Review Article

JHSMR Journal of Health Science and Medical Research

Harnessing Probiotics as a Nexus of Food Safety, Public Health, and Environmental Sustainability

Chinenyenwa M.D. Ohia, Ph.D.[1,2], Olutayo I. Falodun, Ph.D. [3], Chinyere C. Ezemba, Ph.D.[4]

[1]Department of Environmental Health Sciences, Faculty of Public Health, College of Medicine, University of Ibadan, Queen Elizabeth II Road, Agodi 200285, Ibadan, Oyo State 200284, Nigeria.

[2]Nanobios Lab, Department of Biosciences and Bioengineering, Indian Institute of Technology (IIT), Bombay, 400076, India.

[3]Department of Microbiology, University of Ibadan, Ibadan, Oyo State 200284, Nigeria.

[4]Chychy Gilgal Laboratory and Consulting Services Ichida, Anambra State 422012, Nigeria.

Received 22 September 2025 ● Revised 5 November 2025 ● Accepted 17 November 2025 ● Published online 10 July 2026

Abstract:

Probiotics, defined as live microorganisms, provide health advantages when ingested in sufficient quantities. They have progressed from Élie Metchnikoff's early hypothesis of lactic acid bacteria promoting longevity to a scientifically grounded field spanning clinical, nutritional, and environmental domains. Traditionally associated with *Lactobacillus*, *Bifidobacterium,* probiotics now include strains of *Bacillus*, *Pediococcus,* and *Saccharomyces boulardii*, expanding their functional repertoire. Contemporary evidence highlights their roles not only in maintaining gastrointestinal balance but also in allergy management, metabolic regulation, skin health, and modulation of the gut–brain axis. These benefits are mediated through immune modulation, enhancement of intestinal barrier function, and support of microbial diversity. Despite this progress, several challenges remain unresolved, including strain-specific variability, inconsistent efficacy across populations, and safety considerations in vulnerable groups. Additionally, fragmented global regulatory frameworks limit standardization of claims, labeling, and clinical adoption, while the ecological implications and sustainability of large-scale probiotic production are emerging concerns. This review provides a structured synthesis of probiotics in four domains: natural and engineered sources, mechanisms of action, contributions to human health, and broader implications for food safety, public health, and environmental sustainability. Integrating classical insights with recent advances highlights the promise of probiotics as broad-spectrum tools for preventive and therapeutic health. Looking forward, developments in microbiome science, bioengineering, and personalized nutrition offer opportunities to refine probiotic applications. Systematic attention to regulatory harmonization, safety, and sustainability will be critical to unlocking their full potential as cornerstones of modern health strategies.

Contact: Chinenyenwa M.D. Ohia, Ph.D.
Department of Environmental Health Sciences, Faculty of Public Health, College of Medicine, University of Ibadan, Queen Elizabeth II Road, Agodi 200285, Ibadan, Oyo State, 200284, Nigeria.
E-mail: ohiacmd@gmail.com

J Health Sci Med Res
doi: 10.31584/jhsmr.20261394
www.jhsmr.org

Keywords: Environmental sustainability, food safety, One Health, probiotics, public health

Introduction

Probiotics, often described as "friendly bacteria," are live microorganisms that, when administered in adequate amounts, confer measurable health benefits to the host[1–4]. Traditionally, the most widely studied probiotic genera include *Lactobacillus* and *Bifidobacterium*, but in recent decades, other microbes such as specific strains of *Bacillus*, *Pediococcus*, and the yeast *Saccharomyces boulardii* have also been recognized for their functional properties[1,5–7]. The concept of probiotics has a rich historical foundation, tracing back to Élie Metchnikoff's early 20th-century hypothesis that consumption of lactic acid bacteria (LAB) could promote longevity by modulating intestinal health. This early insight has since expanded into a comprehensive scientific understanding of probiotics as key modulators of the gut microbiota, immune responses, and systemic health outcomes.

Today, probiotics are not only integrated into clinical practice for preventing and managing gastrointestinal disorders, but they are also widely consumed as dietary supplements and functional foods. Their applications extend beyond digestive health to include roles in allergy management, metabolic regulation, mental health through the gut–brain axis, and even skin health[3,8,9].

However, despite this growing body of evidence and commercial popularity, significant knowledge gaps persist. Questions remain about the consistency of probiotic efficacy across different populations, optimal dosing strategies, safety in vulnerable groups, such as infants, the elderly, and immunocompromised individuals, and the lack of harmonized global regulatory frameworks. Additionally, the contribution of probiotics to sustainable food systems and environmental health is an emerging area of inquiry, particularly as society seeks eco-friendly solutions to health and nutrition challenges.

As a result of this gap, this review provides a structured exploration of probiotics in four domains: (1) their natural and engineered sources, (2) their mechanisms of action in host systems, (3) their contributions to human well-being across different health dimensions, and (4) their broader implications for food safety, public health, and environmental sustainability. By integrating both classical perspectives and contemporary research findings, this review aimed to clarify the evolving role of probiotics and highlight future directions for research, regulation, and practical application.

