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+15878858911
editorial-office@sciformat.ca

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PROBIOTIC INTERVENTIONS IN GASTROINTESTINAL PHYSIOLOGY AND PATHOPHYSIOLOGY: A SYSTEMATIC REVIEW OF MODERN THERAPEUTIC FRAMEWORKS AND FUTURE INNOVATIONS

Aleksandra Potempa *(Corresponding Author, Email: alexandrapotempa@gmail.com)*
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0004-2698-4957

Liwia Prorok
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0008-3762-514X

Aleksandra Oszczypała
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0006-5809-3934

Michał Petkow
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0008-3398-9069

Katarzyna Lipska
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0003-5670-7726

Monika Szyszkowska
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0006-5367-0026

Zuzanna Strojek
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0005-8857-5670

Aleksandra Ustaszewska
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0001-5651-5906

Zofia Parol
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0007-0885-2637

Mateusz Żyła
Medical University of Warsaw, 61 Żwirki i Wigury Street, 02-091 Warsaw, Poland
ORCID ID: 0009-0003-9005-620X

ABSTRACT

The human gastrointestinal tract is a vast and dynamic system where interactions between host cells and microbial populations regulate the condition of systemic health. Probiotics, defined as live microorganisms that administered in sufficient amounts provide a health benefit to the host, have progressed from conventional dietary supplements to advanced biotherapeutic treatments. This systematic review presents a comprehensive analysis of the physiological and pathophysiological roles of probiotics focusing on developments between 2013 and 2026. Probiotics enhance the intestinal barrier by modulating tight junction proteins, competitively excluding enteric pathogens and orchestrating immune responses via dendritic cell and regulatory T-cell pathways. Clinical data collected from recent umbrella meta-analyses shows considerable effectiveness at reducing the risk of antibiotic-associated diarrhea, managing symptoms of irritable bowel syndrome in a strain specific manner and leading to remission in ulcerative colitis. This review addresses the increase in usage of next-generation probiotics, such as Akkermansia muciniphila, and the role of genetically engineered bacteria in the targeted delivery of anti-inflammatory agents and reactive oxygen species scavengers. Additionally, the transition toward personalized medicine is discussed through the combination of multi-omics and artificial intelligence allowing to predict probiotic responsiveness in individuals. Despite recent progress, the field faces serious challenges in terms of harmonizing regulations and standardizing safety measures in vulnerable populations. This review aims to summarize current knowledge on probiotic interventions while identifying the critical knowledge gaps that need to be addressed in order to advance the next era of precision microbiome-based therapies.

KEYWORDS

Probiotics, Next-Generation Probiotics, Akkermansia muciniphila, Gastrointestinal Physiology, Inflammatory Bowel Disease, Ulcerative Colitis, Crohn's Disease, Irritable Bowel Syndrome, Antibiotic-Associated Diarrhea, Epithelial Barrier, Immunomodulation, Metabolomics, Genetically Engineered Microbes, and Multi-omics

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1. Introduction

For more than a century, the relationship between humans and the microbes living in their gastrointestinal tract has been under investigation, but the processes of this symbiosis have only just begun to be understood.The word „probiotics" was first used by Werner Kollath in 1953 to describe active compounds necessary for maintaining health (Kollath, 1953). In the subsequent decades the term was redefined by global authority. The Food and Agriculture Organization (FAO) of the United Nations and the World Health Organization (WHO) define probiotics as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" (Kollath, 1953; FAO/WHO, 2002; Hill et al., 2014; FDA, 2025; ISAPP, 2014). This definition places a high standard for scientific substantiation, demanding that all microbial strains labelled as probiotics, show survival, a quantifiable effective dose and a proven health benefit in the intended host. In the current physiological paradigm, the gut microbiota is seen as a crucial metabolic organ. The adult gastrointestinal system contains about 10^{13} to 10^{14} bacteria, which represent a microbial biomass comparable to the total amount of human somatic cells (Li et al., 2025). These microorganisms help ferment undigested food fibres in the colon to produce essential metabolites, such as short-chain fatty acids (SCFAs), and synthesise important micronutrients, such as Vitamin K, riboflavin, and folate (Kollath, 1953; FAO/WHO, 2002). In addition to metabolic support, probiotics are important for the maintenance of the integrity of the intestinal mucosal barrier, detoxification of xenobiotics and environmental pollutants and inhibition of the development of opportunistic infections (Kollath, 1953; FAO/WHO, 2002; Patra et al., 2022).

