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Probiotics: Significance in Human Health

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Abstract: *Probiotics have gained significant attention due to their diverse health benefits and applications in functional foods and therapeutics. The concept of probiotics dates back to the early work of Metchnikoff, later refined through scientific advancements and formalized by the FAO/WHO definition as live microorganisms that confer health benefits when administered in adequate amounts. This chapter discusses the historical background, classification, sources, selection criteria, mechanisms of action, health benefits, and safety aspects of probiotics. Probiotic microorganisms, particularly lactic acid bacteria and Bifidobacteria, play a key role in maintaining gut microbiota balance, enhancing the intestinal epithelial barrier, producing antimicrobial substances, and modulating the immune system. Advances in molecular techniques have improved the identification and characterization of probiotic strains, ensuring their effectiveness and safety, although concerns such as strain specificity and antibiotic resistance remain important considerations. The chapter also highlights recent developments and future perspectives, including next-generation probiotics and personalized therapeutic approaches, emphasizing their potential in improving human health.*

Keywords*:* DNA–DNA hybridization, pulsed-field gel electrophoresis, synbiotics and postbiotics

I. INTRODUCTION

Probiotics are widely used in functional foods and dietary supplements due to their potential health benefits. The term *probiotic*, first introduced by Werner Kollath in 1953, which is known to be a derivative of the Latin word pro and the Greek word bio meaning "for life." And the term refers to microorganisms that promote health. The FAO and WHO Expert Consultation (2001) defined probiotics as *"live microorganisms which, when administered in adequate amounts, confer a health benefit on the host,"* a definition that has since been widely accepted globally. As research and probiotic products increased, concerns about misuse of the term and regulatory issues also emerged. To reassess the concept and provide updated guidance, the International Scientific Association for Probiotics and Prebiotics (ISAPP) convened a panel of international experts in 2013 to review and clarify the definition of probiotics. Various bacterial genera such as *Lactococcus*, *Pediococcus*, *Enterococcus*, *Streptococcus*, *Propionibacterium*, and *Bacillus* are commonly recognized as potential probiotic microorganisms.

Table 1 Categories of live microorganisms for human use as defined by the expert panel

From: The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic

Description	Claim	Criteria*	Minimum level of evidence required to make claim	Comments
Not probiotic				
Live or active cultures	"Contains live and active cultures"	Any food fermentation microbe(s) Proof of viability at a minimum	No product-specific efficacy studies needed	The terms 'live' or 'active' do not imply probiotic activity

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Description	Claim	Criteria*	Minimum level of evidence required to make claim	Comments
		level reflective of typical levels seen in fermented foods, suggested to be 1×10^9 CFU per serving		Fermented foods containing live cultures might also qualify as a 'probiotic' if they meet the criteria for that category (e.g. evidence that yogurt can improve lactose digestion in lactose maldigesters would qualify it as a 'probiotic'[74,75])
Probiotic				
Probiotic in food or supplement without health claim	"Contains probiotics"	A member(s) of a safe species, which is supported by sufficient evidence of a general beneficial effect in humans OR a safe microbe(s) with a property (e.g. a structure, activity or end product) for which there is sufficient evidence for a general beneficial effect in humans Proof of viability at the appropriate level used in supporting human studies	Well-conducted human studies (e.g. these could involve RCT(s), observational studies, systematic reviews or meta-analyses supporting the observed general beneficial effect for the taxonomical category concerned) The evidence does not have to be generated for the specific strain included in the product	Extrapolation of evidence must be based on reasonable expectations that the strain(s) incorporated in the product would have similar general beneficial effects in humans This evidence could be based on taxonomical or functional comparisons
Probiotic in food or supplement with a specific health claim	Specific health claim, such as "helps to reinforce the body's natural defences in children" or "helps reduce the risk of antibiotic-associated	Defined probiotic strain(s) Proof of delivery of viable strain(s) at efficacious dose at end of shelf-life	Convincing evidence needed for specific strain(s) or strain combination in the specified health indication Such evidence includes well-conducted studies in humans, including: positive meta-analyses on specific strain(s) or strain combinations, as	Well-designed observational studies are useful to detect the effect of foods on health in 'real life', that is, outside the controlled environment of an RCT (e.g. data on health benefits by dietary fibre are mostly observational)