Probiotics sources and relevance

Probiotics are derived from a variety of natural and industrial sources, with fermented foods serving as one of the most traditional and widely recognized reservoirs. Common examples include yogurt, kefir, sauerkraut, kimchi, miso, and certain types of cheeses, all of which provide a diverse range of beneficial microorganisms that have co-evolved with human dietary practices for centuries. These foods are not only culturally significant across different regions of the world but also serve as accessible vehicles for delivering viable probiotic strains in everyday diets[7]. Beyond naturally fermented products, probiotics are deliberately incorporated into dietary supplements in the form of capsules, powders, sachets, and tablets (Table 1), offering consumers standardized doses and targeted microbial formulations. They are also increasingly embedded into functional foods and beverages such as probiotic-fortified milk, juices, snack bars, and even infant formulas, reflecting the growing demand for convenient, health-promoting products.

From a safety perspective, most probiotic strains have been evaluated and classified as *Generally Recognized as Safe* (GRAS) by regulatory agencies, including the

Table 1 Natural and commercial sources of probiotics

Source	Microorganisms involved	Type	Health relevance
Human Colostrum	*Lactobacillus, Bifidobacterium*	Natural	Infant gut colonization, immune development
Yogurt	*Lactobacillus, Streptococcus*	Natural/commercial	Gut health, lactose digestion
Kefir	Lactic acid bacteria+Yeasts	Natural	Antimicrobial, immune modulation
Sauerkraut & Kimchi	*Leuconostoc, Lactobacillus*	Natural	Digestive health, antioxidant effects
Miso & Tempeh	*Bacillus subtilis* (Tempeh)	Natural	Protein-rich, gut health
Pickles (fermented)	Various LAB	Natural	Digestive support, microbiome balance
Supplements	*Lactobacillus, Bifidobacterium*, etc.	Commercial	Specific strain-targeted effects
Fortified foods/beverages	Strain-specific probiotics	Functional food	Custom-formulated for health outcomes

U.S. Food and Drug Administration and the European Food Safety Authority, based on long-standing human consumption and rigorous toxicological assessments[10-11] (Table 1). This designation underscores their reliability for general use, although careful strain-specific evaluations remain important, particularly for vulnerable populations such as infants, the elderly, and immunocompromised individuals.

The relevance of probiotics lies primarily in their role in supporting balanced intestinal microbiota. A well-regulated microbial community within the gut contributes to efficient digestion, nutrient absorption, and resistance to pathogenic invasion. Moreover, emerging evidence highlights that probiotics exert systemic benefits beyond the gastrointestinal tract, influencing metabolic health, immune system regulation, and even neurobehavioral outcomes through the gut–brain axis[12-13]. Regular consumption of probiotic-rich foods or supplements, therefore, promotes not only digestive health but also broader physiological stability, positioning probiotics as key agents in preventive nutrition and integrative medicine.

Mechanisms of action and benefits

Probiotics exert their health-promoting effects through multiple, interrelated mechanisms that act at the molecular, cellular, and systemic levels[14-18]. These mechanisms not only influence gastrointestinal stability (Table 2) but also extend to metabolic, immunological, and neurological functionS[19-26]. The major pathways include the following:

Pathogen inhibition: One of the primary roles of probiotics is their antagonistic activity against pathogenic microorganisms. Probiotic strains compete with pathogens for essential nutrients and adhesion sites along the intestinal epithelium, thereby limiting pathogen colonization and biofilm formation[27]. In addition, many strains secrete antimicrobial substances such as organic acids (lactic and acetic acids), hydrogen peroxide, and bacteriocins, which lower gut pH and create an unfavorable environment for harmful microbes[28]. By disrupting the ecological niches of pathogens like *Clostridium difficile*, *Escherichia coli*, and *Salmonella*, probiotics contribute to infection prevention and restoration of microbiota balance following antibiotic treatment.

Immune modulation: Probiotics interact closely with the host's immune system, influencing both innate and adaptive responses. They can enhance macrophage activity, stimulate natural killer (NK) cells, and regulate dendritic cell signaling, which collectively improve the body's ability to detect and eliminate harmful agents. On the adaptive

Table 2 Mechanism of action and related health outcomes of probiotics use

Mechanism	Health Benefit	Examples	References
Microbial balance restoration	Management of irritable bowel syndrome (IBS), antibiotic-associated diarrhea, restoration of balance disrupted by diet, stress, or antibiotics	*L. rhamnosus* GG	19
Pathogen inhibition	Effectively competes with pathogens for nutrients/space and adhesion sites	*L. plantarum* vs. E. coli	20
Gut barrier enhancement	Prevents translocation of pathogens, digestive health	*L. casei* CRL 431	19
Immunomodulation	Increased antibody e.g. cytokine production (IL-6, IL-10), immune cells activation, balanced immune system	*L. paracasei* CNCM I-1518	21, 22
Modulation of gut-brain axis	Reduction in anxiety, stress and depression, influences mental health well being	Multistrain probiotics in trials	23
Lactose digestion enhancement	Lactose intolerance relief, nutrient adsorption, possible weight management, metabolic health	*L. acidophilus* LBKV-3	24
Inflammatory response regulation	Reduced allergic reactions, acne, eczema, overall skin health	Fermented milk blends	25
Phagocytic activity stimulation	Boosted innate immune response	*B. lactis* HN019	26

side, probiotics influence the production of immunoglobulin A (IgA) and modulate cytokine profiles by promoting anti-inflammatory cytokines (e.g., IL-10) while reducing pro-inflammatory mediators (e.g., TNF-α, IL-6). Furthermore, certain strains enhance the function of regulatory T-cells (Tregs), maintaining immune tolerance and preventing overactive immune responses that contribute to allergies and autoimmune disorders[29-31].

