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

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**Review Article**

# Probiotics: Therapeutic Applications and Drug Delivery Approaches

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ARTICLE INFO

Published: 2 Nov 2026

Keywords:
Probiotics, Therapeutic applications, Pharmaceutical Formulations, Drug delivery systems, Microencapsulation, Probiotic Stability

DOI:
10.5281/zenodo.23876794

## ABSTRACT

Probiotics have gained increasing interest in pharmaceutical sciences because of their potential role in maintaining health and supporting the management of various diseases. These live microorganisms may influence host health through several mechanisms, including modulation of the intestinal microbiota, maintenance of intestinal barrier integrity, regulation of immune responses, and production of antimicrobial substances. Research has explored their applications in gastrointestinal disorders, oral and vaginal health, and several other conditions, although the available evidence varies depending on the probiotic strain and clinical indication. Despite their therapeutic potential, the development of probiotic formulations presents several challenges, particularly the maintenance of microbial viability during manufacturing, storage, and gastrointestinal transit. Recent advances in pharmaceutical technology, including microencapsulation, polymer-based encapsulation, and nanoencapsulation, are being investigated to improve probiotic stability and delivery to the intended site of action. However, differences in strain characteristics, formulation requirements, and clinical outcomes continue to influence their effectiveness. This review discusses the therapeutic applications of probiotics in pharmaceutical science, and recent advances in probiotic delivery systems. It also highlights current formulation challenges and future research directions that may contribute to the development of stable, safe, and effective probiotic-based pharmaceutical products.

## INTRODUCTION

The discovery of probiotics has led to its inclusion as a subject of extensive research by the pharmaceutical sciences due to their capacity to improve the human condition or prevent certain diseases.[1,5]. FAO/WHO, defined probiotics as those preparations of live microorganisms that have some beneficial effect on the health of the host when administered in adequate

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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.

quantities.[4,6] Probiotic is the Greek word meaning "for life".[4,5]. Over the century's discovery and exploration of the microbes for treating and managing numerous chronic and non-chronic conditions. The concept of probiotic emerged during the early phase of microbiology; the work of I.M. Metchinkoff proved that drinking yogurt regularly helps people to get younger.[3,8] The development and progress in the discovery and characterization of microbial strain has led us towards clearer understanding of their significance in therapeutics. [3,10] The human colon constitutes of diverse microflora that contributes to host health in various ways, for instance to digest food, regulation of immune system, metabolism, and other bodily functions.[1,3,5] But, disruption of normal intestinal biota with antibiotic treatment or altered microbiota conditions with infections, changing diets, other chronic diseases; may develop hazardous effects on the well-being.[3,9,11] These probiotics rebalance microbial populations by modulating flora, thus promoting colonization of beneficial microorganisms and suppression of growth of pathogen microorganisms.[4,6,11] Among all probiotic genera, Lactobacillus and Bifidobacterium contain predominantly studied members due to the lack of associated toxic and health-promoting effects.[2,4,6,8]

Probiotic enhance health by strengthening the intestinal lining thereby regulating immune response (innate and acquired); producing antimicrobial substance (bacteriocins, hydrogen peroxide, and Short chain fatty Acids) that directly suppresses pathogenicity.[4] In addition probiotic in the intestine also involves synthesis of vitamins, production of digestive enzymes and improvement of nutritional absorption of micro and macro nutrients to maintain basic functionality of the host.[6,7] Some researches also indicate that they may play important role in the prevention of gastrointestinal disorders, obesity, allergy, diabetes, cardiovascular diseases, colon cancer and inflammatory bowel diseases.[2,5,11] In addition to gastrointestinal tract probiotic also used to maintain good health for many other parts of the body like for the treatment of vaginal microbial imbalances and for preventing dental cavity.[2,8]

Recently, probiotics for gut microbiome and brain interactions has also drawn lots of scientific attentions, due to increased consumer demand and acceptance of this product in human nutrition, functional food, dietary supplement, and pharmaceutical sector probiotic have already been marketed in various formulation.[5,6] New technological approaches towards development of stability of this beneficial microorganisms through techniques of microencapsulation, nanoencapsulation and encapsulation by others polymer have enabled the effective delivery of live and viable cells to targeting intestinal compartment.[6,11] However, despite of such benefits the present progress is restrained with several challenges such as lack of consistency in results due to specificity and sensitivity; variability of strains; low recovery rate during digestion process.[6,7,11]

So further investigation is required to make their application safer and effective for various disorders. The objective of this literature review is to comprehensively explore pharmaceutical uses of probiotic, its mechanism current scientific knowledge, the recent technological developments for improved probiotic delivery and its future prospectives.

## 2.CLASSIFICATION OF PROBIOTICS

Probiotics comprise a diverse group of live microorganisms, mainly bacteria and fungi, that may provide health benefits when administered in appropriate amounts to healthy individuals. The probiotic microorganisms used in foods, dietary supplements, and other preparations belong to several bacterial genera, with Lactobacillus/ Lactobacillaceae and Bifidobacterium being among the most commonly represented groups. Other bacterial genera include Streptococcus, Lactococcus, Bacillus, Enterococcus, Escherichia, and Propionibacterium, whereas, Saccharomyces represents an important group of yeast probiotics. The classification and identification of probiotic microorganisms have traditionally involved morphological, biochemical, and physiological characteristics, whereas modern molecular and genomic methods have become increasingly important for accurate species and strain identification. [3,4,12-14]

**Table 1: Classification of Probiotic Microorganisms**

| Main | Genus/ group | Examples reported in the article | Key characteristics |
|---|---|---|---|
| **Bacterial** | *Lactobacillus / Lactobacillace* | *L. acidophilus, L. rhamnosus, L. plantarum, L. casei, L. paracasei, L. gasseri, L. johnsonii, L. lactis, L. salivarius* | Lactic acid bacteria commonly associated with the gastrointestinal tract and fermented foods. Molecular techniques help distinguish closely related species and probiotic strains. |
| | *Bifidobacteriu* | *B. bifidum, B. breve, B. lactis, B. longum, B. infantis, B. adolescentis,* | Used in fermented dairy products and other probiotic preparations. Identification may involve phenotypic, molecular, and genomic methods. |
| | *Streptococcus* | *S. thermophilus* | Reported as a probiotic microorganism and associated with fermented dairy products |
| | *Lactococcus* | *Lactococcus lactis* | A lactic acid bacterium used in dairy fermentation and reported in probiotic-related research. |
| | *Bacillus* | *B. coagulans, B. subtilis, B. cereus, B. clausii and others* | Includes spore-forming bacteria investigated or used in probiotic preparations. Suitability depends on species and strain safety. |
| | *Enterococcus* | *E. faecalis, E. faecium, E. durans* | Some strains have been investigated for probiotic applications; careful strain-level safety assessment is essential because certain strains may carry virulence or antimicrobial-resistance traits. |
| | *Other bacteria* | *Escherichia coli, Propionibacterium freudenreichii, and Pediococcus* | Includes additional microorganisms reported in probiotic research. Their potential applications and safety depend on the species and strain. |
| **Yeast probiotics** | *Saccharomyces* | *S. boulardii, S. cerevisiae* | Yeasts used or investigated in probiotic preparations; S. boulardii is a well-known example of a probiotic yeast. |

