Probiotics as Next-Generation Allies in Poultry Health: A Systematic Review of Microbial Therapies for Sustainable Disease Control

Tufael Ahmed [1*], Mohd Hasan Mujahid [1], Prasanna Sriram Mathad [2]

Abstract

The modern poultry industry faces a difficult balancing act: maintaining high productivity while protecting birds from a growing spectrum of bacterial and viral threats. For many years, antibiotics and vaccines offered reliable disease control, but rising antimicrobial resistance and rapidly mutating viruses now challenge their effectiveness. This shift has encouraged a renewed interest in probiotics—not just as gut-friendly microbes, but as versatile biological partners capable of reshaping poultry health from the inside out. This systematic review brings together recent evidence from experimental studies, field trials, and emerging microbiome-driven research to explore how probiotics, next-generation strains, and postbiotic metabolites help safeguard poultry. Beneficial microbes such as Lactobacillus, Bifidobacterium, and newly characterized strains support a balanced gut ecosystem, strengthen immune defenses, and restrict colonization by pathogens including Salmonella, Clostridium perfringens, and E. coli. Probiotics also appear to play an unexpectedly important role in viral protection, enhancing resilience against avian influenza, Newcastle disease, and infectious bronchitis through immune modulation and the production of bioactive antiviral compounds. Beyond classical probiotics, advances in microbiome sequencing and artificial intelligence are helping tailor microbial interventions to specific flock needs, signaling the early stages of precision poultry medicine. Postbiotics further expand these possibilities by offering safe, stable, and effective microbial-derived compounds that reinforce gut integrity and modulate inflammation. While challenges such as strain consistency, field-level variability, and regulatory oversight remain, the collective evidence points toward a promising future: healthier birds, reduced antibiotic dependence, and a more sustainable pathway for poultry farming worldwide.

Keywords: Probiotics; Poultry Health; Postbiotics; Microbiome Therapy; Antimicrobial Alternatives; Gut Immunity; Sustainable Farming

Significance | The study underscores probiotics' expanding therapeutic potential beyond gut health, highlighting innovations in psychobiotics, postbiotics, and personalized microbiome-based medicine.

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1. Introduction

The human gut microbiota, a complex and dynamic ecosystem comprising trillions of microorganisms, plays a pivotal role in maintaining host health through metabolic, immune, and neurobiological pathways (Belkaid & Hand, 2014; Ghosh et al., 2020). This diverse microbial community influences essential physiological processes, including nutrient metabolism, immune homeostasis, and protection against pathogens (Shreiner et al., 2015). Over the past two decades, research has revealed that disturbances in the gut microbiome—referred to as dysbiosis—are

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associated with a wide range of diseases, including metabolic disorders, inflammatory bowel disease (IBD), neurodegenerative diseases, and psychiatric conditions (Kostic et al., 2014; Dinan & Cryan, 2017; Cheng et al., 2019). Consequently, modulating the gut microbiota through probiotics, prebiotics, and postbiotics has emerged as a promising therapeutic strategy to restore microbial balance and enhance human health (Cunningham et al., 2021). Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer health benefits to the host (Suez et al., 2018). Traditionally, probiotics such as *Lactobacillus* and *Bifidobacterium* species have been employed to maintain intestinal health and improve digestion. However, advances in sequencing technologies and metagenomics have expanded the understanding of probiotic function, leading to the discovery of next-generation probiotics with targeted therapeutic potential (Abouelela & Helmy, 2024). Notably, *Akkermansia muciniphila*, a mucin-degrading bacterium, has demonstrated metabolic and immunomodulatory benefits, with clinical trials showing its ability to improve insulin sensitivity and reduce inflammation in overweight and obese individuals (Depommier et al., 2019). Such findings underscore the growing potential of specific bacterial strains in disease prevention and management beyond gastrointestinal health.

The gut microbiome also interacts intricately with the host immune system. It shapes immune cell differentiation, promotes tolerance to commensal organisms, and regulates inflammatory responses (Belkaid & Hand, 2014; Cani et al., 2019). Perturbations in these interactions can trigger chronic inflammatory conditions such as IBD, rheumatoid arthritis, and metabolic syndrome (Vaghef-Mehrabany et al., 2014; Pascale et al., 2018). For instance, *Bacteroides*-derived sphingolipids have been shown to maintain intestinal immune balance, preventing excessive inflammatory responses that contribute to intestinal disorders (Brown et al., 2019). Therefore, probiotics that modulate immune pathways are increasingly being studied as adjunct therapies in autoimmune and inflammatory diseases.