Gut barrier reinforcement: The intestinal epithelial barrier is crucial for preventing the translocation of toxins, allergens, and pathogenic microbes into systemic circulation. Some probiotic strains strengthen this barrier by upregulating tight junction proteins such as occludin and claudin, thereby reducing intestinal permeability ("leaky gut"). This fortification minimizes local inflammation and systemic endotoxemia, which are linked to chronic conditions like inflammatory bowel disease (IBD) and metabolic syndrome. Additionally, probiotics can stimulate mucus production and enhance the secretion of antimicrobial peptides from epithelial cells, further fortifying host defenses[32-33].

Metabolic and neurological effects: Beyond local gut effects, probiotics influence host metabolism and neurobiology. They contribute to lipid metabolism by modulating bile salt hydrolase activity, which affects cholesterol reabsorption, and they enhance glucose regulation by improving insulin sensitivity and influencing short-chain fatty acid (SCFA) production, especially butyrate. SCFAs also serve as signaling molecules that regulate energy balance and inflammation[34]. Importantly, probiotics communicate with the central nervous system via the gut–brain axis. Through mechanisms involving vagus nerve signaling, modulation of neurotransmitters (e.g., serotonin, GABA), and regulation of systemic inflammation, certain strains have shown potential in alleviating symptoms of anxiety, depression, and cognitive decline[35-36]. These findings open new frontiers in psychobiotics (probiotics specifically studied for mental health benefits).

It is important to emphasize that these effects are strain-specific, meaning that not all probiotics exhibit the same biological actions. Outcomes also vary widely across individuals depending on host genetics, age, diet, lifestyle, and the baseline composition of the gut microbiome. This variability underscores the importance of precision in probiotic research and the need for personalized approaches to maximize health benefits.

Probiotics and human well-being

The beneficial effects of probiotics extend far beyond the gastrointestinal tract, influencing diverse aspects of human health. Their contributions are increasingly supported by experimental evidence, clinical trials, and meta-analyses, though many of these outcomes are strain-specific and context-dependent. The following domains highlight areas where probiotics have demonstrated relevance for human well-being.

Gastrointestinal health: Probiotics are most strongly associated with gastrointestinal (GI) health, where their efficacy is well documented in both prevention and treatment. Clinical evidence supports their role in reducing the incidence and severity of antibiotic-associated diarrhea (AAD), as well as in managing irritable bowel syndrome (IBS) and IBD, including Crohn's disease and ulcerative colitis. For instance, *Lactobacillus rhamnosus* GG has demonstrated effectiveness in lowering the risk of *Clostridium difficile*-associated diarrhea, a serious complication of antibiotic therapy[37]. Probiotics can also help restore microbiota balance following antibiotic disruption, reduce bloating and abdominal discomfort in IBS patients, and modulate inflammatory pathways implicated in chronic bowel disorders.

Metabolic disorders: Beyond digestive health, probiotics influence metabolic processes linked to obesity, type 2 diabetes, and cardiovascular diseases[38-39]. Research indicates that probiotics may improve insulin sensitivity, modulate glucose metabolism, and positively affect lipid profiles by lowering serum cholesterol and triglyceride levels[40]. These benefits are often mediated through short-chain fatty acid (SCFA) production, bile salt metabolism, and reduced systemic inflammation. However, the findings remain heterogeneous across clinical trials, with several meta-analyses pointing to strain-specific efficacy rather than universal benefits across all probiotics[41]. This suggests that targeted use of specific strains, rather than broad supplementation, may be necessary to optimize metabolic outcomes.

Lactose intolerance: Another well-established area of probiotic benefit lies in the management of lactose intolerance. Strains such as *Lactobacillus acidophilus* and *Bifidobacterium longum* improve lactose digestion by producing β-galactosidase (lactase) enzymes or by enhancing residual lactase activity in the gut[42-45]. This enzymatic activity reduces gastrointestinal symptoms such as bloating, cramping, and diarrhea after lactose ingestion[46]. The incorporation of probiotic cultures into fermented dairy products, such as yogurt, not only enhances palatability but also provides a natural therapeutic option for individuals with lactose malabsorption.

Allergies and immune responses: Probiotics play an important role in modulating allergic and immune responses. Several studies report that probiotic supplementation can reduce serum immunoglobulin E (IgE) levels, alleviate symptoms of allergic rhinitis, and contribute to the prevention of atopic dermatitis (eczema) in infants[17,30,31,47-48]. For example, maternal and infant supplementation with certain *Lactobacillus* and *Bifidobacterium* strains has been associated with a lower incidence of eczema in early childhood[49]. Nevertheless, outcomes vary widely depending on the timing of administration, strain selection, and host factors, indicating the need for precision-based approaches in allergy prevention and management.

Mental health and the gut–brain axis: One of the most rapidly emerging areas of probiotic research relates to their influence on mental health via the gut–brain axis. Probiotics, sometimes termed "psychobiotics" when used for this purpose, can modulate neurotransmitter signaling, regulate systemic inflammation, and influence the hypothalamic–pituitary–adrenal (HPA) axis. Studies suggest that certain strains may reduce symptoms of anxiety and depression, improve stress resilience, and enhance aspects of cognitive performance[35-36]. Proposed mechanisms include increased production of gamma-aminobutyric acid (GABA), serotonin modulation, and vagus nerve activation. While early findings are promising, the evidence base is still developing, and larger, more robust clinical trials are required to establish causality and long-term safety.