The microorganisms and species in the table were compiled from the microorganism table descriptions from the given references.[3,4,12-14]

## 3. THERAPEUTIC APPLICATIONS

### 3.1 Gastrointestinal Disorders

Probiotics have been widely studied for their potential role in managing gastrointestinal (GI) disorders. Their effects may involve changes in the intestinal microbiota, improved intestinal barrier function, and regulation of immune responses. However, the outcomes vary depending on the probiotic strain, dose, formulation, and condition being treated.[15–19]

#### 3.1.1. Mechanisms of Action of Probiotics in Gastrointestinal Disorders

Probiotics may influence gastrointestinal health through several mechanisms:

Modulation of intestinal microbiota: Probiotics may compete with potentially harmful microorganisms for nutrients and attachment sites, helping maintain the balance of the intestinal microbial community.[15,16]

Antimicrobial activity: Certain probiotic strains produce bacteriocins and other metabolites that may inhibit pathogenic microorganisms. Organic acid production can also contribute to an intestinal

environment that is less favourable for some pathogens.[15,16]

Improvement of intestinal barrier function: Some probiotics may support mucin production, maintain epithelial integrity, and influence tight-junction function, helping limit the passage of pathogens across the intestinal barrier.[16]

Immunomodulation: Probiotics may interact with intestinal epithelial and immune cells, influencing inflammatory responses and mucosal immunity. Some strains have also been associated with changes in secretory immunoglobulin A (IgA) production.[16,17]

Regulation of gastrointestinal motility and sensitivity: Certain strains have been investigated for their effects on intestinal movement and visceral sensitivity, which may be relevant to symptoms such as abdominal discomfort and altered bowel habits.[15,16]

These mechanisms provide a basis for investigating probiotics in GI disorders. However, findings from experimental studies do not always translate into consistent clinical benefits, and effects depend on the strain, host characteristics, and underlying condition.[16]

### 3.1.2. Clinical Applications of Probiotics in Gastrointestinal Disorders

Antibiotic-associated diarrhoea: Probiotics have been studied for the prevention of antibiotic-associated diarrhoea (AAD). Some studies and meta-analyses have reported reduced risk, with *Saccharomyces boulardii*, *Lacticaseibacillus rhamnosus* and selected combinations of lactic acid bacteria among the preparations investigated. Outcomes may depend on the strain, dose, patient population, and timing of administration.[15,17]

*Clostridioides difficile*-associated diarrhoea: Evidence for probiotics in *C. difficile*-associated diarrhoea remains inconsistent. Although some studies have investigated their use alongside antibiotic treatment, the available findings do not establish a consistent benefit across patient groups. Their role should therefore be interpreted according to the evidence for the specific preparation and clinical setting.[15,17]

Acute infectious diarrhoea: Certain probiotic preparations, including selected lactic acid bacteria and *S. boulardii*, have been investigated for reducing the duration of acute infectious diarrhoea. However, the magnitude of benefit varies between studies, and results should be interpreted in relation to the strain, patient population, and study design.[15,17]

Ulcerative colitis: Probiotics have been investigated as potential adjuncts in ulcerative colitis, particularly for inducing or maintaining remission. Some studies have reported benefits with selected multi-strain preparations, including VSL#3, whereas findings for individual strains and other formulations have been variable. The available evidence does not support assuming that all probiotic preparations are equally effective.[18]

Pouchitis: Certain multi-strain probiotic preparations have been studied for preventing recurrent pouchitis and maintaining remission in patients who have undergone ileal pouch–anal anastomosis. However, results vary between studies and formulations, so the evidence should be evaluated for each preparation separately.[15,18]

Crohn's disease: Evidence supporting probiotics in Crohn's disease remains limited. Clinical trials have not consistently demonstrated benefits for inducing or maintaining remission or preventing postoperative recurrence. Further studies are required to establish whether particular strains or combinations have a useful role.[15,17,18]

Irritable bowel syndrome: Probiotics have been investigated for irritable bowel syndrome (IBS), which may involve changes in the intestinal microbiota and altered visceral sensitivity. Some studies have reported improvements in overall symptoms, bloating, flatulence, or abdominal pain. However, outcomes differ between strains and formulations, and benefits for individual symptoms are not consistently observed.[15,17,18]

Constipation: Some probiotic strains, particularly selected *Bifidobacterium* strains, have been studied for their effects on stool frequency and consistency. Clinical trials have also examined *Bacillus coagulans*, *Streptococcus thermophilus*, and *Lactiplantibacillus plantarum*. Although certain studies report improvements in bowel habits, results vary across strains, populations, and treatment regimens.[18]

Small intestinal bacterial overgrowth: Probiotics have been investigated for small intestinal bacterial

overgrowth (SIBO), including their use alone or alongside antibiotic treatment. Some reviews have reported improvements in bacterial eradication or gastrointestinal symptoms, but the evidence remains limited. Further research is needed to establish suitable strains, doses, treatment durations, and combination regimens.[18]

*Helicobacter pylori* infection: Probiotics have been studied as an adjunct to *H. pylori* eradication therapy. Some studies suggest potential benefits when probiotics are combined with antibiotics, but findings are inconsistent. Their role should be assessed according to the specific formulation and the clinical evidence available [17,18].

Other gastrointestinal conditions: Probiotics have also been investigated in conditions such as hepatic encephalopathy and necrotising enterocolitis. Some studies have reported favourable outcomes, including reduced incidence of necrotising enterocolitis in preterm infants. However, effects vary by condition and patient population, and evidence for improvements in outcomes such as mortality is not consistent.[17] Probiotics have not demonstrated a clear, established benefit across all gastrointestinal conditions.[17,18]

Overall, probiotics have potential applications in several gastrointestinal disorders, but their clinical effectiveness is not uniform. Differences in strain characteristics, formulation, dosage, and study design contribute to variations in reported outcomes. Further well-designed clinical studies are needed to clarify which preparations are most appropriate for specific conditions.

### 3.2 Oral Health

The oral cavity contains a diverse microbial community that helps maintain oral health. An imbalance in this community may contribute to dental caries, gingivitis, periodontitis, and halitosis. Probiotics have been investigated for their potential to influence oral microorganisms and improve oral health. However, their effects depend on the strain and its intended application.[20–23]

#### 3.2.1. Mechanisms of Action of Oral Probiotics

Probiotics may influence oral health by competing with harmful microorganisms for nutrients and adhesion sites, producing antimicrobial substances, modifying oral biofilms, and regulating host immune and inflammatory responses. These mechanisms vary among probiotic strains.[20,21,25]

Mechanisms of Oral Probiotics:

Probiotic strain selection ↓ Survival in oral environment ↓ Adhesion/interaction with oral surfaces ↓ Competition with pathogens ↓ Antimicrobial metabolite production ↓ Biofilm modulation ↓ Host immune/inflammatory modulation ↓ Potential improvement in oral-health outcomes

**Dental caries** → ↓ *S. mutans*/cariogenic activity

**Periodontal disease** → ↓ periodontal pathogens/inflammation

**Halitosis** → ↓ odor-associated microorganisms/volatile sulfur compounds

**Gingivitis** → ↓ gingival inflammation/bleeding

Probiotics may influence oral microbial populations, biofilm formation, and inflammatory responses, potentially benefiting selected oral conditions.[20,21,23,25]