Although probiotic products are now widely available (a global market of over USD 61.15 billion in 2021), large gaps in scientific understanding still exist (Polaris Market Research, 2022). While the genera *Lactobacillus*

and *Bifidobacterium* have been classically thought to have universal beneficial effects, an increasing number of researchers have stressed that the therapeutic efficacy is highly strain-specific (Maftei et al., 2026). At present, we do not have a complete understanding of the exact dose-response relationships necessary for the treatment of different pathophysiological states and there is a pressing need for standardisation of safety reporting, especially relating to the long term effects of next-generation probiotics (NGPs) (Maftei et al., 2026). The host microbiome interacts with exogenous probiotic strains in an unpredictable way, resulting in large variability in the results of clinical trials (Maftei et al., 2026; Li et al., 2026). Our goal is to review current knowledge on probiotic treatments in gastrointestinal physiology and pathology with a critical evaluation of current therapy paradigms and possible technological advances in the field.

2. Search Strategy

To ensure a rigorous and exhaustive evaluation of the current scientific landscape, a systematic search strategy was employed to identify relevant literature published between 2013 and early 2026. This period was selected to capture the most recent advancements in molecular biology, genetics, and microbiome research that have fundamentally expanded our understanding of probiotic-host interactions (Maftei et al., 2026).

2.1 Information Sources and Keyword Selection

The search was conducted across multiple high-impact medical and scientific databases, including MEDLINE (via PubMed), EMBASE, Scopus, the Cochrane Central Register of Controlled Trials, and Google Scholar (Li et al., 2023; Maftei et al., 2025). The search utilized a combination of Medical Subject Headings (MeSH) and free-text keywords to ensure a broad reach.

2.2 Inclusion and Exclusion Criteria

The selection of studies followed a strict protocol to maintain a high level of evidence-based synthesis. The primary focus was on randomized controlled trials (RCTs), systematic reviews, and meta-analyses, particularly "umbrella" meta-analyses which provide a comprehensive assessment of existing research (Maftei et al., 2025).

Table 1. Inclusion and Exclusion Criteria for Literature Selection

Inclusion Criteria	Exclusion Criteria
Studies involving human adults or pediatric populations evaluating probiotic efficacy (Maftei et al., 2025).	Case reports, editorials, poster presentations, and conference abstracts (Maftei et al., 2025).
Comparative studies with a placebo, standard care, or no-treatment control group (Li et al., 2023; Maftei et al., 2025).	Studies published in languages other than English (Maftei et al., 2025).
Research reporting on clinical outcomes such as symptom scores, remission rates, or biomarker changes (e.g., cytokines, SCFAs) (Maftei et al., 2025; Horvath et al., 2025).	In vitro studies that lack a clear translational link to host pathophysiology.
Evaluation of single-strain or multi-strain probiotic formulations (Li et al., 2023; Maftei et al., 2025).	Trials where the probiotic effect could not be isolated from other concurrent treatments.

2.3 Data Synthesis and Quality Assessment

The study selection process adhered to the PRISMA (Preferred Reporting Items for a Systematic Review and Meta-Analysis) guidelines to ensure transparency and reproducibility (Maftei et al., 2025). Quality assessment of the included meta-analyses was performed using the AMSTAR 2 (A

Measurement Tool to Assess Systematic Reviews) tool, which evaluates methodological flaws and the certainty of evidence (Maftei et al., 2025; Maftei et al., 2024). The synthesis focused on identifying core themes, such as the mechanisms of probiotic action, strain-specific efficacy in gastrointestinal disorders, and emerging therapeutic frameworks that incorporate personalized medicine.

3. Physiological Foundations of Probiotic Action

The therapeutic utility of probiotics is founded upon their ability to engage in a multifaceted dialogue with the host. These interactions occur at the physical, biochemical, and immunological levels, contributing to the maintenance of homeostasis within the gastrointestinal tract.