Other emerging areas: In addition to the above, research is beginning to explore the role of probiotics in oral health (e.g., reducing dental caries and periodontal disease), dermatological conditions such as acne and psoriasis, and even cancer prevention through modulation of gut microbiota and immune pathways. These emerging applications reflect the expanding recognition of probiotics as multifunctional agents that contribute to systemic well-being beyond traditional gastrointestinal contexts.

Side effects associated with probiotics

Probiotics are largely regarded as being safe for a healthy population. However, individuals with underlying medical conditions, including systemic infections, deleterious metabolic activities, excessive immune stimulation, and gene transfer, are highly sensitive to the intake of probiotics. The interactions that occur between the microbes in the intestine impact and influence the overall health condition of the host. Adverse effects due to the consumption of probiotics have been well reported. Thus, a good understanding of the characteristics of the relationships between probiotic structure and function would help reduce any possible side effects. Hence, it is imperative to have a full understanding of the mechanisms of activity of probiotic bacteria. Some of the risks associated with the unrestricted dietary intake of probiotics include: Probiotic sepsis, allergic rhinitis and more serious asthma, wheezing bronchitis, intra-abdominal abscess, and atopic sensitization, among others[50-51].

Probiotics as consumer products: opportunities and challenges

There are significant opportunities for the market growth of probiotics due to rising health awareness and demand for functional foods[52-55]. Understanding the lifecycle of probiotics as consumer products is essential for evaluating their broader implications for food safety, public health, and environmental sustainability. Figure 1 provides a visual representation of the key stages in the development, utilization, and post-consumption fate of probiotics. Each phase is interconnected, with critical feedback mechanisms that inform future product innovation, sustainability practices, and policy frameworks. This systems-oriented progression perspective highlights the relevance of circular economy principles in optimizing the lifecycle of probiotics for safer, more sustainable, and health-promoting applications across human and environmental domains.

Challenges and limitations

While the benefits of probiotics are widely documented, challenges in their use include:

Strain-specific efficacy: Not all strains within a genus exert health effects, and outcomes cannot be generalized[29].

Viability and stability: Many probiotics do not survive gastric acidity or bile salts, limiting their efficacy[7].

Safety concerns: In immunocompromised individuals, probiotics can, on rare occasions, cause infections or transfer antibiotic resistance genes.

Variability in host response: Age, microbiota composition, and diet influence outcomes, complicating clinical standardization.

Other significant barriers to market entry, especially in low- and middle-income countries, include:

Regulatory frameworks: Regulatory oversight varies significantly across regions, reflecting the diversity of standards applied to these products[56-58]. In the EU, probiotics are regulated as "novel foods" and must demonstrate safety and efficacy before approval, while in the U.S., they are often marketed as dietary supplements with less stringent pre-market requirements[59]. In addition, limited resources and capacity for regulatory oversight

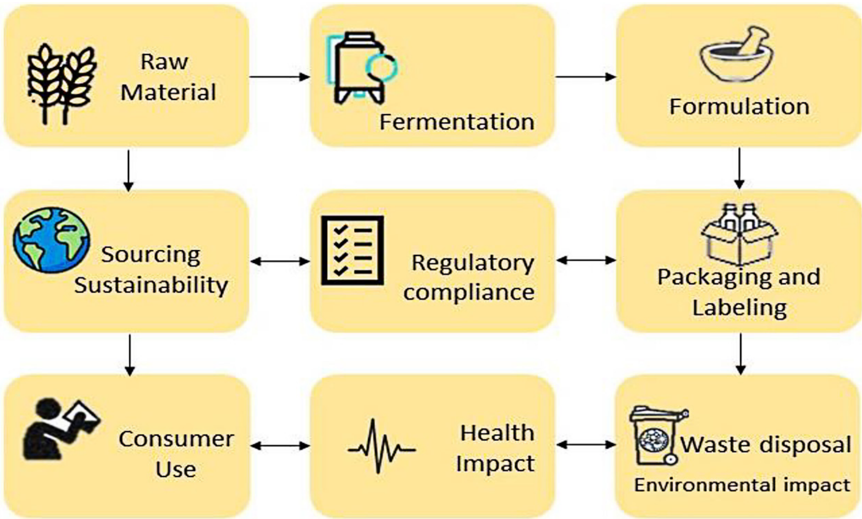

Figure 1 Lifecycle of probiotic products from raw materials to environmental impact

and enforcement across countries hinder the effective regulation of probiotics[52]. Standardizing these regulations has the potential to enhance product quality, which is critical to ensure efficacy and consumer trust.

Labelling: Accurate labeling provides essential information to consumers, supporting informed choices and safe use[60–61]. The labelling of probiotics is essential for ensuring consumer awareness and safety. Key requirements across different countries include details such as the genus, species, strain, and Colony-Forming Units (CFUs) at the product's shelf-life endpoint. Also, health claims must be accompanied by a disclaimer[62], strain-specific quantities, and storage conditions[63]. The regulation and labelling of probiotics have far-reaching implications for food safety, public health, and environmental health (Table 3). As probiotics become more prevalent in the markets, understanding these implications is crucial for policymakers, manufacturers, and consumers.