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Description	Claim	Criteria*	Minimum level of evidence required to make claim	Comments
	diarrhoea"		per principles outlined by Cochrane, PASSCLAIM, or GRADE; well-conducted RCT(s) OR strong evidence from large observational studies	Sample sizes must be large enough to manage confounding factors
Probiotic drug	Specific indication for treatment or prevention of disease, such as "useful for the prevention of relapse of ulcerative colitis"	A defined strain(s) of live microbe Proof of delivery of viable probiotic at efficacious dose at end of shelf-life Risk–benefit assessment justifies use	Appropriate trials to meet regulatory standards for drugs	What constitutes a drug claim varies among countries

*Unless otherwise indicated, all criteria indicated must be met.

Abbreviations: CFU, colony forming unit; GRADE, Grades of Recommendation Assessment, Development and Evaluation; PASSCLAIM, Process for the Assessment of Scientific Support for Claims on Food; RCT, randomized controlled trial.

History

In 1899, Henry Tissier isolated *Bifidobacteria* from the stools of breast-fed infants and observed that these bacteria were abundant in healthy individuals, suggesting their role in treating infant diarrhoea. In the early 20th century, Ilya Ilyich Metchnikoff linked the longevity of Bulgarian peasants to their regular consumption of yogurt containing *Lactobacillus* species. He described this idea in his 1907 book *The Prolongation of Life*, proposing that beneficial microbes could improve human health by modifying intestinal microflora. Further scientific discoveries strengthened probiotic research, including Eduard Buchner's (1907) work on yeast fermentation and Minoru Shirota's (1930) isolation of *Lactobacillus casei* strain Shirota, which led to the development of the probiotic drink Yakult in 1935. The term "probiotic," meaning "for life," was first introduced by Werner Kollath in 1953, and later refined by Roy Fuller (1989), who defined probiotics as live microbial supplements that improve intestinal microbial balance and benefit the host.

Probiotic strains must possess several essential characteristics to ensure their efficacy and safety. They should be of well-defined origin with proper taxonomic identification, supported by molecular characterization. A suitable probiotic must demonstrate safety, including non-pathogenicity, absence of toxigenic activity, and no transferable antibiotic resistance genes. Functionally, the strain should survive gastrointestinal conditions, including resistance to low pH and bile salts, and exhibit the ability to adhere to intestinal epithelial cells for transient colonization. Additionally, it should confer proven health benefits, such as antimicrobial activity against pathogens, modulation of the immune system, or improvement of gut barrier function. From a technological perspective, the strain must be stable during processing and

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storage, maintain high viability throughout shelf life, and be suitable for large-scale industrial production. These criteria collectively ensure the selection of effective and reliable probiotic strains.

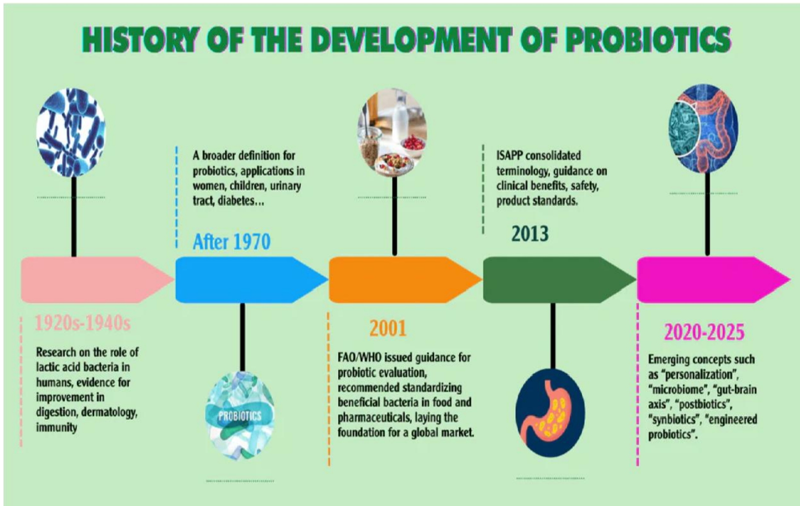

Figure 1: History of the development of Probiotics

Mechanism of Action of Probiotics

Recent studies have shown significant progress in probiotic research, particularly in the selection of probiotic strains and understanding their health benefits. Probiotics exert their effects through several mechanisms, including enhancing the intestinal epithelial barrier, adhering to intestinal mucosa, producing antimicrobial substances, and competitively inhibiting pathogenic microorganisms. They also produce beneficial metabolites such as short-chain fatty acids, regulate immune responses, and improve gut barrier integrity. Through these actions, probiotics help maintain intestinal health and contribute to the prevention and management of various diseases.