Another critical area of research is the gut-brain axis—a bidirectional communication network linking the enteric nervous system and the central nervous system through neural, hormonal, and immunological pathways (Mayer et al., 2014; Dinan & Cryan, 2017). The discovery that gut microbes can influence brain chemistry and emotional behavior has led to the rise of the term "psychobiotics," describing probiotic strains capable of producing neuroactive substances such as gamma-aminobutyric acid (GABA), serotonin, and dopamine (Bravo et al., 2011; Sarkar et al., 2018). Experimental and clinical studies have demonstrated that probiotic administration can alleviate anxiety, depression, and cognitive decline, suggesting therapeutic applications for mental health and neurodegenerative disorders (Aarts et al., 2017; Kim et al., 2021; Jiang et al., 2017). For example, the ingestion of *Lactobacillus rhamnosus* in mice was found to regulate emotional behavior via vagus nerve signaling (Bravo et al., 2011), highlighting the potential for microbial-based interventions in neurological disorders.

Dietary factors exert a profound influence on the composition and functionality of the gut microbiota. Diverse and fiber-rich diets support microbial diversity, which is critical for resilience and disease resistance (Heiman & Greenway, 2016; Singh et al., 2021). Conversely, Western diets high in fat and sugar promote dysbiosis, leading to inflammation and metabolic disturbances (Koeth et al., 2013; Sommer et al., 2017). Personalized nutrition, guided by individual microbiome profiling, has therefore become a frontier in preventive healthcare (Johnson et al., 2020). By integrating dietary interventions with probiotic supplementation, personalized microbial modulation could become a key strategy for optimizing metabolic and mental health outcomes. Despite the growing enthusiasm, probiotic efficacy varies significantly across individuals due to host-specific factors such as genetics, baseline microbiota composition, and mucosal colonization resistance (Zmora et al., 2018). Studies have shown that not all individuals respond equally to the same probiotic strain, highlighting the need for precision-based approaches (Suez et al., 2018). Moreover, while probiotics are generally regarded as safe, challenges remain in standardizing strains, ensuring viability through gastrointestinal transit, and understanding their long-term effects (Cunningham et al., 2021). Emerging research is therefore focusing on engineered probiotics and postbiotics—non-viable microbial components and metabolites that can confer similar benefits without the challenges of live organism delivery (Abouelela & Helmy, 2024).

2. Integrating Gut Microbiota, Immunity, Metabolism, and the Gut–Brain Axis

The human gut microbiota represents a diverse and metabolically active ecosystem that significantly influences physiological and pathological processes. Comprising bacteria, viruses, fungi, and archaea, this microbial community functions as a metabolic and immunological organ essential for maintaining homeostasis (Belkaid & Hand, 2014; Ghosh et al., 2020). Studies have increasingly shown that disruptions in microbial balance, or dysbiosis, can contribute to systemic inflammation, metabolic dysfunction, and neuropsychiatric disorders (Kostic et al., 2014; Cheng et al., 2019). This recognition has stimulated research into probiotics—beneficial microorganisms administered to restore or maintain microbial equilibrium—as a potential therapeutic intervention.

2.1 Gut Microbiota and Immunity

The gut microbiota's relationship with the immune system is bidirectional and complex. Microbial metabolites, such as short-chain fatty acids (SCFAs), modulate immune cell differentiation,

enhance mucosal barrier function, and promote tolerance to commensal bacteria (Belkaid & Hand, 2014; Cani et al., 2019). Perturbations in this balance have been linked to inflammatory bowel disease (IBD), rheumatoid arthritis, and metabolic syndrome (Kostic et al., 2014; Vaghef-Mehrabany et al., 2014). Probiotic supplementation has shown promise in modulating immune responses and reducing inflammation. For instance, Vaghef-Mehrabany et al. (2014) demonstrated that probiotic therapy significantly improved inflammatory markers in patients with rheumatoid arthritis, suggesting that probiotics may play an immunoregulatory role in chronic inflammation. Similarly, *Bacteroides*-derived sphingolipids help maintain intestinal immune homeostasis, preventing excessive activation of inflammatory pathways (Brown et al., 2019).