Probiotics at the node of food safety, public health, and environmental sustainability

Probiotics occupy a pivotal role at the intersection of food safety, human well-being, public health, and environmental sustainability. As illustrated in Figure 2, probiotics are not merely functional food components; they also serve as integrative agents linking microbiological safety, nutritional quality, health promotion, and ecological impact. Their production, regulation, and use are influenced by factors such as food system hygiene, disease prevention, gut microbiome balance, and waste management practices.

Food safety

Live microorganisms require strict safety monitoring to prevent contamination and ensure product consistency[64–66]. Mislabeling or adulteration can lead to ineffective or harmful products, especially in low- and middle-income countries with weak regulatory oversight[67–68]. A Robust regulatory framework is essential for consumer protection, informed use, and accessibility[64–66,69].

Public health

Probiotics hold promise for reducing global health burdens such as diarrheal diseases, antibiotic resistance, and noncommunicable diseases. Safe production, inclusion

Table 3 Regulatory requirements for probiotics and implications for safety and health

Aspect	Description/requirements	Implication
Regulatory oversight	Varies globally; weak in LMICs	Leads to market infiltration of substandard products
Labeling requirements	Genus, species, strain, CFU, shelf life, health claims	Informs consumer choice, builds trust
Health claims	Must be evidence-based in regulated countries	Prevents misinformation
Risk communication	Storage conditions, dosage, contraindications	Enhances safe use
Environmental standards	Waste management, biodegradability of packaging	Reduces environmental burden

LMICs=low middle-income countries, CFUs=colony-forming units

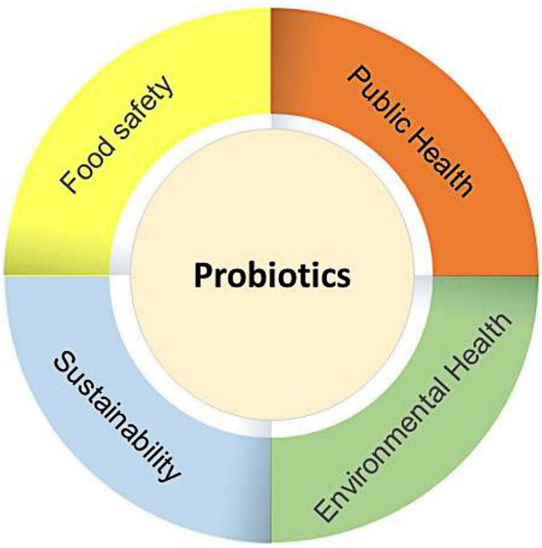

Figure 2 Circular One-Health framework of probiotics, its use and impacts

of verified benefits, and clear labeling, backed by regulation, all positively impact public health[57,64–66]. Furthermore, sound scientific evidence is required to support health claims, ensuring consumers receive accurate information and limiting exaggerated health promotion and marketing claims[57,64].

Environmental health and sustainability: The lifecycle of probiotics—from production to disposal—can impact ecosystems. The environmental footprint encompasses raw material use, energy demand, and waste disposal. Encouraging sustainable practices, such as eco-friendly fermentation, energy-efficient production processes, and proper waste management, can reduce the risks of microbial contamination or antimicrobial resistance spread in ecosystems and contribute to overall environmental health[65–66,70–71]. Regulations should promote sustainable practices, especially proper disposal of expired or contaminated probiotics, to reduce environmental contamination, antimicrobial resistance, and ecosystem disruption[57,65,72–73].

Conclusion

Probiotics represent a broad-spectrum tool for enhancing human health, with applications that extend far beyond traditional gastrointestinal benefits. Their roles in maintaining digestive balance, supporting metabolic regulation, mitigating allergic responses, and even influencing mental well-being through the gut–brain axis underscore their potential as integral components of preventive and therapeutic healthcare. By contributing to immune modulation, reinforcing the intestinal barrier, and promoting microbial diversity, probiotics serve as important allies in both clinical practice and everyday nutrition.

However, several critical challenges remain unresolved. Inconsistent global regulations make it difficult to standardize claims, labeling, and safety requirements, thereby limiting consumer trust and clinical adoption. Strain-specific variability also complicates both research and practice, as benefits cannot be generalized across all probiotics, necessitating precise identification and targeted application. Additionally, issues surrounding the sustainability of large-scale probiotic production and the ecological implications of their use are emerging concerns that warrant greater attention.

Looking ahead, advances in microbiome science, next-generation sequencing, and bioengineering offer promising opportunities to refine probiotic development and delivery. The future of probiotics may lie in personalized approaches, where formulations are tailored to individual genetic, dietary, and microbiome profiles, thereby maximizing efficacy and minimizing risks. For probiotics to realize their full potential as a cornerstone of modern health strategies, these scientific, regulatory, and sustainability challenges must be systematically addressed through rigorous research, policy harmonization, and innovation in product design.