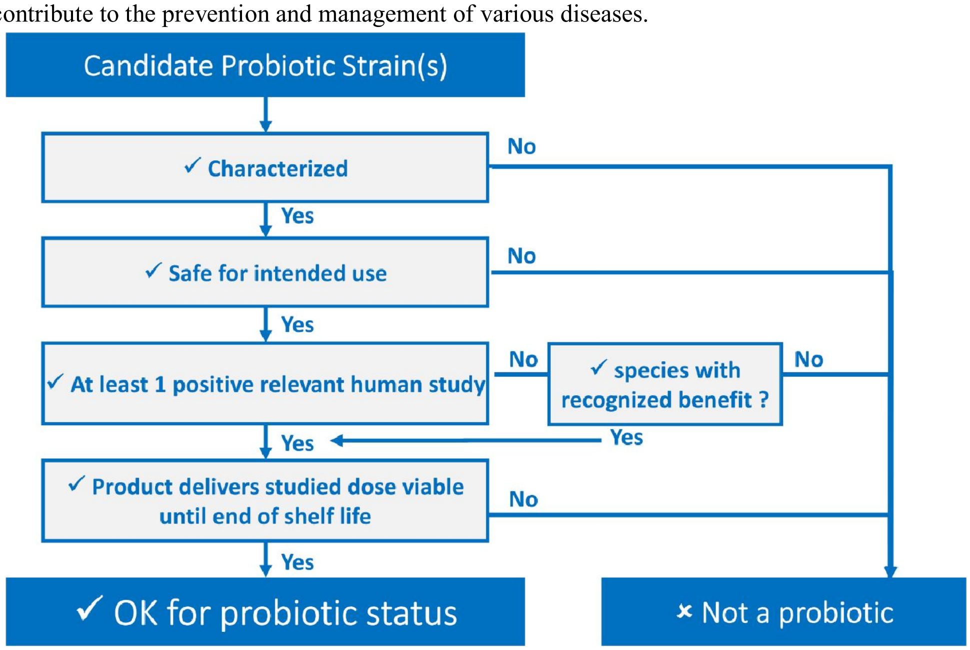

Figure 2: Selection of Probiotic strains

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Microorganisms in Probiotics

Over the past two decades, interest in probiotic research has increased significantly, leading to more than 6000 scientific publications, many appearing in high-impact journals. The most commonly used probiotic microorganisms include lactic acid bacteria and Bifidobacteria, although other bacteria and certain yeasts are also utilized. The biological effects of probiotics are strain-specific, meaning the benefits observed with one strain cannot be assumed for another. Therefore, accurate identification of probiotic strains using molecular techniques such as 16S rRNA gene sequencing, DNA–DNA hybridization, pulsed-field gel electrophoresis, and RAPD analysis, along with phenotypic characterization, is essential.

Health Benefits of Probiotics

Probiotics provide numerous health benefits by maintaining the balance and activity of the gut microbiota, which consists of diverse microorganisms in the digestive system. They promote the growth of beneficial bacteria while inhibiting harmful microorganisms, thereby supporting overall gut health. Probiotics have also been reported to help manage digestive disorders such as irritable bowel syndrome, inflammatory bowel disease, and diarrhoea. In addition, they enhance immune function by stimulating antibody production and activating immune cells, improving the body's defence against infections. Certain probiotic strains, such as *Lactobacillus*, also help maintain urogenital health and reduce antibiotic-associated diarrhoea by restoring microbial balance in the gut.