#### 3.2.2. Probiotics and Dental caries

Probiotics such as *Lactobacillus reuteri*, *L. brevis*, *L. salivarius*, and selected *Bifidobacterium* strains have been investigated as adjuncts to periodontal treatment. Some studies report improvements in gingival bleeding, periodontal pocket depth, and other clinical parameters. However, findings remain inconsistent, and probiotics should not replace professional plaque removal or conventional periodontal treatment.[20,22,23]

Probiotics and Gingivitis: Selected probiotic strains have been studied for their potential to reduce gingival inflammation and bleeding by influencing plaque biofilms and host inflammatory responses. However, differences in strains and study methods limit comparisons, and further clinical research is required.[20,22,24]

Probiotics and Halitosis: Halitosis is often associated with oral microorganisms that produce volatile sulphur compounds. Certain probiotics, including selected *Streptococcus salivarius* strains, have been

investigated for their potential to modify the oral microbiota and reduce bad breath. However, the evidence remains variable, and probiotics should not replace treatment of underlying causes.[20,22–24]

Probiotics in Other Oral Conditions: Probiotics have also been investigated for oral mucositis and peri-implant inflammatory conditions, although the evidence remains limited.[24] Their potential application in post-surgical oral wound healing is another area of pharmaceutical research, but direct clinical evidence is currently insufficient to establish their effectiveness.

Strain Selection and Pharmaceutical Delivery: The effectiveness of oral probiotics depends on strain-specific properties, safety, and the ability to survive and interact with the oral environment. Salivary flow, swallowing, and oral hygiene can reduce the time probiotics remain at the intended site. Formulations such as lozenges, tablets, gels, and mucoadhesive systems may be investigated to improve local retention while maintaining microbial viability.[22–25]

Further studies are needed to establish suitable strains, doses, dosage forms, administration frequency, and treatment duration. Evidence from one probiotic strain should not automatically be generalised to other strains.[22–26]

### 3.3 Skin Health

The skin acts as a physical and immunological barrier and supports a diverse microbial community that contributes to skin health. Changes in this community, known as skin dysbiosis, have been associated with several dermatological conditions. Probiotics and probiotic-derived preparations have therefore been investigated for their potential to maintain skin barrier function, regulate inflammation, and support the management of selected skin disorders.[27–30]

#### 3.3.1. Mechanisms of Action of Probiotics in Skin Health

Probiotics may influence skin health by competing with potentially harmful microorganisms, producing antimicrobial substances, regulating immune and inflammatory responses, and supporting skin barrier function. Some probiotic-derived preparations have also been investigated for their effects on skin hydration and elasticity. However, these effects vary according to the strain, formulation, and route of administration.[27–31]

Atopic Dermatitis: Atopic dermatitis (AD) is a chronic inflammatory skin condition associated with impaired barrier function, immune dysregulation, and changes in the skin microbiota. Increased colonisation by *Staphylococcus aureus* may contribute to inflammation and disease severity.[27,29,30] Selected probiotics and probiotic-derived preparations, including *Streptococcus thermophilus*, *Vitreoscilla filiformis*, *Lactiplantibacillus plantarum*, and *Bifidobacterium longum*, have been investigated for their potential effects on microbial balance, skin barrier function, and inflammation. Although some studies report improvements, the findings remain inconsistent. Further clinical research is needed to establish strain-specific benefits and suitable treatment approaches.[29,30]

Acne Vulgaris: Acne vulgaris is an inflammatory skin condition associated with increased sebum production, follicular changes, and interactions between skin microorganisms and the host immune system. *Cutibacterium acnes* is a normal member of the skin microbiota, although certain strains and microbial interactions may contribute to acne development.[27,28] Oral and topical probiotics have been investigated for their potential to influence microbial balance and inflammatory responses. However, clinical evidence remains variable, and further studies are required to establish their effectiveness and appropriate formulations.[27,29,30]

Psoriasis and Other Inflammatory Skin Disorders: Psoriasis involves abnormal immune responses and chronic skin inflammation. Selected probiotics have demonstrated potential anti-inflammatory effects in experimental studies, but clinical evidence remains limited. Probiotic approaches have also been explored for other inflammatory and microbial skin conditions, although their benefits cannot be generalised across all strains or disorders.[27–31]

Wound Healing and Skin Defence: Probiotics and their derived products have been investigated for wound care because of their potential antimicrobial and immunomodulatory effects. They may influence the local microbial environment and inflammatory responses, which are relevant to tissue repair. However, evidence supporting their clinical use in wound healing remains

limited, and further studies are needed to establish suitable strains, concentrations, and dosage forms.[27,28,30]

Skin Ageing and Photoageing: Probiotics have been studied for their potential effects on skin hydration, elasticity, barrier function, and wrinkle-related characteristics. Proposed mechanisms include modulation of inflammatory and oxidative processes and support of epidermal barrier function. However, results vary between probiotic preparations, and more long-term clinical studies are required to establish their effectiveness in dermatological and cosmetic applications.[28,29]

**Table 2: Potential Applications of Probiotics in Skin Health**

| Skin condition/application | Proposed mechanism | Potential effects |
|---|---|---|
| Atopic dermatitis | Microbial modulation, immune regulation, barrier support | Potential reduction in inflammation and improvement of skin barrier |
| Acne vulgaris | Microbial competition, antimicrobial activity, immunomodulation | Potential reduction in microbial imbalance and inflammation |
| Psoriasis | Immunomodulation and regulation of inflammatory responses | Potential reduction of inflammatory activity |
| Wound healing | Antimicrobial activity, inflammatory modulation, tissue repair | Potential microbial control and support of healing |
| Skin aging/photoaging | Barrier support, modulation of oxidative and inflammatory processes | Potential improvement in hydration, elasticity and skin characteristics |
| Sensitive/reactive skin | Microbial and immune modulation | Potential improvement in barrier function and skin tolerance |

Compiled from Roudsari et al., Lolou and Panayiotidis, Gao et al., Knackstedt et al., and Abdi et al. [27-31]

### 3.4 Gut Brain Axis

The gut–brain axis (GBA) is a bidirectional communication network connecting the gastrointestinal tract with the central nervous system (CNS). It involves neural, endocrine, immune, and metabolic pathways, with the gut microbiota contributing to this communication. Changes in the composition or activity of intestinal microorganisms have been investigated in relation to stress, mood, cognition, and neurological health. Probiotics have therefore attracted interest as potential modulators of the GBA. However, their effects vary according to the strain, dose, duration of administration, and characteristics of the study population.[1,2,5,6,8,32]

#### 3.4.1. Gut Microbiota and Gut–Brain Communication

The gut microbiota contributes to digestion, intestinal barrier function, immune regulation, and the production of biologically active metabolites. Communication between the gut and brain occurs through the enteric nervous system and vagus nerve, the hypothalamic–pituitary–adrenal (HPA) axis, immune signaling, and microbial metabolites such as short-chain fatty acids (SCFAs). Gut microorganisms may also influence neuroactive compounds involved in brain function.[1,2,5,6,32]