References

1. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document: the international scientific association for probiotics and prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol 2014;11:506–14.
2. Gaggìa F, Baffoni L, Alberoni D. Probiotics for honeybees' health. In: Gioia DD, Biavati B, editors. Probiotics and prebiotics in animal health and food safety. Cham: Springer International Publishing; 2017;p.219-45.
3. George F, Daniel C, Thomas M, Singer E, Guilbaud A, Tessier FJ, Revol-Junelles AM, Borges F, Foligné B. Occurrence and dynamism of lactic acid bacteria in distinct ecological niches: a multifaceted functional health perspective. Front Microbiol 2018;9:2899.
4. Damián MR, Cortes-Perez NG, Quintana ET, Ortiz-Moreno A, Garfias Noguez C, Cruceño-Casarrubias CE, et al. Functional foods, nutraceuticals and probiotics: a focus on human health. Microorganisms 2022;10:1065.
5. Roy S, Dhaneshwar S. Role of prebiotics, probiotics, and synbiotics in management of inflammatory bowel disease: current perspectives. World J Gastroenterol 2023;29:2078.
6. Sanders ME. Probiotics: definition, sources, selection, and uses. Clin Infect Dis 2008;46(Suppl 2):S58–61.
7. Marco ML, Sanders ME, Gänzle M, Arrieta MC, Cotter PD, De Vuyst L, et al. The international scientific association for Probiotics and Prebiotics (ISAPP) consensus statement on fermented foods. Nat Rev Gastroenterol Hepatol 2021;18:196-208.
8. Mishra P, Mishra SK. Role of microbial flora and probiotics in host immune homeostasis. J Appl Pharm Sci 2018;8:136–49.
9. Kerry RG, Patra JK, Gouda S, Park Y, Shin HS, Das G. Benefaction of probiotics for human health: a review. J Food Drug Anal 2018;26:927–39.
10. Arshad FA, Mehmood R, Hussain S, Khan MA, Khan MS. Lactobacilli as probiotics and their isolation from different sources. Br J Res 2018;5:43.
11. Food and Agriculture Organization of the United Nations (FAO), & World Health Organization (WHO) 2001. Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria. [Monographon the Internet]. Rome: FAO/WHO Secretariat; 2001 [cited 2025 Jul 29]. Available from: https://www.fao.org/3/y6398e/y6398e.pdf
12. Zhang C, Derrien M, Levenez F, Brazeilles R, Ballal SA, Kim J, et al. Ecological robustness of the gut microbiota in response to ingestion of transient food-borne microbes. ISME J 2016;10:2235-45.
13. Sarkar A, Lehto SM, Harty S, Dinan TG, Cryan JF, Burnet PW. Psychobiotics and the manipulation of bacteria–gut–brain signals. Trends Neurosci 2016;39:763-81.
14. Hemaiswarya S, Raja R, Ravikumar R, Carvalho IS. Mechanism of action of probiotics. Braz Arch Biol Technol 2013; 56:113–9.
15. Kleerebezem M, Binda S, Bron PA, Gross G, Hill C, van Hylckama Vlieg JE, et al. Understanding mode of action can drive the translational pipeline towards more reliable health benefits for probiotics. Curr Opin Biotechnol 2019;56:55–60.
16. Plaza-Diaz J, Ruiz-Ojeda FJ, Gil-Campos M, Gil A. Mechanisms of action of probiotics. Adv Nutr 2019;10(Suppl 1):S49–66.
17. Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics mechanism of action on immune cells and beneficial

effects on human health. Cells 2023;12:184. doi: 10.3390/cells12010184.