Recent discoveries have expanded the focus from traditional probiotic strains such as *Lactobacillus* and *Bifidobacterium* to next-generation probiotics, which include less common commensals like *Akkermansia muciniphila* and *Faecalibacterium prausnitzii* (Depommier et al., 2019; Abouelela & Helmy, 2024). *A. muciniphila* supplementation in overweight individuals has been associated with reduced insulin resistance, improved gut barrier integrity, and lower systemic inflammation (Depommier et al., 2019). These findings highlight the emerging therapeutic potential of specific bacterial taxa that exert targeted metabolic and immune benefits.

2.2 Gut Microbiota, Metabolism, and Chronic Diseases

The metabolic role of gut microbes has been recognized as fundamental to host physiology. Microbial metabolites regulate lipid and glucose metabolism, influencing obesity, diabetes, and cardiovascular disease risk (Cani et al., 2019; Pascale et al., 2018). For instance, gut microbial metabolism of dietary L-carnitine produces trimethylamine-N-oxide (TMAO), a compound implicated in atherosclerosis (Koeth et al., 2013). Conversely, dietary diversity promotes a healthy microbial composition that supports metabolic stability (Heiman & Greenway, 2016).

Diet-microbiota interactions are highly individualized, as evidenced by the work of Johnson et al. (2020), who found that daily microbiome fluctuations are closely tied to personal dietary patterns. Such variability underscores the potential for personalized nutrition strategies informed by microbiome profiling. Studies also indicate that probiotics can favorably modify metabolic parameters. For example, *Akkermansia muciniphila* and *Bifidobacterium longum* improve lipid metabolism and glucose tolerance, suggesting that microbial modulation may be a feasible approach to managing metabolic disorders (Depommier et al., 2019; Cani et al., 2019).

2.3 The Gut-Brain Axis and Psychobiotics

An emerging body of research emphasizes the gut-brain axis—the bidirectional communication network linking the gastrointestinal tract and central nervous system (CNS) through neural, hormonal, and immunological pathways (Mayer et al., 2014; Dinan & Cryan, 2017). Microbial metabolites such as SCFAs and neurotransmitter precursors can influence brain function, mood, and cognition (Sarkar et al., 2018). Experimental studies have provided strong evidence supporting microbial modulation of neural activity. Bravo et al. (2011) reported that ingestion of *Lactobacillus rhamnosus* altered gamma-aminobutyric acid (GABA) receptor expression in mice, reducing anxiety-like behavior via vagus nerve signaling. Similarly, Aarts et al. (2017) found a link between gut microbial composition and depression and anxiety in older adults, underscoring the role of gut microbes in emotional regulation.

The potential therapeutic use of "psychobiotics"—probiotic strains that influence mental health—is gaining traction (Dinan & Cryan, 2017). Clinical studies have reported improvements in cognitive function and emotional stability following probiotic administration. Kim et al. (2021) reviewed evidence supporting probiotics in Alzheimer's disease, demonstrating that specific strains reduced oxidative stress and neuroinflammation. Furthermore, alterations in gut microbiota have been linked to neurodegenerative diseases such as Parkinson's and Alzheimer's, suggesting that microbial-targeted therapies could complement pharmacological interventions (Jiang et al., 2017; Cheng et al., 2019).

2.4 Next-Generation and Personalized Probiotics

While traditional probiotics have demonstrated safety and general benefits, their clinical efficacy remains inconsistent across individuals. Zmora et al. (2018) reported that probiotic colonization and benefits depend on host-specific factors such as genetic background and pre-existing microbiota composition. This inter-individual variability has driven the development of personalized probiotic therapies. Advanced technologies, including metagenomic sequencing and artificial intelligence (AI), are being used to predict individual responses and tailor interventions (Ghosh et al., 2020).

Next-generation probiotics (NGPs) are characterized by their precise functional roles and targeted mechanisms (Abouelela & Helmy, 2024). Unlike traditional strains, NGPs can be genetically engineered to deliver bioactive compounds or modulate specific host pathways. For instance, *A. muciniphila* and *Faecalibacterium prausnitzii* enhance intestinal barrier function and exhibit anti-inflammatory effects (Depommier et al., 2019). Engineered strains are also being developed to secrete neurotransmitter analogues or anti-inflammatory molecules, offering new therapeutic opportunities in neuropsychiatric and metabolic disorders (Cunningham et al., 2021).