3.1 Competitive Exclusion and Pathogen Inhibition

The essence of probiotic action is competitive exclusion - a process where beneficial microbes actively prevent pathogens from colonization (Patra et al., 2022; Maftei et al., 2025). This defensive maneuver is a combination of physical displacement, resource competition, and chemical warfare (Kollath, 1953; Patra et al., 2022; Li et al., 2023).

Probiotics, particularly those belonging to the *Lacticaseibacillus*, *Limosilactobacillus*, and *Bifidobacterium* genera, exhibit high affinity for the mucosal surfaces of the gut (Patra et al., 2022). These microorganisms produce a thick biological barrier by filling up the binding receptors on epithelial cells. This barrier makes it difficult for opportunistic bacteria like *Escherichia coli*, *Salmonella* and *Clostridioides difficile* to establish themselves (Patra et al., 2022; Maftei et al., 2025; Chen et al., 2025). This trait is highly strain-specific; for instance, *Lactobacillus rhamnosus* GG is renowned for its ability to adhere to human intestinal epithelial cells (Culturelle, 2025).

In addition to competing for a physical niche, probiotics generate a number of chemicals that have a direct anti-pathogenic effect:

- Organic acids: Lactic and acetic acids are produced by fermentation of carbohydrates by lactic acid bacteria, and these acids result in a considerable reduction in the luminal pH. This acidic climate is not conducive to many harmful germs (Kollath, 1953; FAO/WHO, 2002; Farahani et al., 2025).
- Bacteriocins: antimicrobial peptides synthesised by the ribosome and generated by different probiotic strains. They attack certain cell wall components of competing bacteria, essentially serving as “natural antibiotics” (Kollath, 1953; FAO/WHO, 2002; Farahani et al., 2025).
- Hydrogen peroxide: Some *Lactobacillus* strains generate H2O2 which leads to oxidative stress to nearby anaerobic pathogens (Kollath, 1953; Farahani et al., 2025).

3.2 Reinforcement of the Intestinal Mucosal Barrier

The intestinal barrier is a structure composed of a physical (mucus and epithelial cells), a chemical (antimicrobial peptides) and an immunological layer (GALT). Probiotics are critical in strengthening this barrier, therefore preventing the translocation of luminal antigens - a syndrome often referred to as "leaky gut” (Kollath, 1953; Chen et al., 2025).

A key target of probiotic action is the modulation of tight junction (TJ) proteins, such as claudins, occludin, and zonula occludens-1 (ZO-1). These proteins maintain the apical seal between adjacent epithelial cells. Probiotic interventions have been shown to increase the expression and proper localization of these proteins, thereby reducing intestinal permeability (Kollath, 1953; Chen et al., 2025; Patra et al., 2022). Additionally, certain strains, notably *Akkermansia muciniphila*, stimulate the production of mucins by goblet cells. This paradoxical deterioration and stimulation cycle leads to a thicker, more resilient mucus layer that serves as the primary physical defense against invaders (Chen et al., 2025; Derrien et al., 2004; Geerlings et al., 2021; Cani et al., 2022).

3.3 Immunomodulation and Signaling Pathways

Probiotics are modulators of the host's innate and adaptive immune systems. They engage with the gut-associated lymphoid tissue (GALT) through pattern recognition receptors (PRRs), such as Toll like receptors (TLRs), located on the surface of epithelial and dendritic cells (Kollath,1953; Geerlings et al., 2021). This interaction initiates a signaling cascade supporting immune homeostasis:

1. Dendritic Cell Maturation: probiotics can influence the maturation and function of dendritic cells (DCs), which are the primary antigen-presenting cells in the gut; this results in increased activity of Regulatory T-cells (Tregs) (Kollath, 1953; Chen et al., 2025).
2. T-cell Differentiation: by promoting the differentiation of Tregs, probiotics help balance the immune response, preventing the excessive pro-inflammatory activity of Th17 and Th1 cells, which is crucial for avoiding chronic inflammation and autoimmune responses in the gut (Kollath, 1953; Chen et al., 2025).
3. Cytokine Regulation: probiotic signaling promotes the release of anti-inflammatory cytokines like IL-10 and TGF-\beta, while simultaneously inhibiting the production of pro- inflammatory factors such as TNF-\alpha, IL-6, and IL-12 (Maftei et al., 2024; Munir et al., 2022; Chen et al., 2025).
4. Secretory IgA (sIgA) Stimulation: probiotics enhance the production of sIgA by B- cells. sIgA is the predominant antibody class in the gut and is essential in the immunological exclusion of pathogens and toxins (Hill et al., 2014).
5.