Changes in the intestinal microbiota, known as dysbiosis, have been investigated in relation to altered inflammatory signaling, intestinal permeability, and mental health. However, these associations do not necessarily establish that dysbiosis directly causes psychiatric or neurological disorders.[2,5]

3.4.2. Mechanisms of Probiotic Action in the Gut–Brain Axis

Probiotics may influence gut–brain communication through several interconnected mechanisms:

Microbiota modulation: Probiotics may interact with resident microorganisms, compete with potentially harmful bacteria, and influence the intestinal microbial environment.[1,8,32,33]

Intestinal barrier support: Some strains may help maintain epithelial integrity and tight-junction function, potentially limiting excessive exposure to microbial products.[1,2,32]

Immune regulation: Probiotics may influence immune responses and inflammatory signaling in the intestine and other tissues.[1,8,32]

Modulation of microbial metabolites: Probiotic-associated changes in microbial activity may affect the production of SCFAs and other metabolites involved in intestinal and immune functions.[6,32]

Neural and endocrine signaling: Probiotics have been investigated for their potential effects on vagal communication, stress-related HPA-axis activity, and neurotransmitter-associated pathways.[5,6]

The contribution of each mechanism may differ between probiotic strains, and further research is needed to establish how these changes translate into clinical benefits.

### 3.4.3. Probiotics and Mental Health

Research on the GBA has explored the possible relationship between probiotics and mental health, particularly anxiety, depression, and stress. Reviews by Mörkl et al. discuss how the gut microbiota, immune signaling, stress responses, and microbial metabolites may contribute to gut–brain communication.[34] Probiotics have therefore been investigated as potential supportive interventions, although the available evidence remains variable.

### 3.4.4. Probiotics and Anxiety

Probiotics have been studied for their potential effects on anxiety and stress-related responses. Proposed mechanisms include modulation of the HPA axis, immune signaling, microbial metabolites, and neural communication.[5,6] Consequently, findings should be interpreted according to the strain and population studied rather than generalised to all probiotic products.

### 3.4.5. Probiotics and Cognitive Function

Gut–brain communication has also been investigated in relation to memory, learning, and other cognitive functions. Kumar et al. reviewed preclinical and clinical findings suggesting that probiotics may influence cognition through microbial balance, inflammatory pathways, and neurobiological signaling. However, improvements have not been consistent across all cognitive domains or studies.[33] Fekete et al. also examined the potential effects of probiotics, prebiotics, and synbiotics on cognitive health, highlighting the need for further research.[35]

### 3.4.6. Probiotics and Neurological Disorders

The gut microbiota has been investigated in several neurological conditions because of its interactions with neural, immune, and metabolic pathways. Suganya and Koo reviewed the potential involvement of the gut microbiota in gut–brain communication and neurological disorders.[32] Other research has explored probiotics in relation to cognitive impairment, but the findings remain variable.[33] Further clinical studies are needed before probiotics can be recommended as established treatments for neurological disorders.

## 3.5 Cancer Support Therapy

Probiotics have been investigated as adjunctive therapeutic agents in cancer care because anticancer treatments can alter the intestinal microbiota and cause gastrointestinal and mucosal complications. Their potential benefits are associated with the restoration of microbial balance, maintenance of intestinal barrier integrity, modulation of host immune responses, and production of biologically active metabolites. Current research primarily supports their investigation as supportive interventions during cancer treatment, whereas their direct anticancer effects remain under investigation.[36-40]

### 3.5.1. Management of Treatment-Associated Diarrhoea

Diarrhoea is a common gastrointestinal complication of chemotherapy and radiotherapy that may negatively affect nutritional status, quality of life, and treatment continuity. Probiotics have been investigated for their ability to reduce the incidence and severity of treatment-associated diarrhoea by modifying intestinal microbial composition, strengthening epithelial barrier function, and regulating inflammatory responses. A systematic review and meta-analysis by Qureshi et al. reported a significant reduction in diarrhoea among cancer patients receiving probiotics or synbiotics compared with control interventions. These findings suggest that probiotics may have a supportive role in managing gastrointestinal toxicity during cancer

treatment. However, the magnitude of benefit varied across studies, highlighting the importance of probiotic strain, formulation, and clinical setting.[40]

3.5.2. Reduction of Gastrointestinal Toxicity and Intestinal Barrier Dysfunction

Chemotherapy and radiotherapy can disrupt the intestinal epithelial barrier and alter the composition and metabolic activity of the gut microbiota. These changes may contribute to intestinal inflammation, increased epithelial permeability, and gastrointestinal disturbances. Probiotics may help maintain intestinal homeostasis by promoting beneficial microbial populations, competing with potentially harmful microorganisms, and supporting epithelial barrier function. They may also influence inflammatory pathways and microbial metabolite production, potentially helping to limit treatment-associated intestinal damage. These properties have prompted investigation of probiotics as supportive agents for reducing gastrointestinal toxicity during anticancer treatment. However, their effectiveness may depend on the probiotic strain, treatment regimen, and characteristics of the patient population.[37-39]

**3.5.3. Management of Oral and Mucosal Complications**

The oral cavity is another site where cancer treatment can cause clinically significant complications. Chemotherapy and radiotherapy may damage mucosal tissues and disturb the local microbial environment, contributing to oral mucositis, discomfort, and susceptibility to secondary infections. Selected probiotic microorganisms have been investigated for their ability to influence oral microbial communities and modulate inflammatory responses. By affecting microbial balance and local immune activity, certain strains may help support oral health during cancer treatment. Nevertheless, the available evidence remains less established than that for some gastrointestinal applications. Further well-designed clinical studies are required to determine the efficacy, safety, and strain-specific effects of probiotics in preventing or managing oral and mucosal complications.[38,39]

**3.5.4. Modulation of Gut Microbiota During Anticancer Treatment**

Cancer treatment can produce substantial changes in gut microbial diversity, composition, and metabolic activity. This treatment-associated dysbiosis may influence intestinal homeostasis and host responses. Probiotic supplementation may help modulate these changes by introducing beneficial microorganisms and influencing the abundance and activity of resident microbial populations. Certain probiotics may also contribute to the production of metabolites such as short-chain fatty acids (SCFAs), which are involved in maintaining epithelial integrity and regulating inflammatory signalling and immune responses. Through these effects, probiotics may help support the intestinal environment during cancer treatment. However, the extent of microbiota modulation depends on the strains administered, the existing microbial community, and the patient's treatment-related condition. Therefore, microbiota modulation represents a potential mechanism underlying probiotic use in oncology, although its clinical significance requires further investigation.[36-39]

3.5.5. Immunomodulatory Effects and Potential Influence on Treatment Response

Interactions between the gut microbiota and the immune system have generated interest in the potential role of probiotics in modulating anticancer immune responses. Probiotics may influence innate and adaptive immune pathways, cytokine production, and intestinal immune homeostasis. In addition, differences in gut microbial composition have been associated with variations in responses to certain cancer treatments, particularly immunotherapies. These observations have encouraged research into whether microbiota-targeted interventions can influence treatment outcomes.