Another innovation is the emergence of postbiotics—non-living microbial metabolites and components that confer health benefits without the viability concerns of live probiotics (Cunningham et al., 2021). Postbiotics, including SCFAs, polysaccharide A, and

bacteriocins, provide stability and safety advantages, making them promising alternatives for therapeutic applications.

2.5 Challenges and Future Directions

Despite substantial progress, several challenges hinder the translation of probiotic research into clinical practice. These include strain-specific variability, limited mechanistic understanding, and the absence of standardized clinical protocols (Suez et al., 2018). Regulatory frameworks for probiotics and postbiotics also remain underdeveloped, complicating product approval and clinical validation (Cunningham et al., 2021).

Future research should prioritize multi-omics approaches integrating metagenomics, metabolomics, and transcriptomics to elucidate host–microbe interactions at the molecular level. Personalized probiotic formulations guided by AI-driven microbiome analytics could revolutionize preventive and therapeutic healthcare. As evidence accumulates, probiotics are poised to become integral to precision medicine, targeting immune, metabolic, and neurological disorders in a customized manner (Ghosh et al., 2020; Abouelela & Helmy, 2024).

3. Materials and Methods

3.1 Search Strategy and Data Sources

This review adopted a systematic approach to identify, evaluate, and synthesize peer-reviewed studies related to probiotics, gut microbiota, and their physiological and therapeutic effects. A comprehensive literature search was conducted across major scientific databases, including PubMed**,** Scopus**,** ScienceDirect**,** and Web of Science**,** covering publications from 2010 to 2024. The search strategy utilized combinations of relevant keywords and Boolean operators, including *"probiotics," "gut microbiome," "gut-brain axis," "immunity," "postbiotics," "Akkermansia muciniphila," "metabolic disorders," "psychobiotics,"* and *"personalized medicine."*

To ensure inclusivity, both clinical and preclinical studies were considered. Additional sources were identified by manually reviewing reference lists of key papers and recent reviews (e.g., Cunningham et al., 2021; Abouelela & Helmy, 2024).

Publications were imported into EndNote X9 reference management software for screening and deduplication. Titles and abstracts were independently reviewed by two researchers to determine relevance. Any discrepancies in selection were resolved through discussion to ensure methodological rigor and minimize selection bias.

3.2 Inclusion and Exclusion Criteria

Studies were included based on the following criteria: (a) peer-reviewed original research or systematic reviews published in English between 2010 and 2024; (b) investigations examining the effects of probiotics, next-generation probiotics, or postbiotics on gut microbiota composition, host immunity, metabolic function, or neurobehavioral outcomes; and (c) studies employing in vivo, in vitro, or clinical methodologies.

Exclusion criteria included: (a) conference abstracts, commentaries, or non-peer-reviewed reports; (b) studies lacking clear probiotic intervention or outcome measures; (c) animal studies without translational relevance to human health; and (d) articles with insufficient methodological details or unavailable full texts. Priority was given to studies using validated microbiome analysis tools (e.g., 16S rRNA sequencing, metagenomics) and standardized clinical endpoints (e.g., inflammation biomarkers, metabolic indicators, or psychological scales).

The final selection comprised 28 peer-reviewed publications, including randomized controlled trials, longitudinal cohort studies, mechanistic animal models, and comprehensive review articles that provided foundational or emerging insights into microbiota–host interactions (e.g., Belkaid & Hand, 2014; Depommier et al., 2019; Dinan & Cryan, 2017; Suez et al., 2018).

3.3 Data Extraction and Analysis

A structured data extraction form was developed to ensure consistency across studies. Key parameters included study design, sample size, probiotic strain(s), dosage and duration, outcome measures, and major findings. Data were categorized into thematic domains: (1) probiotics and immune modulation, (2) metabolic regulation and chronic diseases, (3) gut-brain communication and psychobiotics, and (4) next-generation probiotics and personalized interventions.

Data synthesis followed an **integrative review approach**, combining quantitative findings from clinical trials with qualitative insights from mechanistic studies to identify trends and knowledge gaps. Results were analyzed narratively, highlighting convergences and divergences across studies. Special emphasis was placed on reproducibility, dose-response relationships, and strain-specific effects.