3.4 The Role of Postbiotics and Microbial Metabolites

The concept of "postbiotics" has emerged to describe the beneficial effects of inanimate microorganisms and their components. This includes microbial metabolites that exert significant therapeutic potential (Salminen et al., 2021). The most studied metabolites are short-chain fatty acids (SCFAs), produced through the fermentation of dietary fibers (Kollath, 1953; Li et al., 2025; Patra et al., 2022).

Table 2. Physiological Benefits of Key Microbial Metabolites (Postbiotics)

Metabolite	Primary Source/Mechanism	Physiological Benefit
Butyrate	Fermentation by *Faecalibacterium prausnitzii* and *Roseburia* (Cani et al., 2022; Bhattacharya et al., 2025).	Energy source for colonocytes; increases tight junction resistance via histone acetylation; anti-inflammatory (Li et al., 2025; Patra et al., 2022; Bhattacharya et al., 2025).
Acetate	Wide range of *Bifidobacterium* and *Lactobacillus* species (Li et al., 2025; Munir et al., 2022).	Regulates luminal pH; serves as a precursor for butyrate through cross-feeding; systemic metabolic regulation (Li et al., 2025; Patra et al., 2022; Gautier et al., 2021).
Propionate	Produced via the succinate or propanediol pathways (Li et al., 2025; Gautier et al., 2021).	Influences liver gluconeogenesis and satiety signaling via the gut-brain axis (Li et al., 2025; Patra et al., 2022; Gautier et al., 2021).
Indoles	Tryptophan metabolism by various commensal bacteria (Kollath, 1953; Cani et al., 2022; Patra et al., 2022)	Act as ligands for the aryl hydrocarbon receptor (AhR), promoting barrier integrity and immune tolerance (Kollath, 1953; Cani et al., 2022; Patra et al., 2022)

4. Clinical Pathophysiology: Probiotic Interventions in Gastrointestinal Disease

The use of probiotics in clinical settings has transitioned from general support to targeted interventions for specific gastrointestinal disorders. The success of these treatments is increasingly linked to strain-specific traits and the dose-response characteristics of the formulations.

4.1 Irritable Bowel Syndrome (IBS)

IBS is one of the most common functional gastrointestinal disorders, characterized by abdominal pain, bloating, and irregular bowel patterns. Dysbiosis is a major contributor to IBS pathophysiology and probiotic interventions aim to restore microbial balance. Recent systematic reviews of randomized placebo-controlled trials (RPCTs) have identified specific strains that exhibit consistent effect (Maftei et al., 2026).

Table 3. Efficacy of Specific Probiotic Strains in Irritable Bowel Syndrome (IBS)

Probiotic Strain	Target Symptom in IBS	Observed Clinical Efficacy
Bifidobacterium longum 35624	Global IBS symptoms, abdominal pain, straining.	Effectively reduces pain severity and straining; insufficient for bloating or gas (Maftei et al., 2026).
Lactobacillus rhamnosus GG	Abdominal pain (Pediatric and adult populations).	Significant reduction in pain at doses of 6 \times 10^{9} CFU over 8 weeks (Maftei et al., 2026).
Lactiplantibacillus plantarum 299v	Abdominal pain, flatulence, incomplete evacuation.	Probiotic groups reported higher significant improvement in digestive symptoms vs. placebo (Maftei et al., 2026).
Saccharomyces cerevisiae CNCM I-3856	Core IBS symptoms.	Associated with general improvement and reduced abdominal pain intensity (Maftei et al., 2026).
Bacillus coagulans Unique IS2	Global symptoms and quality of life.	Demonstrated significant reduction in abdominal pain intensity (Maftei et al., 2026).