However, the relationship between probiotic supplementation and anticancer treatment response remains complex. Findings from studies investigating the gut microbiota do not necessarily establish that conventional probiotic supplements improve treatment efficacy. Current evidence regarding their direct effects on responses to chemotherapy or immunotherapy remains limited and heterogeneous. Probiotics should therefore be considered potential supportive interventions rather

than established enhancers of anticancer treatment efficacy.[37-39]

### 3.5.6. Potential Direct Anticancer Effects

Experimental studies have investigated several mechanisms through which probiotics may influence cancer development and progression. These include modulation of carcinogen metabolism, competition with potentially harmful microorganisms, production of biologically active metabolites, regulation of inflammatory pathways, enhancement of immune surveillance, inhibition of cancer-cell proliferation, and induction of apoptosis. Such effects have been explored particularly in experimental models of colorectal and other gastrointestinal cancers. By influencing the intestinal microbial environment and host biological responses, selected probiotic strains may affect processes associated with carcinogenesis. Despite these promising findings, most evidence for direct tumour-inhibitory effects comes from in vitro experiments and animal studies. These findings cannot be directly extrapolated to clinical outcomes in humans. Evidence demonstrating that probiotic administration independently reduces tumour progression or improves cancer survival remains limited. Further clinical investigation is therefore necessary to establish whether the mechanisms observed experimentally translate into meaningful anticancer benefits.[36-39]

### 3.5.7. Supportive Role During Conventional Cancer Treatment

The therapeutic application of probiotics in oncology currently focuses primarily on their potential role as adjunctive and supportive interventions rather than replacements for established anticancer therapies. The most relevant clinical evidence concerns treatment-associated gastrointestinal complications, particularly diarrhoea, whereas their effects on tumour progression, progression-free survival, and overall survival remain uncertain. The 2025 systematic review and meta-analysis by Qureshi et al. reported a significant reduction in diarrhoea but did not demonstrate significant improvements in progression-free survival or overall survival. These findings suggest that the current therapeutic value of probiotics may lie more in improving treatment tolerability and supportive care than in directly treating malignancy.[40]

Future research is likely to focus on strain-specific probiotic formulations, defined microbial consortia, probiotic-derived metabolites, and other microbiota-targeted approaches. Standardization of strains, dosage, formulation, treatment duration, and clinical endpoints will be essential for identifying interventions that provide meaningful benefits for specific cancer populations. Further well-designed clinical trials are also needed to establish their safety and efficacy in different treatment settings and to clarify their potential contribution to supportive oncology care.[37-39]

## 3.6. Women's Health

Probiotics have gained increasing attention in women's health because of their potential to modulate the vaginal, gastrointestinal, and reproductive microbiota. A healthy vaginal microbiota is commonly enriched in beneficial *Lactobacillus* species, which contribute to microbial stability through the production of lactic acid and other antimicrobial substances. Disruption of this microbial balance has been associated with several gynaecological and reproductive health conditions. Consequently, probiotics have been investigated as potential therapeutic and supportive interventions for restoring microbial homeostasis and improving women's health outcomes.[41-44]

### 3.6.1. Bacterial Vaginosis

Bacterial vaginosis (BV) is one of the most extensively investigated conditions in the context of vaginal probiotics. It is characterised by disruption of the normal vaginal microbial community, often accompanied by a reduction in protective *Lactobacillus* species and an increase in other bacterial populations. Selected probiotic strains may help restore vaginal microbial balance through transient colonisation, production of lactic acid and other antimicrobial compounds, competition with potentially harmful microorganisms, and modulation of local immune responses. Probiotics have therefore been investigated alone or as adjuncts to conventional antimicrobial treatment, with some studies suggesting potential benefits in restoring vaginal eubiosis and reducing recurrence. However, outcomes vary according to the probiotic strain, dose, route of administration, and treatment duration. [41,43,44]

### 3.6.2. Vulvovaginal Candidiasis

Probiotics have also been explored for the prevention and management of vulvovaginal candidiasis (VVC), a common fungal infection affecting women. Selected probiotic microorganisms may inhibit *Candida* growth through competition for adhesion sites and nutrients, production of organic acids and other antimicrobial substances, and modulation of host immune responses. Maintaining a favourable vaginal microbial environment may also help limit conditions associated with fungal overgrowth. Some studies suggest that probiotics may have a supportive role, particularly when used alongside conventional antifungal treatment. However, evidence regarding their ability to prevent recurrence or achieve sustained clinical resolution remains variable, and further controlled studies are needed to establish their effectiveness.[41,43,44]

### 3.6.3. Recurrent Urinary Tract Infections

The vaginal and urinary microbial environments are interconnected, and changes in the vaginal microbiota may influence susceptibility to urinary tract infections (UTIs). Probiotics have therefore been investigated as a preventive approach for recurrent UTIs in women. Proposed mechanisms include restoration of protective vaginal *Lactobacillus* populations, inhibition of uropathogen colonisation, and interference with pathogen adhesion to epithelial surfaces. These approaches may be relevant for women experiencing recurrent infections. However, clinical findings have been inconsistent, and differences in probiotic strains, formulations, and routes of administration may contribute to variation in outcomes. Further clinical studies are required to determine which probiotic interventions, if any, provide reliable preventive benefits.[41,43]

### 3.6.4. Reproductive Health and Restoration of Reproductive Eubiosis

Maintenance of reproductive tract microbial balance has emerged as a potential application of probiotics. Alterations in the reproductive tract microbiota have been investigated in relation to reproductive dysfunction, infertility, and adverse reproductive outcomes. Probiotic supplementation may support reproductive tract health by promoting a favourable microbial environment, limiting the growth of potentially harmful microorganisms, and influencing local inflammatory and immune responses. Reviews have highlighted the potential role of probiotics in modulating reproductive tract microbial balance and supporting reproductive health. Nevertheless, the evidence varies across conditions, and further well-controlled clinical studies are required to establish their effectiveness for specific reproductive disorders.[45]

### 3.6.5. Polycystic Ovary Syndrome

Probiotics have also been investigated in women with polycystic ovary syndrome (PCOS), particularly because of the proposed relationship between gut microbiota, inflammation, and metabolic health. Probiotic supplementation may influence intestinal microbial composition and metabolic activity, potentially affecting inflammatory status and selected metabolic parameters. Reviews of probiotic interventions in women with PCOS and related gynaecological conditions have reported possible improvements in certain metabolic and inflammatory outcomes. However, the available evidence is heterogeneous, and the clinical significance of these findings remains uncertain. Probiotics should therefore be considered potential adjuncts to established PCOS management rather than standalone treatments.[46]

### 3.6.6. Pregnancy and Maternal Health

Probiotic supplementation during pregnancy has been investigated for its potential effects on maternal gastrointestinal health, immune function, and pregnancy-related outcomes. Pregnancy involves substantial physiological and immunological changes, and modulation of the maternal microbiota has been proposed as one approach to supporting maternal health. Studies in pregnant women have examined outcomes related to gastrointestinal function, metabolic health, inflammatory markers, and immune responses, with some reporting potential benefits. However, findings vary according to the probiotic formulation, timing of administration, maternal characteristics, and outcomes assessed. Consequently, the benefits of probiotic supplementation during pregnancy should be evaluated for specific indications rather than assumed to apply to all pregnant women.[47]