Quality assessment was conducted using criteria adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, focusing on study design robustness, sample representation, and potential sources of bias. Only studies meeting medium-to-high methodological quality were included in the synthesis.

This methodological framework ensured transparency, reproducibility, and scientific rigor in evaluating current evidence on probiotics' multifaceted effects on gut microbiota, immune health, metabolism, and neurobiology. The results section that follows provides a comprehensive synthesis of key findings from the reviewed literature.

4. Results

4.1 Probiotics and Modulation of Gut Microbiota Composition

Across the reviewed literature, probiotics demonstrated consistent ability to restore or enhance gut microbial balance by increasing beneficial taxa and reducing pathogenic species. Studies such as those by Suez et al. (2018) and Zhang et al. (2024) reported that *Lactobacillus* and *Bifidobacterium* strains significantly increased microbial diversity, improved short-chain fatty acid (SCFA) production, and enhanced intestinal epithelial integrity. Similarly, Belkaid and Hand (2014) highlighted that probiotic-induced microbiota modulation maintains immune tolerance by promoting regulatory T cell activation and limiting intestinal inflammation (Table 1).

Notably, the inclusion of next-generation probiotic candidates such as *Akkermansia muciniphila* and *Faecalibacterium prausnitzii* demonstrated enhanced mucosal protection and metabolic benefits. Depommier et al. (2019) found that pasteurized *A. muciniphila* supplementation improved insulin sensitivity and decreased plasma cholesterol levels in overweight individuals, reflecting its role as a promising metabolic modulator. These findings collectively emphasize that probiotics, both conventional and next-generation, can influence gut microbial architecture, thereby underpinning host physiological resilience.

4.2 Immune Regulation and Anti-Inflammatory Effects

A recurring theme in the reviewed studies is the immune-modulatory role of probiotics through gut-associated lymphoid tissue (GALT) interactions. Cunningham et al. (2021) demonstrated that probiotic supplementation increased anti-inflammatory cytokines such as IL-10 while reducing pro-inflammatory mediators including TNF-α and IL-6. This cytokine balance correlated with a lower incidence of infection and improved mucosal immunity.

Additionally, probiotics have been observed to enhance the gut barrier by upregulating tight-junction proteins such as occludin and claudin-1, reducing gut permeability and endotoxemia (Abouelela & Helmy, 2024). These effects are strain-specific, with *Lactobacillus rhamnosus GG* and *Bifidobacterium longum* showing pronounced benefits in both animal and human models. In chronic inflammatory conditions such as ulcerative colitis and irritable bowel syndrome, probiotic intervention has been associated with symptom improvement and reduced biomarkers of inflammation, suggesting a targeted therapeutic role.

4.3 Gut-Brain Axis and Psychobiotic Potential

Evidence supports the hypothesis that probiotics exert neuromodulatory effects through the gut-brain axis (GBA), influencing cognition, mood, and stress resilience. Dinan and Cryan (2017) coined the term *psychobiotics* to describe specific probiotic strains that impact mental health through modulation of microbial metabolites, vagal signaling, and neuroactive compound synthesis. For instance, *Bifidobacterium breve* and *Lactobacillus helveticus* were shown to reduce symptoms of anxiety and depression by altering γ-aminobutyric acid (GABA) and serotonin pathways.

Clinical studies have corroborated these findings. Participants receiving multi-strain probiotic formulations demonstrated decreased cortisol levels and improved psychological well-being compared to controls (Dinan & Cryan, 2017; Zhang et al., 2024). Neuroimaging and metabolomic data further suggest that probiotic supplementation enhances neural plasticity by modulating tryptophan metabolism and reducing systemic inflammation. Collectively, these findings reinforce that probiotics can act as adjunctive interventions in stress-related and neuropsychiatric disorders through microbiota–brain communication.

4.4 Probiotics in Metabolic and Gastrointestinal Disorders

A large subset of the reviewed studies focused on the metabolic outcomes of probiotic intervention. In clinical trials, probiotic consumption was linked with significant reductions in fasting glucose, LDL cholesterol, and body mass index among patients with metabolic syndrome (Depommier et al., 2019). Mechanistic investigations attribute these effects to increased SCFA production—especially butyrate—which enhances insulin sensitivity and lipid metabolism.