18. Gopalakrishnan V, Helmink BA, Spencer CN, Reuben A, Wargo JA. The influence of the gut microbiome on cancer, immunity, and cancer immunotherapy. Cancer Cell 2018;33:570–80.
19. Mörbe UM, Jørgensen PB, Fenton TM, von Burg N, Riis LB, Spencer J, et al. Human gut-associated lymphoid tissues (GALT); diversity, structure, and function. Mucosal Immunol 2021;14:793–802.
20. Mokoena MP. Lactic acid bacteria and their bacteriocins: classification, biosynthesis and applications against uropathogens: a mini-review. Molecules 2017;22:1255.
21. Fakharian F, Asgari B, Nabavi-Rad A, Sadeghi A, Soleimani N, Yadegar A, et al. The interplay between Helicobacter pylori and the gut microbiota: an emerging driver influencing the immune system homeostasis and gastric carcinogenesis. Front Cell Infect Microbiol 2022;12:953718.
22. Al-Qadami GH, Secombe KR, Subramaniam CB, Wardill HR, Bowen JM. Gut microbiota-derived short-chain fatty acids: impact on cancer treatment response and toxicities. Microorganisms 2022;10:2048.
23. Kober AH, Riaz Rajoka MS, Mehwish HM, Villena J, Kitazawa H. Immunomodulation potential of probiotics: a novel strategy for improving livestock health, immunity, and productivity. Microorganisms 2022;10:388.
24. Minj J, Chandra P, Paul C, Sharma RK. Bio-functional properties of probiotic Lactobacillus: current applications and research perspectives. Crit Rev Food Sci Nutr 2021;61:2207–24.
25. Cristofori F, Dargenio VN, Dargenio C, Miniello VL, Barone M, Francavilla R. Anti-inflammatory and immunomodulatory effects of probiotics in gut inflammation: a door to the body. Front Immunol 2021;12:578386.
26. Simón R, Docando F, Nuñez-Ortiz N, Tafalla C, Díaz-Rosales P. Mechanisms used by probiotics to confer pathogen resistance to teleost fish. Front Immunol 2021;12:653025.
27. Wilson KH, Perini F. Role of competition for nutrients in suppression of *Clostridium difficile* by the colonic microflora. Infect Immun 1988;56:2610–4.
28. de Almada CN, Almada CN, Martinez RC, Sant'Ana AS. Paraprobiotics: Evidences on their ability to modify biological responses, inactivation methods and perspectives on their application in foods. Trends Food Sci Technol 2016;58:96-114.
29. Ouwehand AC, Salminen S, Isolauri E. Probiotics: an overview of beneficial effects. Antonie Van Leeuwenhoek 2002;82:279-89.
30. Eslami M, Bahar A, Keikha M, Karbalaei M, Kobyliak NM, Yousefi B. Probiotics function and modulation of the immune system in allergic diseases. Allergol Immunopathol (Madr) 2020;48:771–88.
31. Prakash S, Nicoletti C, McAleer JP, Su H, Huang J, Zhang J, et al. Effect of probiotics on respiratory tract allergic disease and gut microbiota. Front Nutr 2022;9:821900.
32. Bron PA, Kleerebezem M, Brummer RJ, Cani PD, Mercenier A, MacDonald TT, et al. Can probiotics modulate human disease by impacting intestinal barrier function? Br J Nutr 2017;117:93-107.
33. Galdeano CM, Perdigón G. Role of viability of probiotic strains in their persistence in the gut and in mucosal immune stimulation. J Appl Microbiol 2004;97:673–81.
34. Chambers ES, Preston T, Frost G, Morrison DJ. Role of gut microbiota-generated short-chain fatty acids in metabolic and cardiovascular health. Curr Nutr Rep 2018;7:198-206.
35. Ng QX, Peters C, Ho CY, Lim DY, Yeo WS. A meta-analysis of the use of probiotics to alleviate depressive symptoms. J Affect Disord 2018;228:13-9.
36. Kim CS, Cha J, Sim M, Jung S, Chun WY, Baik HW, Shin DM. Probiotic supplementation improves cognitive function and mood with changes in gut microbiota in community-dwelling older adults: a randomized, double-blind, placebo-controlled, multicenter trial. J Gerontol A Biol Sci Med Sci 2021;76:32-40.
37. Goldenberg JZ, Yap C, Lytvyn L, Lo CK, Beardsley J, Mertz D, et al. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children. Cochrane Database Syst Rev 2017:CD006095. doi: 10.1002/14651858.CD006095.pub4.
38. Everard A, Belzer C, Geurts L, Ouwerkerk JP, Druart C, Bindels LB, Guiot Y, Derrien M, Muccioli GG, Delzenne NM, De Vos WM. Cross-talk between Akkermansia muciniphila and intestinal epithelium controls diet-induced obesity. Proc Natl Acad Sci USA 2013;110:9066-71.
39. Oudat Q, Okour A. The role of probiotics in modulating gut microbiota and metabolic health for weight management: a mini review. Acta Microbiologica Hellenica 2025;70:5. doi: 10.3390/amh70010005.

40. Mendes MCS, Paulino DS, Brambilla SR, Camargo JA, Persinoti GF, Carvalheira JBC. Microbiota modification by probiotic supplementation reduces colitis-associated colon cancer in mice. World J Gastroenterol 2018;24:1995–2008.
41. Tao YW, Gu YL, Mao XQ, Zhang L, Pei YF. Effects of probiotics on type II diabetes mellitus: a meta-analysis. J Transl Med 2020;18:30.
42. Urbańska M, Szajewska H. The efficacy of *Lactobacillus reuteri* DSM 17938 in infants and children: a review of the current evidence. Eur J Pediatr 2014;173:1327–37.
43. Urbańska M, Gieruszczak-Białek D, Szajewska H. Systematic review with meta-analysis: *Lactobacillus reuteri* DSM 17938 for diarrhoeal diseases in children. Aliment Pharmacol Ther 2016;43:1025–34.
44. Azcarate-Peril MA, Ritter AJ, Savaiano D, Monteagudo-Mera A, Anderson C, Magness ST, et al. Impact of short-chain galactooligosaccharides on the gut microbiome of lactose-intolerant individuals. Proc Natl Acad Sci USA 2017;114:e367–75.
45. Zhang GQ, Hu HJ, Liu CY, Zhang Q, Shakya S, Li ZY. Probiotics for prevention of atopy and food hypersensitivity in early childhood: a PRISMA-compliant systematic review and meta-analysis of randomized controlled trials. Medicine 2016;95:e2562.
46. He T, Priebe MG, Zhong Y, Huang C, Harmsen HJ, Raangs GC, Antoine JM, Welling GW, Vonk RJ. Effects of yogurt and bifidobacteria supplementation on the colonic microbiota in lactose-intolerant subjects. J Appl Microbiol 2008;104:595-604.
47. Olsen R, Greisen G, Schrøder M, Brok J. Prophylactic probiotics for preterm infants: a systematic review and meta-analysis of observational studies. Neonatology 2016;109:105–12.
48. Klein A, Friedrich U, Vogelsang H, Jahreis G. *Lactobacillus acidophilus* 742 and *Bifidobacterium animalis* subsp. *lactis* DGCC 420 modulate unspecific cellular immune response in healthy adults. Eur J Clin Nutr 2008;62:584–93.
49. Cuello-Garcia CA, Brożek JL, Fiocchi A, Pawankar R, Yepes-Nuñez JJ, Terracciano L, et al. Probiotics for the prevention of allergy: a systematic review and meta-analysis of randomized controlled trials. J Allergy Clin Immunol 2015;136:952-61. doi: 10.1016/j.jaci.2015.04.031
50. Zawistowska-Rojek A, Tyski S. Are probiotic really safe for humans? Pol J Microbiol 2018;67:251-8.
51. Gul S, Durante-Mangoni E. Unraveling the puzzle: health benefits of probiotics—a comprehensive review. J Clin Med 2024;13:1436. doi: 10.3390/jcm13051436.
52. Abesinghe AMNL, Priyashantha H, Prasanna PHP, Kurukulasuriya MS, Ranadheera CS, Vidanarachchi JK. Inclusion of probiotics into fermented buffalo (*Bubalus bubalis*) milk: an overview of challenges and opportunities. Fermentation 2020;6:121.
53. Westerik N, Kort R, Sybesma W, Reid G. *Lactobacillus rhamnosus* probiotic food as a tool for empowerment across the value chain in Africa. Front Microbiol 2018;9:1501.
54. Mokoena MP, Mutanda T, Olaniran AO. Perspectives on the probiotic potential of lactic acid bacteria from African traditional fermented foods and beverages. Food Nutr Res 2016;60:29630.
55. Setta MC, Matemu A, Mbega ER. Potential of probiotics from fermented cereal-based beverages in improving health of poor people in Africa. J Food Sci Technol 2020;57:3935–46.
56. Sanders ME, Levy DD. The science and regulations of probiotic food and supplement product labeling. Ann N Y Acad Sci 2011;1219:E1–23.
57. Hoffmann DE, Fraser CM, Palumbo F, Ravel J, Rowthorn V, Schwartz J. Probiotics: achieving a better regulatory fit. Food Drug Law J 2014;69:237.
58. Arora M, Baldi A. Regulatory categories of probiotics across the globe: a review representing existing and recommended categorization. Indian J Med Microbiol 2015;33(Suppl):S2–10.
59. Sanders ME, Merenstein DJ, Ouwehand AC, Reid G, Salminen S, Cabana MD, Paraskevakos G, Leyer G. Probiotic use in at-risk populations. J Am Pharm Assoc 2016;56:680-6. doi: 10.1016/j.japh.2016.07.001.
60. Kaur S, Kaur R, Rani N, Sharma S, Joshi M. Sources and selection criteria of probiotics. In: Advances in Probiotics for Sustainable Food and Medicine. Singapore: Springer; 2021. p.27–43.
61. Singh S, Gupta R, Chawla S, Gauba P, Singh M, Tiwari RK, et al. Natural sources and encapsulating materials for probiotics delivery systems: recent applications and challenges in functional food development. Front Nutr 2022;9:971784.
62. Food and Drug Administration (FDA). [homepage on the Internet]. Guidance for industry: evidence-based review system for the scientific evaluation of health claims. Silver Spring, MD:

FDA; 2020. [cited 2025 Jul 29]. Available from: https://www.fda.gov/media/71986/download

63. European Food Safety Authority (EFSA). Scientific and technical guidance for the preparation and presentation of the notification and application for authorisation of a health claim. EFSA J 2020;18:e05938.
64. Arora M, Kaur N, Arora M, Bansal P. Critical review on food safety standard regulations: a real scrutinizing authority or a misleading player for probiotic products. Appl Clin Res Clin Trials Regul Aff 2019;6:71–85.
65. Fukushima Y, Iino H. Probiotics in food safety and human health: current status of regulations on the use of probiotics in foods in Japan. In: Goktepe I, Juneja VK, Ahmedna M, editors. Probiotics in food safety and human health. CRC Press USA; 2006;p.431–59.
66. Chugh P, Misra S, Dhar MS, Raghuwanshi S. Regulatory aspects relevant to probiotic products. In: Dadar M, Mojgani N, editors. Probiotics, prebiotics, synbiotics, and postbiotics: human microbiome and human health. Singapore: Springer Nature Singapore; 2023;p.513–34.
67. Dwivedi MK, Amaresan N, Sankaranaryanan A, Kemp H, editors. Probiotics in the prevention and management of human diseases: a scientific perspective. Academic Press; 2021.
68. Spök A, Arvanitakis G, McClung G. Status of microbial based cleaning products in statutory regulations and ecolabelling in Europe, the USA, and Canada. Food Chem Toxicol 2018;116:10–9.
69. Siddiqui SA, Khan S, Mehdizadeh M, Nirmal NP, Khanashyam AC, Fernando I, et al. Consumer studies focus on prebiotics, probiotics, and synbiotics in food packaging: a review. Curr Food Sci Technol Rep 2023;1:13–29.
70. Foligné B, Daniel C, Pot B. Probiotics from research to market: the possibilities, risks and challenges. Curr Opin Microbiol 2013;16:284–92.
71. Food and Agriculture Organization of the United Nations (FAO), & World Health Organization (WHO). Probiotics in food: Health and nutritional properties and guidelines for evaluation. FAO/WHO. [homepage on the Internet]. Rome: FAO/WHO; 2021 [cited 2025 Jul 29]. Available from: https://www.fao.org/3/i8677en/I8677EN.pdf
72. Zavišić G, Popović M, Stojkov S, Medić D, Gusman V, Jovanović Lješković N, et al. Antibiotic resistance and probiotics: knowledge gaps, market overview and preliminary screening. Antibiotics (Basel) 2023;12:1281.
73. Lok B, Buettner A, Denk P, Ortner E, Fell T. Exploring odor minimization in post-consumer plastic packaging waste through the use of probiotic bacteria. Sustainability 2020;12:9432.