Interestingly, not all probiotics are effective for IBS. Meta-analyses have shown that *Escherichia coli* Nissle 1917 and *Lactobacillus casei* Shirota did not demonstrate sufficient effects on abdominal pain or bloating in this specific patient population, highlighting the critical importance of strain-specific selection (Maftei et al., 2026).

4.2 Inflammatory Bowel Disease (IBD)

Inflammatory Bowel Disease (IBD) consists of Ulcerative Colitis (UC) and Crohn's Disease (CD) and is characterised by chronic idiopathic inflammation of the gastrointestinal system. Probiotics are increasingly used as supplementary therapy to induce and maintain remission by modulating the gut-liver axis and improving barrier function (Maftei et al., 2024; Chen et al., 2025; Patra et al., 2022).

The evidence for Ulcerative Colitis is quite compelling. Multi-strain probiotics, notably with *Lactobacillus*, *Bifidobacterium* and *Streptococcus*, have shown higher benefits than placebo in generating clinical remission (Maftei et al., 2024; UEG Journal, 2024). Subgroup analyses suggest that the combination of probiotics with standard medication such as 5-ASA (mesalazine) may be more helpful in achieving remission and preventing than either therapy alone (Maftei et al., 2024; UEG Journal, 2024).

The results in Crohn's Disease have been largely disappointing. Currently, broad meta-analyses and European recommendations do not support the use of standard probiotics in Crohn's disease because of a lack of evidence of benefit for achieving remission or postoperative recurrence prevention (UEG Journal, 2024). This difference can be owing to the more complex nature of inflammation and accompanying microbial signatures in CD, compared to UC.

4.3 Antibiotic-Associated Diarrhea (AAD)

The use of broad-spectrum antibiotics frequently leads to the disruption of the gut microbiota, leading to AAD and potentially life-threatening *Clostridioides difficile* infections. Probiotics have been used to reduce these risks. An umbrella meta-analysis of interventional studies found that probiotic supplementation was associated with a 56% reduction in the risk of diarrhea (RR 0.44; 95% CI 0.37–0.52) (Maftei et al., 2025).

Further analysis suggests that multi-strain formulations can provide the strongest protective effect (RR0.40 compared to single strains). The success rate is most apparent when probiotics are administered early in the antibiotic course and for a duration of at least 2 to 4 weeks (Li et al., 2023; Maftei et al., 2025).

4.4 Metabolic and Chronic Conditions

Recent studies have broadened the use of probiotics from the gastrointestinal system to metabolic health.

- Insulin Resistance and Diabetes Multi-strain probiotics have been proven to minimise the gastrointestinal side effects (eg, diarrhoea and abdominal discomfort) of metformin thereby improving drug tolerance (Ratajczak et al., 2026).
- NAFLD and MASH: Probiotics modify the gut-liver axis, lowering endotoxicemia and liver inflammation by the alteration of production of microbial enzymes involved in steroid and fatty acids metabolism (Patra et al., 2022).
- Burn Wounds and Skin Health: Topical and oral probiotics such as *Lactiplantibacillus plantarum* have shown to suppress infections like *Pseudomonas aeruginosa* and promote wound healing by releasing antimicrobial compounds (Farahani et al., 2025).

5. Modern Therapeutic Frameworks: Toward Precision Probiotics

The field is changing from a one-size-fits-all approach to more sophisticated therapy frameworks that focus on individualisation and accuracy. This transformation is based on the principles of Predictive, Preventive and Personalised Medicine (3PM) (Li et al., 2026).

5.1 Multi-Omics and AI Integration

The advent of high-throughput technology has enabled the integration of cross-sectional and longitudinal multi-omics data to predict the results of probiotic treatments.

- Genomics and Culturomics: Comparative investigation of the gut microbiome enables for the identification of health-associated taxa and the construction of functionally improved strains (Li et al., 2026).
- Metabolomics: Researchers can now track biochemical signatures (e.g., imidazole propionate or particular SCFAs) that represent the interplay of genes, food and microbiome using standardised platforms. These signals are predictive of the functional liver capacity and drug metabolism potential (Biocrates, 2025).
- Artificial Intelligence: Deep learning models are applied to predict postprandial glycaemic responses, inferred food-microbe-metabolite interactions, and allows doctors to personalise therapies based on an individual's baseline microbiome profile (Li et al., 2026).