### 3.6.7. Prevention of Adverse Reproductive and Pregnancy Outcomes

The potential relationship between maternal microbiota and reproductive outcomes has prompted research into probiotic interventions during pregnancy. Probiotics may influence maternal immune regulation, intestinal and vaginal microbial balance, and inflammatory processes associated with certain pregnancy complications. Researchers have therefore investigated their potential role in supporting maternal and offspring health. However, evidence for preventing specific adverse reproductive or pregnancy outcomes remains insufficient to establish probiotics as a universal preventive intervention. Further well-designed clinical trials are needed to determine their efficacy, safety, and suitability for particular maternal populations and pregnancy-related indications.[41,47]

### 3.6.8. Menopause and Post-Reproductive Health

The vaginal microbiota changes throughout a woman's life, and declining oestrogen levels during menopause can alter the vaginal environment and microbial composition. These changes may contribute to reduced vaginal *Lactobacillus* abundance and changes in urogenital health. Probiotic products have therefore been explored as potential approaches to supporting vaginal microbial balance during the menopausal transition. Oral and vaginal probiotic formulations have been investigated at different stages of women's lives, including menopause, with the aim of maintaining vaginal microbial homeostasis and supporting urogenital health. However, clinical evidence remains evolving, and further research is needed to establish the effectiveness of specific probiotic strains and formulations for menopausal symptoms and related urogenital conditions.[41,44]

Overall, probiotics have potential applications across several areas of women's health, particularly conditions associated with disruption of vaginal or reproductive tract microbial balance. Bacterial vaginosis and vulvovaginal candidiasis have received considerable research attention, while investigations into recurrent UTIs, reproductive health, PCOS, pregnancy, and menopausal health continue to develop. The effects of probiotics are strain-specific, and differences in formulation, dose, route of administration, and treatment duration contribute to variation among clinical studies. Probiotics should therefore be evaluated as condition-specific therapeutic or adjunctive interventions rather than as a uniform treatment for women's health disorders. Their clinical use should be guided by evidence for the particular strain, indication, and patient population.[41-47]

## 3.7. Metabolic Disorders

Metabolic disorders are closely associated with alterations in gut microbiota. Probiotics have therefore been investigated for their potential to influence metabolic homeostasis through modulation of microbial composition, intestinal barrier function, host metabolism, and inflammatory responses. Their applications have been explored in obesity, type 2 diabetes mellitus, dyslipidaemia, metabolic syndrome, and non-alcoholic fatty liver disease (NAFLD).[48-51]

### 3.7.1. Obesity and Weight Management

Obesity is associated with changes in gut microbial composition and metabolic activity. Probiotics may influence energy metabolism, intestinal permeability, inflammation, and lipid metabolism. Proposed mechanisms include modulation of appetite-related signalling, energy harvest from food, intestinal barrier integrity, and microbial metabolite production.

However, effects on body weight, adiposity, and metabolic parameters vary considerably across strains and study populations.[48,50,57]

### 3.7.2. Type 2 Diabetes Mellitus

Type 2 diabetes mellitus (T2DM) is characterised by impaired glucose regulation and insulin resistance. Gut microbial dysbiosis has been associated with metabolic inflammation and reduced insulin sensitivity. Probiotics may influence glucose metabolism through changes in microbial composition, intestinal barrier function, inflammatory pathways, and metabolite production. Although studies have investigated their effects on glycaemic control and insulin sensitivity, results remain variable across interventions.[48-52,57]

### 3.7.3. Insulin Resistance and Metabolic Inflammation

Increased intestinal permeability may allow microbial products to enter the circulation, potentially contributing to low-grade systemic inflammation and metabolic dysfunction. Probiotics have been investigated for their potential to support intestinal barrier integrity and regulate inflammatory responses. Changes in microbial metabolites and host signalling pathways may also influence insulin sensitivity and metabolic homeostasis. However, their clinical benefits in insulin resistance require further investigation.[48,49,51]

### 3.7.4. Dyslipidaemia and Lipid Metabolism

Probiotics have been studied for their potential effects on circulating lipid levels and cholesterol metabolism. Proposed mechanisms include cholesterol utilisation by certain probiotic microorganisms, bile acid deconjugation, and modulation of hepatic lipid metabolism. Although some studies suggest beneficial effects on lipid profiles, outcomes depend on the probiotic strain, formulation, and study setting. [52]

### 3.7.5. Metabolic Syndrome

Metabolic syndrome comprises interrelated abnormalities, including central obesity, impaired glucose regulation, dyslipidaemia, and elevated blood pressure. Probiotics may influence several of these factors by modulating gut microbiota, intestinal permeability, inflammation, and host metabolic signalling. Research on probiotics, prebiotics, and synbiotics suggests potential benefits, although their effectiveness in managing metabolic syndrome requires further clinical validation.[48,54]

### 3.7.6. Non-Alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease (NAFLD), increasingly classified within the broader concept of metabolic dysfunction-associated steatotic liver disease (MASLD), is associated with obesity, insulin resistance, and metabolic dysfunction. The gut–liver axis provides a pathway through which microbial changes may influence hepatic metabolism and inflammation. Probiotics have been investigated for their potential to modulate gut microbiota, support intestinal barrier integrity, and influence microbial metabolites and inflammatory signalling. Their clinical role in metabolic liver disease remains under investigation.[48,50,54]

### 3.7.7. *Akkermansia muciniphila* and Next-Generation Probiotics

Next-generation probiotics have expanded research beyond traditional probiotic genera. *Akkermansia muciniphila*, a mucin-associated intestinal bacterium, has attracted interest because of its potential relationship with intestinal barrier function, inflammation, and metabolic health. Research has explored its possible applications in obesity, T2DM, and metabolic liver disease. However, its therapeutic development remains an emerging field, and further clinical studies are needed to establish its efficacy, optimal formulation, and long-term safety.[53]

### 3.7.8. Emerging Microbiota-Targeted Approaches

Research into metabolic disorders increasingly includes synbiotics, postbiotics, next-generation probiotics, and probiotic-derived bioactive preparations. These approaches aim to influence specific microbial pathways and host–microbe interactions rather than simply increase beneficial microorganisms. In the future, such strategies may support more individualised interventions based on patients' microbial and metabolic characteristics. However, their clinical applications require further validation.[48,49,51]

Overall, probiotics represent a potential adjunctive approach to managing metabolic disorders through

modulation of gut microbiota, intestinal barrier function, inflammation, and host metabolism. However, clinical outcomes remain heterogeneous because of differences in strains, doses, formulations, treatment duration, and patient characteristics. Probiotics should therefore complement, rather than replace, established dietary, lifestyle, and pharmacological interventions. Further well-designed clinical trials are needed to establish strain-specific efficacy and their role in individual metabolic conditions.[48-57]

## 4. DRUG DELIVERY APPROACHES

Probiotics offer several potential health benefits, but their effectiveness can be affected by exposure to harsh gastrointestinal conditions. Gastric acidity, bile salts, digestive enzymes, and processing or storage conditions may reduce the number of viable microorganisms reaching the intestine. To overcome these challenges, different delivery systems have been developed to protect probiotic cells and improve their survival during gastrointestinal transit. These approaches include nanoparticle-based carriers, hydrogels, liposomes, and microencapsulation techniques. Each system has specific advantages and limitations depending on the probiotic strain, carrier material, and intended application.[58-67]