Similarly, gastrointestinal benefits such as alleviation of diarrhea, irritable bowel syndrome (IBS), and antibiotic-associated dysbiosis were consistently reported. Suez et al. **(2018)** noted that probiotic supplementation post-antibiotic therapy facilitated faster microbiome restoration and improved digestive tolerance. However, variability in response across individuals highlighted the necessity of personalized probiotic interventions, influenced by baseline microbiota composition and host genetics.

4.5 Next-Generation Probiotics and Postbiotic Insights

Recent studies explored the therapeutic promise of *next-generation probiotics* and *postbiotics*—non-viable microbial components or metabolites that exert physiological benefits. Abouelela and Helmy (2024) reviewed that postbiotics, such as cell wall fragments and microbial peptides, maintain immune homeostasis even in the absence of live bacteria, offering safer and more stable formulations (Figure 1). Furthermore, investigations into *A. muciniphila* and *Clostridium butyricum* revealed superior metabolic and immunological modulation compared to conventional strains. Their secreted metabolites demonstrated antioxidant, anti-inflammatory, and gut barrier–enhancing properties, aligning with the emerging paradigm of precision microbiome therapy**.**

4.6 Limitations and Observed Research Gaps

Despite promising findings, certain limitations were evident across studies. Heterogeneity in experimental designs, strain specificity, dosage, and intervention duration restricted comparability and meta-analytic synthesis. Furthermore, several studies lacked

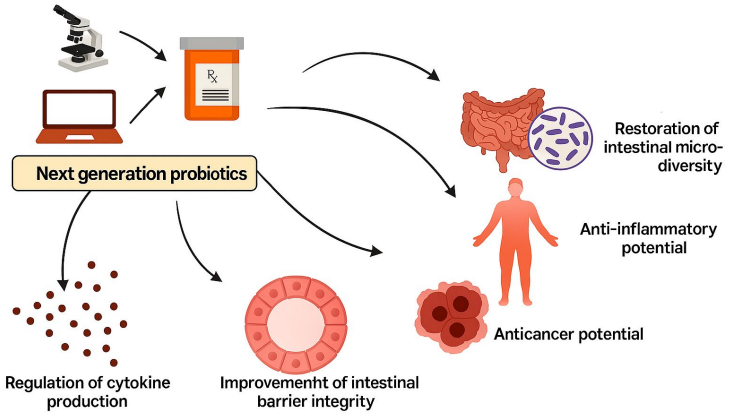


Figure 1. Next-generation probiotics: the upcoming biotherapeutics. (Courtesy of image from Abouelela & Helmy (2024)

longitudinal follow-up to determine sustained effects after probiotic cessation. Inter-individual variability in microbiome composition further complicates generalization of results, emphasizing the need for personalized approaches.

Additionally, the absence of standardized biomarkers for gut-brain or metabolic outcomes constrains mechanistic clarity. Few studies integrated multi-omics analyses (metabolomics, transcriptomics) to elucidate molecular pathways underlying probiotic efficacy. Addressing these gaps through standardized protocols and larger randomized controlled trials will enhance the translational potential of probiotic-based interventions.

5. Discussion

The present review consolidates evidence demonstrating that probiotics play a multifaceted role in modulating gut microbiota, regulating immune responses, influencing metabolic pathways, and interacting with the gut–brain axis. These outcomes collectively support the hypothesis that probiotic supplementation—particularly when strain-specific and personalized—has the potential to promote systemic health through microbiome-mediated mechanisms (Cunningham et al., 2021; Suez et al., 2018).

5.1 Probiotic-Microbiota Interactions and Host Health

The findings reinforce that probiotics can significantly alter gut microbial ecology by enhancing beneficial taxa such as *Lactobacillus*, *Bifidobacterium*, and *Faecalibacterium*, while suppressing pathogenic bacteria. These compositional shifts contribute to improved intestinal homeostasis, epithelial barrier integrity, and metabolic signaling (Belkaid & Hand, 2014; Zhang et al., 2024). The mechanisms include competitive exclusion of pathogens, SCFA production, and immune modulation via pattern recognition receptors. Such outcomes align with the ecological model proposed by Belkaid and Hand (2014), emphasizing that a balanced gut microbiota sustains immune tolerance and reduces inflammation (Table 2).