5.2 Personalized Probiotic Therapy Frameworks

A crucial understanding in contemporary medicine is that probiotic colonization is profoundly personalized. Research indicates that certain individuals are „permissive" to colonization, whilst others exhibit resistance, conditional of synthetic biology to generate smarter biotherapeutics (Li et al., 2026).

Table 4. Conceptual Frameworks for Personalized and Precision Probiotic Therapy

Framework Strategy	Description	Clinical Goal
Stratified Probiotics	Probiotics tailored for specific host subpopulations (e.g., sex-specific effects on CD4+ T- cells) (Li et al., 2026).	Optimizing efficacy for defined demographic or clinical groups
Personalized Probiotics	Formulations tailored to an individual's unique physiological and microbial profile (Li et al., 2026).	Ensuring successful colonization and target engagement for the individual
Predictive Modeling	Using molecular and microbial biomarkers to forecast responsiveness (Li et al., 2026).	Avoiding treatment failure and reducing unnecessary healthcare costs

6. Future Innovations and Next-Generation Probiotics (NGPs)

The future of probiotic therapy lies in the exploration of non-traditional microbial species and the application of synthetic biology to create smarter biotherapeutics.

6.1 *Akkermansia muciniphila*: The Archetypal NGP

Akkermansia muciniphila (AKK) has been identified in 2004 and since then has become one of the most promising candidates for treating metabolic and inflammatory diseases. AKK constitutes 1-4% of the total gut microbiota and is characterized by its unique ability to degrade mucin as its primary energy source (Derrien et al., 2004; Geerlings et al., 2021; Cani et al., 2022). This metabolic activity provides several health benefits:

- Barrier Restoration: By stimulating the turnover of the mucus layer, AKK thickens the intestinal barrier and promotes the expression of tight junction proteins (Geerlings et al., 2021; Cani et al., 2022).
- Metabolic Homeostasis: AKK has been shown to reduce blood glucose levels and improve insulin sensitivity (Geerlings et al., 2021; Cani et al., 2022; Bhattacharya et al., 2025).
- Anti-inflammatory Effects: AKK produces extracellular vesicles and outer membrane proteins that modulate host immune responses, particularly in the context of metabolic syndrome and ulcerative colitis (Geerlings et al., 2021; Cani et al., 2022).

In 2025 research also explored the idea of combination therapies such as the use of AKK alongside sodium butyrate, which showed synergistic effects in normalizing metabolic parameters in diabetic models compared to either treatment alone (Bhattacharya et al., 2025).

6.2 Genetically Engineered Microbes (GEMs)

Synthetic biology and gene editing techniques like CRISPR-Cas9 are allowing to develop probiotics tailor for precise therapeutic delivery.

- Targeted Cytokine Delivery: Strains like *Lactococcus lactis* have been engineered to express anti-inflammatory cytokines like IL-10. These strains provide direct delivery to inflamed tissues in IBD, reducing systemic side effects (Chen et al., 2025).
- ROS Scavenging: GEMs can be programmed to sense inflammation and respond by releasing reactive oxygen species (ROS) scavengers, helping reduce oxidative damage in the gut (Chen et al., 2025).
- Real-time Monitoring: Some engineered probiotics function as "biosensors," capable of monitoring inflammation levels in the gut and dynamically adjusting the release of therapeutic molecules (Chen et al., 2025).

6.3 Breakthrough Trends in Delivery Systems

Innovations presented at Probiota 2025 and 2026 highlight the transition from simple bacterial counts to understanding complex metabolic networks (DSM-Firmenich, 2025).

- Precision Delivery Systems: Technologies like Microbiome Targeted TechnologyTM (MTTTM) use multi-layered coatings to protect active ingredients (like B-vitamins or live strains) from gastric acid, ensuring precise release in the colon where beneficial microbe concentration is highest (DSM-Firmenich, 2025).
- Healthy Aging Focus: Research is tracking how age-related declines in SCFA production can be mitigated through target metabolic network interventions, rather than simple supplementation (DSM-Firmenich, 2025).