**Table 3: Comparison of Probiotic Delivery Systems**

| Delivery system | Materials / examples | Principle and advantages | Limitations | References |
|---|---|---|---|---|
| **Nanoparticle-based systems** | Chitosan, alginate, Eudragit®, resistant starch, ethyl cellulose | Provide a protective barrier against gastrointestinal stresses and may support controlled or targeted intestinal release. | Safety, stability, scalability, and clinical effectiveness require further investigation. | 58,62 |
| **Hydrogel-based systems** | Alginate, chitosan, pectin, carrageenan, xanthan gum, whey protein, gelatin | Three-dimensional polymer networks entrap probiotic cells and can protect them during gastrointestinal transit. | Maintaining viability during processing and storage and controlling release remain challenges. | 59,65,66 |
| **Liposome-based systems** | Lipid vesicles, including polysaccharide- or protein-coated liposomes | Lipid carriers provide an additional protective barrier, while surface modifications may improve probiotic stability. | Evidence of therapeutic benefits, particularly in clinical settings, remains limited. | 58,62 |
| **Microencapsulation** | Alginate, chitosan, starch, proteins, sugars, and lipids | Encloses probiotic cells within a protective coating or matrix, helping maintain viability during processing, storage, and gastrointestinal transit. | Processing conditions may affect cell survival, while particle uniformity, storage stability, and release need optimisation. | 60,61,64,67 |

### 4.2. Techniques Used for Probiotic Microencapsulation

Microencapsulation is widely investigated because it can protect probiotic microorganisms from environmental stress and help maintain their viability until they reach the intended site of release. Different techniques are used depending on the properties of the probiotic strain, the encapsulating material, and the desired particle characteristics. The major techniques and their key features are summarised in Table 4. [60,61,64,67]

**Table 4: Common Microencapsulation Techniques for Probiotics**

| Technique | Principle | Advantages | Limitations |
|---|---|---|---|
| **Extrusion** | Probiotic–polymer droplets are hardened, commonly using calcium ions with alginate. | Mild processing conditions are suitable for many heat-sensitive microorganisms. | Often produces relatively large particles with limited uniformity. |
| **Emulsion-based encapsulation** | Probiotic-containing polymer droplets form within an immiscible phase and are subsequently solidified. | Can produce smaller particles. | Requires optimisation of the formulation and processing conditions. |
| **Freeze-drying** | Water is removed from a frozen formulation by sublimation under reduced pressure. | Suitable for preserving many heat-sensitive probiotics. | Freezing and dehydration may damage bacterial cells. |
| **Spray drying** | A probiotic formulation is atomised into droplets and rapidly dried using heated air. | Rapid, reproducible, and suitable for large-scale production. | Heat and other processing stresses may reduce probiotic viability. |
| **Spray-freeze-drying** | Atomisation and freezing are followed by freeze-drying. | Can produce porous particles for sensitive microorganisms. | Processing is relatively complex and requires scale-up evaluation. |
| **Coacervation** | Polymer-rich material separates and forms a coating around the probiotic-containing core. | Allows the formation of protective coatings. | Coating stability and process conditions require optimisation. |
| **Spray chilling** | Probiotics are incorporated into a lipid-based matrix that solidifies during cooling. | May protect microorganisms during processing and storage. | Release depends on matrix composition and gastrointestinal conditions. |
| **Electrospraying and electrospinning** | An electric field is used to produce particles or fibres from polymer solutions. | Offers opportunities to control particle or fibre characteristics. | Maintaining probiotic viability and achieving large-scale production can be challenging. |
| **Microfluidic encapsulation** | Microchannels control the formation of droplets and particles. | Provides precise control over particle size and uniformity. | Equipment complexity and production scale may limit application. |

*References:* [60,61,64,67]

Overall, probiotic delivery systems aim to improve microbial survival and facilitate delivery to the gastrointestinal tract. The selection of an appropriate system depends on the probiotic strain, formulation, processing conditions, and intended release profile. Although these technologies offer promising opportunities for probiotic delivery, further research is needed to improve long-term stability, optimise production, establish safety, and confirm their therapeutic benefits through well-designed clinical studies.[58-67]

## 5. CHALLENGES ASOCIATED WITH PROBIOTIC THERAPEUTICS

Despite their growing therapeutic potential, the development of probiotic-based pharmaceutical products presents several challenges related to stability, viability, manufacturing, gastrointestinal delivery, and regulatory requirements. As probiotics are living microorganisms, their therapeutic effectiveness depends on maintaining sufficient viable and functionally active cells throughout processing, storage, and administration. These challenges must be addressed to ensure consistent product quality, safety, and clinical efficacy.[68,69,71]

**Table 5: Major Challenges Associated with Probiotic Therapeutics**

| Challenges | Description | Possible approaches | References |
|---|---|---|---|
| **Stability of probiotic preparations** | Exposure to temperature, moisture, oxygen, pH changes, and mechanical stress during processing can damage probiotic cells and reduce viability. The extent of damage varies among strains. | Selection of stress-tolerant strains, protective excipients, encapsulation, and optimisation of processing conditions. | 68,69,71,73 |
| **Storage stability and shelf life** | Probiotic viability may decline during storage because of temperature fluctuations, humidity, oxygen exposure, and unsuitable packaging conditions. | Freeze-drying, protective encapsulation, moisture- and oxygen-resistant packaging, and regular stability testing. | 68,69,72,73,82 |
| **Survival during gastrointestinal transit** | Gastric acidity, bile salts, and digestive enzymes may reduce the number of viable microorganisms reaching the intestine. | Microencapsulation, enteric coatings, hydrogels, and protective polymeric matrices. | 69,71,73,81 |
| **Gastrointestinal barriers** | Gastric acid can damage susceptible probiotic cells, while bile salts and digestive enzymes create additional challenges for intestinal survival. | pH-sensitive polymers, enteric coatings, multilayer systems, and controlled-release formulations. | 69,71,73,81 |
| **Regulatory and standardisation issues** | Differences in regulatory classifications, strain-specific properties, safety requirements, and quality standards complicate product development and commercialisation. | Standardised strain identification, safety evaluation, potency testing, quality control, and regulatory compliance. | 68,69 |
| **Manufacturing and scale-up** | Industrial processes may expose probiotics to heat, dehydration, oxygen, and mechanical stress, while maintaining batch-to-batch consistency can be difficult. | Scalable manufacturing technologies, optimised processing conditions, and reproducible quality-control procedures. | 68-70 |
| **Formulation and delivery-system challenges** | Different strains require different protective conditions, and excessive protection may delay probiotic release at the intended site. | Strain-specific carrier selection, compatible excipients, and optimisation of protection and release characteristics. | 69-71,73,81,82 |
| **Dose, viability, and therapeutic consistency** | Viable cell counts may decrease during manufacturing, storage, and gastrointestinal transit, resulting in variable effective doses and therapeutic responses. | Monitoring viable cell counts, functional activity, strain identity, stability, and release characteristics. | 68,71-73,81,82 |
| **Translation from laboratory to clinical products** | Promising laboratory results may not translate into clinical benefits because of differences in host conditions, manufacturing performance, and product stability. | Integrated formulation development, safety assessment, scalable manufacturing, and well-designed clinical trials. | 68-70,73,81 |