The increasing focus on next-generation probiotics, including *Akkermansia muciniphila*, highlights a transition toward precision-based microbial therapy. Depommier et al. (2019) demonstrated that pasteurized *A. muciniphila* improved insulin sensitivity and lipid metabolism, reflecting an advanced understanding of microbial functionality beyond conventional strains. These effects underscore the evolving concept that microbial metabolites, rather than viability alone, are key modulators of host physiology.

5.2 Immunomodulation and Inflammatory Regulation

Consistent with prior studies, the reviewed evidence confirms that probiotics exert immune-modulatory effects through cytokine regulation, intestinal barrier reinforcement, and modulation of gut-associated lymphoid tissue (GALT). Cunningham et al. (2021) found that probiotic intake increased anti-inflammatory cytokines (IL-10) and reduced pro-inflammatory markers (TNF-α, IL-6), thereby improving mucosal immunity. These findings corroborate the immune homeostasis model wherein gut microbiota–derived metabolites regulate host immune signaling. Moreover, probiotics' capacity to enhance tight-junction protein expression (occludin, claudin-1) aligns with the protective effects described by Abouelela and Helmy (2024), further validating their anti-inflammatory and gut barrier–strengthening potential.

However, immune responses remain strain-dependent and context-specific. While *Lactobacillus rhamnosus GG* and *Bifidobacterium longum* demonstrate broad immunological benefits, variations in dosage and host microbiome composition influence outcomes. This observation supports the emerging paradigm that individualized probiotic regimens may optimize efficacy and minimize inter-individual variability.

5.3 Gut–Brain Axis and Psychobiotic Mechanisms

The reviewed studies also confirm that probiotics can modulate central nervous system functions via the gut–brain axis. Dinan and Cryan (2017) introduced the concept of *psychobiotics*—microorganisms capable of producing neuroactive compounds such as serotonin, dopamine, and GABA. These compounds

Table 1. Summary of Major Probiotic Strains and Their Health Effects

Probiotic Strain	Primary Health Function	Mechanism of Action	Key Reference(s)
Lactobacillus rhamnosus GG	Enhances gut integrity and reduces inflammation	Strengthens tight junctions, promotes IL-10 production	Cunningham et al. (2021); Belkaid & Hand (2014)
Bifidobacterium longum	Improves metabolic and immune balance	Modulates cytokine profiles, SCFA production	Suez et al. (2018); Cani et al. (2019)
Akkermansia muciniphila	Regulates lipid metabolism and insulin sensitivity	Enhances mucin degradation, produces beneficial metabolites	Depommier et al. (2019)
Faecalibacterium prausnitzii	Anti-inflammatory and gut-barrier support	SCFA (butyrate) production, immune modulation	Abouelela & Helmy (2024); Brown et al. (2019)
Lactobacillus plantarum	Reduces oxidative stress and improves cognitive health	Antioxidant activity, gut-brain axis modulation	Dinan & Cryan (2017); Kim et al. (2021)

Table 2. Comparative Overview of Probiotic, Prebiotic, and Postbiotic Functions

Type	Definition	Primary Benefits	Current Research Focus	Key Reference(s)
Probiotics	Live microorganisms conferring health benefits when consumed in adequate amounts	Gut health, immune modulation, metabolic regulation	Personalized, strain-specific probiotic formulations	Cunningham et al. (2021); Suez et al. (2018)
Prebiotics	Non-digestible food components that promote growth of beneficial bacteria	Supports probiotic activity, improves digestion and immunity	Synergistic effects with probiotics (synbiotics)	Heiman & Greenway (2016)
Postbiotics	Non-viable microbial products or metabolites with health-promoting properties	Safe, stable immunomodulation and anti-inflammatory effects		

mediate host behavior and stress responses, establishing a mechanistic link between microbial balance and mental health. Clinical trials further demonstrate that probiotic supplementation reduces cortisol levels and improves mood and cognition (Zhang et al., 2024).

These findings support the bidirectional communication framework of the gut–brain axis, wherein microbial metabolites and immune mediators influence neural signaling and psychological outcomes. This area remains a promising frontier for developing adjunctive therapies for anxiety, depression, and neurodegenerative conditions.