7. Safety and Regulatory Frameworks

As probiotic products get more complicated, the need for comprehensive safety evaluations and consistent standards increases.

7.1 Safety Challenges in Clinical Use

Although probiotics are generally safe for healthy people, evidence suggests their safety profile varies substantially by host condition. Immunocompromised and intensive care patients have reported translocation and bacteremia (Maftei et al., 2026; ISAPP, 2025).

The key safety considerations requiring standardised reporting are:

- Acquisition of Antimicrobial Resistance (AMR) Genes: Screening of probiotics for mobile genomic elements capable of transferring AMR genes to pathogens (Maftei et al., 2026).
- Virulence Factors: Verifying the non-existence of genes that could potentially contribute to toxin generation or tissue invasion (Maftei et al., 2026).
- Genomic stability: Particularly for NGPs and GEMs, long-term stability of the microbial genome in the host needs to be confirmed (Maftei et al., 2026).

7.2 Regulatory Divergence

Currently, there is a lack of international harmonization regarding probiotic regulation.

- European Union: The registration of Live Biotherapeutics (LBPs) falls under medicinal product directives (Directive No. 2001/83/EC), requiring multi-stage clinical trials and GMP compliance (Maftei et al., 2026).
- United States: Probiotics are largely regulated as dietary supplements under a framework that focuses on risk assessment (GRAS status) without requiring pre-market approval for efficiency (Maftei et al., 2026).
- Russian Federation: Probiotics are often positioned as dietary supplements solely intended to supplement the daily diet, while medicinal probiotics are managed separately by the Ministry of Health (Maftei et al., 2026).

The high cost of research and development necessary for producing new and successful strains, along with rigorous safety standards, continue to create a major challenge for manufacturers pursuing clinical acceptance (Polaris Market Research, 2022).

8. Summary and Conclusions

Probiotic interventions have become fundamental to modern gastrointestinal therapeutic frameworks, providing a powerful means to modulate the complex host-microbe interface. From the foundational mechanisms of competitive exclusion and barrier reinforcement to the cutting-edge innovations in genetically engineered microbes and next-generation probiotics like *Akkermansia muciniphila*, the field is advancing toward a new era of precision medicine.

Research highlights that the success rate of these interventions is highly dependent on strain specificity, dosage, and the individual's baseline microbiome profile. While probiotics offer significant potential for managing IBS, IBD, and antibiotic-associated complications, the shift from empirical supplementation to evidence-based biotherapeutics requires addressing several obstacles. Standardising dose-response relationships, harmonising international regulatory standards, and formulating comprehensive safety evaluations for at-risk populations are critical measures for the future. The combination of multi-omics data and artificial intelligence will enable physicians to migrate from a trial-and-error approach to a paradigm where probiotic therapy is tailored to the individual patients needs. This evolution will be important to realising the full promise of microbiome-based therapies to promote human health and manage chronic disease.

Author's contribution

Software: Aleksandra Potempa, Mateusz Żyła, Aleksandra Ustaszewska
Check: Aleksandra Oszczypała, Katarzyna Lipska, Monika Szyszkowska, Liwia Prorok
Formal analysis: Liwia Prorok, Michał Petkow, Zofia Parol, Zuzanna Strojek
Investigation: Aleksandra Oszczypała, Aleksandra Ustaszewska, Zofia Parol
Resources: Katarzyna Lipska, Aleksandra Oszczypała, Mateusz Żyła, Monika Szyszkowska
Data curation: Mateusz Żyła, Katarzyna Lipska, Aleksandra Potempa, Michał Petkow
Writing - rough preparation: Aleksandra Potempa, Monika Szyszkowska, Aleksandra Ustaszewska, Zofia Parol
Writing - review and editing: Zuzanna Strojek, Aleksandra Oszczypała, Katarzyna Lipska, Liwia Prorok
Visualization: Mateusz Żyła, Michał Petkow, Monika Szyszkowska, Aleksandra Ustaszewska
Supervision: Aleksandra Potempa, Michał Petkow, Zuzanna Strojek, Liwia Prorok
Project administration: Aleksandra Potempa

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