benefits in allergy and some infections (e.g., vaginosis, periodontitis, ventilator-associated pneumonia) but with variable strength of evidence[47].

### Mental and Cognitive Health:-

- Small but significant reductions in depression and anxiety in meta-analyses, stronger in clinical/psychiatric samples.
- Moderate- to high-quality evidence for improvements in various cognitive outcomes in adults[49].



- Probiotics act partly via the gut-brain axis and anti-inflammatory pathways[48].

### **Clinical Applications of Probiotics:-**

Probiotics are now tested across many medical specialties, but benefits are strain- and disease-specific, and evidence strength varies. The best-supported uses are in gastrointestinal conditions, some infections, and emerging areas like mental and cognitive health.

### **Major Clinical Indications:-**

- Antibiotic-associated diarrhoea (AAD): Large meta-analysis of 42 RCTs (11,305 adults) shows ~37% relative risk reduction; higher doses and *Lactobacillus* strains are most effective[50].
- IBS: For IBS-C, probiotics improve stool consistency and increase fecal bifidobacteria/lactobacilli but not pain or QoL; evidence low quality. In mixed IBS (Rome IV), probiotics reduce abdominal pain and bloating but not global severity or QoL[51].
- Functional constipation in children: Overall, no convincing benefit vs laxatives; current evidence does not support routine use[52].
- H. Pylori therapy: across 534 RCTs, adjunct probiotics modestly improve eradication and halve treatment side effects;

strain-specific optima unclear and many meta-analyses are low quality [53]

### **Safety and Side Effects of Probiotics:**

Probiotics are widely consumed and generally regarded as safe, but safety depends on strain, host vulnerability, dose, and route of administration. Across large meta-analyses, probiotics do not increase overall adverse events compared with placebo, yet rare but serious complications can occur in high-risk groups.

### **Major Types of Adverse Effects :-**

- Infections: Bacteraemia, sepsis, endocarditis, and fungemia have been reported, often involving *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*, especially with central venous catheters, severe illness, or immunosuppression[54].
- Gastrointestinal events: Nausea, diarrheas, bloating, abdominal pain, dyspepsia, and GI ischemia are the most frequent complaints[55].
- Metabolic/immune effects: Harmful metabolic activities, excessive immune stimulation, allergic reactions, and theoretical gene transfer of antibiotic resistance are highlighted concerns[54].
- Neuro-psychiatric and systemic signals: Pharmacovigilance data suggest signals such as agitation, anxiety, asthenia, hepatobiliary and metabolic disorders, mainly in older adults, though absolute numbers are small[56].

### **Prebiotics, Synbiotics, and Postbiotics in Probiotic Research:**

- Prebiotics: Non-digestible carbohydrates (e.g., inulin, FOS, GOS, XOS) that are selectively fermented and promote beneficial microbes, especially bifidobacteria and lactobacilli[57].
- Probiotics: Live, non-pathogenic microorganisms (mostly *Lactobacillus*, *Bifidobacterium*, some *Streptococcus*, *Bacillus*, *Enterococcus*, *Saccharomyces*) that confer health benefits in adequate doses[57].
- Synbiotics: Combinations of specific probiotics + matching prebiotics designed to improve survival, colonization, and function of the probiotic strain[57].
- Postbiotics: Preparations of inanimate microorganisms and/or their components or





metabolites (e.g., SCAs, peptides, polysaccharides, cell wall fragments) that provide health benefits with improved safety and stability versus live cells[58].

### Factors Affecting Probiotic Efficacy:-

**Probiotic efficacy depends on many interacting factors:** microbial (strain and dose), product-related (formulation, manufacturing, stability), host-related (disease, diet, microbiome, geography), and regulatory/quality aspects.

**Strain specificity:** Different strains within the same species can be effective or ineffective for the same indication; efficacy must be assessed at the strain level, not species[59].

**Disease-specificity:** A strain effective for one condition may fail in another (e.g., *L. rhamnosus* GG treats but does not prevent acute pediatric diarrhea[59]

**Mode of use:** Preventive vs therapeutic use can change outcomes for the same strain[59]

**Clinical examples:** Multi-strain formulations often show superior efficacy in ulcerative colitis and pouchitis compared with single strains[60].

**Diet:** Dietary patterns can modulate probiotic effects and may partly explain translation failures from preclinical to human studies[61].

**Geographical and ethnic variation:** Microbiota composition, lifestyle, regulations, and product types vary by region, influencing efficacy and viability of products[62]

**Health status & indication:** Response differs between healthy, at-risk, and diseased populations; mode of therapy must match indication[61].

**Quality control & labeling:** Mislabeling, inadequate viable counts at end of shelf life, and

lack of regulatory oversight threaten efficacy and safety[61].

**Trial design:** Many studies ignore diet and baseline microbiota, contributing to inconsistent results; longer and better-controlled trials are needed, especially for CNS indications[63].

**Current Research and Future Perspectives:-**

Probiotic research has expanded from classic gut health to systemic, neurological and even oncology-related applications. Recent reviews also stress regulation, manufacturing quality, and the shift toward next-generation probiotics, postbiotics, and smart delivery systems. In which future applications are included such as :-

- Personalised Antibiotics
- Microbiome Engineering
- Next Generation Therapies
- Artificial Intelligence etc.

### CONCLUSION

Probiotics represent a promising field in modern medicine, offering potential benefits across a wide range of health conditions. However, further research is needed to establish standardized guidelines and ensure their safe and effective use. The future of probiotics lies in personalized medicine, advanced biotechnology, and a deeper understanding of the human microbiome.

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**HOW TO CITE:** Shubham Tiwari, Rajesh Kumar, Ajeet Pal Singh, Amar Pal Singh, Pardeep Kaur, Review Article on Probiotics, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 9, 1058-1068, <https://doi.org/10.5281/zenodo.22688447>