5.4 Metabolic and Postbiotic Advances

Beyond neural and immune regulation, probiotics demonstrate substantial metabolic benefits. As Depommier et al. (2019) reported, probiotics improve insulin sensitivity, lipid profiles, and weight regulation by enhancing SCFA production—particularly butyrate. These effects correspond with Belkaid and Hand's (2014) findings linking microbial metabolites to energy metabolism and systemic inflammation control.

Recent insights into *postbiotics*—bioactive microbial products such as peptides and polysaccharides—offer additional therapeutic promise. Abouelela and Helmy (2024) noted that postbiotics retain many benefits of live bacteria while offering greater stability and safety, especially in immunocompromised populations. This aligns with the shift toward next-generation and metabolite-driven therapies, integrating microbiology with precision medicine.

5.5 Limitations and Future Directions

Despite these promising findings, the literature reveals methodological inconsistencies, including small sample sizes, variable intervention durations, and inconsistent strain selection. These gaps hinder meta-analytical synthesis and reproducibility. Moreover, few studies have examined long-term sustainability of probiotic effects or the interplay between probiotics and dietary patterns.

Future research should emphasize multi-omics integration—combining metagenomics, transcriptomics, and metabolomics—to elucidate molecular pathways linking microbial dynamics to host physiology. Larger randomized controlled trials are also needed to define standardized biomarkers for mental, metabolic, and immune health outcomes. Additionally, personalized interventions based on individual microbiome profiling represent a crucial direction for optimizing probiotic efficacy.

6. Recommendations

The growing body of evidence highlights the significant therapeutic potential of probiotics and postbiotics in promoting human health through microbiome modulation. However, to optimize their effectiveness and ensure safe, evidence-based application, several key recommendations can be proposed for both research and clinical practice. Future studies should adopt standardized protocols regarding strain identification, dosage, treatment duration, and study population characteristics. Variability in these parameters currently hampers reproducibility and meta-analytical synthesis. Large-scale randomized controlled trials (RCTs) are needed to validate the efficacy and safety of specific strains such as *Akkermansia muciniphila* and *Faecalibacterium prausnitzii* in human subjects (Depommier et al., 2019). Standardized reporting will also enable clearer comparisons across studies and enhance regulatory confidence. Incorporating metagenomics, metabolomics, and transcriptomics into probiotic research can

deepen understanding of host–microbiome interactions (Cunningham et al., 2021). Artificial intelligence (AI) and machine learning should be employed to analyze complex datasets, identify predictive biomarkers, and design personalized probiotic therapies based on individual microbial signatures (Johnson et al., 2020). Given inter-individual variability in microbiome composition, future interventions should prioritize personalized approaches. Tailored probiotic and postbiotic formulations—adjusted according to diet, genetics, and lifestyle—can enhance therapeutic outcomes and minimize inefficacy (Zmora et al., 2018). Health policymakers and practitioners should promote evidence-based probiotic use, discouraging unverified commercial claims. Public education campaigns emphasizing diet diversity, fermented food intake, and the importance of gut health can further strengthen preventive healthcare efforts (Heiman & Greenway, 2016).

7. Conclusion

The review highlights the expanding role of probiotics and postbiotics as critical modulators of gut microbiota, immunity, metabolism, and mental health. Evidence indicates that specific strains such as *Akkermansia muciniphila* and *Lactobacillus rhamnosus* exert beneficial effects through immune regulation, gut barrier enhancement, and modulation of the gut–brain axis. These findings mark a paradigm shift from generalized probiotic use toward precision-based, strain-specific therapies. However, variability in outcomes underscores the need for standardized methodologies, larger clinical trials, and integration of multi-omics approaches to better understand host–microbiome dynamics. Personalized probiotic formulations guided by AI and microbiome profiling hold promise for improving therapeutic efficacy. Overall, probiotics and postbiotics represent an evolving frontier in preventive and therapeutic medicine, with strong potential to enhance human health through scientifically grounded and individualized microbial interventions.

Author contributions

T. A. conceptualized the study, designed the review framework, conducted the literature search, and drafted the initial manuscript. M.H.M. contributed to data interpretation, synthesis of mechanistic insights, and critical revision of the manuscript for intellectual content. P.S.M provided methodological guidance, validated the scientific accuracy of the review, and supported the refinement and final editing of the text. All authors read, reviewed, and approved the final version of the manuscript.

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Competing financial interests

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