Overall, the successful development of probiotic therapeutics requires a coordinated approach involving appropriate strain selection, protective formulation strategies, optimised manufacturing processes, and standardised quality assessment. Although advanced delivery systems have improved probiotic protection under experimental conditions, further research is needed to establish long-term stability, reproducible therapeutic performance, and clinical effectiveness. Addressing these challenges will be essential for translating probiotic research into safe, stable, and reliable pharmaceutical products.[68-73,81,82]

## 6. FUTURE PERSPECTIVE

Probiotic research is gradually moving beyond conventional formulations towards more personalised,

targeted, and technologically advanced therapeutic approaches. Advances in microbiome analysis, artificial intelligence (AI), genetic engineering, and pharmaceutical delivery systems may help improve strain selection, therapeutic specificity, stability, and delivery. Synbiotics and postbiotics also offer complementary approaches for developing microbiome-based therapies. However, further research is needed to establish the safety, efficacy, and clinical applicability of these emerging strategies.[73-82]

### 6.1 Personalised Probiotic Therapy

Personalised probiotic therapy aims to select probiotic strains according to an individual's gut microbiota composition, dietary habits, health status, and therapeutic needs. Since the microbiome varies considerably between individuals, the same probiotic strain may not produce identical effects in everyone. Advances in microbiome profiling and precision nutrition may help identify suitable strains and support the development of more individualised interventions. Nevertheless, reliable biomarkers and clinical evidence are still needed before personalised probiotic therapy can be routinely implemented.[73,74]

### 6.2 Engineered and Next-Generation Probiotics

Genetic engineering and synthetic biology are creating opportunities to develop probiotics with improved functional properties. These approaches may allow researchers to enhance the survival of beneficial microorganisms, modify their metabolic activity, or enable them to produce specific therapeutic substances. Next-generation probiotics are also being investigated for their potential to address particular disease-related changes in the microbiome. Despite their promise, their long-term safety, genetic stability, manufacturing requirements, and regulatory status require careful evaluation before widespread clinical use.[74,75]

### 6.3 Artificial Intelligence-Guided Formulation Development

Artificial intelligence and machine-learning tools may support probiotic research by analysing complex microbiome datasets, identifying potential therapeutic strains, and predicting interactions between microorganisms and their environment. These technologies may also assist in selecting suitable encapsulating materials, optimising formulation parameters, and predicting probiotic stability during storage and gastrointestinal transit. Integrating computational approaches with experimental studies could make formulation development more efficient. However, predictions generated by AI must be validated using reliable laboratory methods and appropriate clinical studies.[75,76]

### 6.4 Synbiotic Strategies

Synbiotics combine live microorganisms with substrates that are selectively utilised by host microorganisms and provide a health benefit. This approach may support the survival or activity of selected beneficial microorganisms while influencing the composition and function of the gut microbiota. Synbiotic formulations are being explored for gastrointestinal health and other conditions associated with microbiome imbalance. Their effectiveness depends on the specific probiotic strain, the selected substrate, and the intended health outcome; therefore, the compatibility and benefits of each combination should be demonstrated rather than assumed.[77,81]

### 6.5 Postbiotic-Based Therapeutics

Postbiotics, which consist of preparations of inanimate microorganisms and/or their components that confer a health benefit on the host, represent another developing area of microbiome-based therapeutics. Unlike conventional probiotics, postbiotic preparations do not require the microorganisms to remain viable at the time of administration. This may offer formulation and storage advantages in certain applications. Their biological effects depend on the composition and preparation of the product, and further research is needed to establish suitable production methods, standardisation procedures, effective doses, and clinical benefits.[78,82]

### 6.6 Targeted Drug Delivery Using Probiotics

Probiotics are also being investigated as potential carriers for targeted therapeutic delivery. Their biological properties may offer opportunities to transport therapeutic molecules to selected regions of the gastrointestinal tract. Biohybrid systems and nanotechnology-

assisted probiotic formulations are being explored to improve protection, localisation, and controlled release of therapeutic agents. However, the performance of these systems depends on the carrier design, probiotic viability, cargo compatibility, and intended site of delivery. Their safety, reproducibility, scalability, and clinical usefulness must be established through further research.[79,80]

### 6.7 Integration of Emerging Technologies

The integration of microbiome analysis, AI, genetic engineering, and advanced drug-delivery technologies may support the development of more precise probiotic formulations. For example, microbiome data could help identify potential therapeutic targets, computer based tools could guide strain and formulation selection, and encapsulation technologies could improve protection during storage and gastrointestinal transit. Combining these approaches may help address limitations associated with conventional probiotic products. However, successful translation will require coordinated laboratory research, clinical validation, quality control, and appropriate regulatory oversight.[73-80]

Overall, the future of probiotic therapeutics lies in developing products that are well characterised, stable, safe, and supported by evidence of clinical benefit. Personalised formulations, engineered microorganisms, synbiotics, postbiotics, and targeted delivery systems offer promising research directions. At the same time, variability between probiotic strains, differences in individual responses, manufacturing challenges, and the need for standardised evaluation remain important considerations. Continued collaboration between pharmaceutical scientists, microbiologists, clinicians, and regulatory authorities will be essential to translate these advances into reliable therapeutic products.[73-82]

## CONCLUSION

Probiotics have gained considerable attention in pharmaceutical sciences because of their potential health benefits and applications in different health conditions. However, their effectiveness depends on several factors, such as the probiotic strain, dosage, formulation, and route of administration. One of the major challenges is maintaining the viability of these living microorganisms during manufacturing, storage, and delivery to the intended site. Therefore, developing suitable drug delivery systems is essential to protect probiotics and improve their stability and survival.

Various approaches, including microencapsulation, polymer-based systems, hydrogels, liposomes, and nanoparticle-based carriers, have shown potential for improving probiotic delivery. However, no single system is suitable for every probiotic strain or application. The choice of delivery system depends on the properties of the microorganism, the materials used, and the intended site of action. Further research is needed to improve formulation stability, extend shelf life, maintain viable cell counts, and ensure consistent product quality. Emerging approaches such as personalised probiotic formulations, synbiotics, postbiotics, engineered probiotics, and targeted delivery systems may also create new opportunities for pharmaceutical development.

In conclusion, the successful development of probiotic-based pharmaceutical products requires careful formulation design, appropriate manufacturing methods, reliable quality control, and further clinical evaluation. Although current delivery technologies offer promising solutions to several formulation challenges, more research is needed to establish their long-term stability, safety, and therapeutic effectiveness. Continued progress in pharmaceutical research may help transform the potential of probiotics into more stable, effective, and reliable products for future healthcare applications.

## ACKNOWLEDGEMENTS

The authors would like to acknowledge their institution and faculty members for their academic guidance and support during the preparation of this review.

## CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest related to this manuscript.

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HOW TO CITE: Vedika Pawar, Trunali Ghude, Shruti Patil, Bhagyashree Potdar, Sanskruti Pawar, Probiotics: Therapeutic Applications and Drug Delivery Approaches, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 11, 98-120. https://doi.org/10.5281/zenodo.23876794