Probiotics enhance host immunity by interacting with both innate and adaptive immune responses in the gut. The intestinal barrier, composed of mucus, epithelial cells, and immune components, acts as the first line of defense, and probiotics help strengthen this barrier by promoting mucus production and improving tight junction integrity. They adhere to the intestinal mucosa through specific proteins, enabling competitive exclusion of pathogens and preventing their colonization. Probiotic bacteria such as *Lactobacillus* and *Bifidobacterium* also produce antimicrobial substances and organic acids, which inhibit harmful microbes and maintain gut balance.

Probiotics stimulate immune cells like dendritic cells and macrophages, which recognize microbial components and trigger cytokine production, enhancing immune responses. They also influence T cells, promoting differentiation into various subtypes and increasing regulatory T cells that help control inflammation. In addition, probiotics enhance B cell activity, leading to increased production of immunoglobulins, especially IgA, which plays a key role in mucosal immunity. Through these mechanisms, probiotics improve both local and systemic immune responses while maintaining immune homeostasis.

Furthermore, probiotics regulate immune signalling pathways by interacting with receptors such as Toll-like receptors, thereby modulating cytokine production and reducing excessive inflammation. They also support the function of intestinal epithelial cells, goblet cells, and Paneth cells, which produce antimicrobial peptides and maintain gut integrity. Overall, probiotics contribute to enhanced immune defense, reduced pathogen invasion, and improved intestinal health, making them important agents in maintaining host immunity.

Probiotics also play an important role in enhancing the intestinal epithelial barrier, which protects the body from harmful microbes and antigens. They help maintain barrier integrity by supporting components such as mucus, antimicrobial proteins, IgA, and tight junctions. Probiotic bacteria, especially *Lactobacillus*, can upregulate genes involved in tight and adheres junctions, improving cell adhesion and barrier function. Additionally, they modulate signaling pathways and protein phosphorylation, thereby strengthening the intestinal barrier and reducing inflammation.

Safety Concerns and Regulations

The topic of probiotic safety has been addressed by several groups. A foundational initiative by the European Food Safety Authority established the Qualified Presumption of Safety approach for live microorganisms used in foods. This guidance is useful for recognizing microbial species with a history of safe use in foods.

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Safety concerns regarding probiotics have been raised by clinicians and researchers, focusing on strain characteristics, product quality, and safe administration. A key step in safety assessment is complete genome sequencing, which helps identify the probiotic strain and detect genes related to pathogenicity, toxin production, or antibiotic resistance. There is particular concern about the possible transfer of antibiotic resistance genes from probiotic bacteria to other microbes in the gut, although the actual risk is still being studied.

Product safety also requires ensuring purity, potency, and correct microbial composition, along with proper testing to prevent contamination by harmful microorganisms. Probiotics must be administered in safe doses and appropriate formulations, especially for vulnerable populations such as infants or critically ill patients. In rare cases, probiotics may cause invasive infections such as bacteraemia or sepsis, particularly in individuals with weakened immune systems or underlying conditions.

Probiotics can also interact with the gut microbiota and influence drug metabolism, which may affect the efficacy or toxicity of certain medications. Most probiotic strains do not permanently colonize the gut, but some newer strains may persist for longer periods, raising questions about long-term safety. While long-term colonization may provide sustained health benefits, it could also potentially alter the existing microbiota or displace beneficial microbes. Therefore, careful safety evaluation, monitoring, and risk–benefit analysis are essential when developing and using probiotic products.

Regulation of probiotics varies globally and focuses on ensuring their safety, efficacy, and quality. Organizations such as the FAO/WHO have established guidelines defining probiotics and recommending proper strain identification, safety assessment, and clinical validation. In the United States, probiotics are regulated by the FDA as dietary supplements, foods, or drugs depending on their intended use, while in Europe, the EFSA evaluates probiotic safety under the Qualified Presumption of Safety (QPS) framework. Regulatory requirements typically include accurate labelling, proof of viable cell count, absence of harmful contaminants, and scientifically substantiated health claims. Despite these frameworks, differences in global regulations and misuse of the term “probiotic” highlight the need for standardized international guidelines and stricter quality control.

Recent Advances in Probiotic Research

Recent advances in probiotic research have significantly expanded our understanding of their functional roles, mechanisms, and applications. The use of omics technologies such as genomics, metagenomics, metabolomics, and transcriptomics has enabled precise identification and characterization of probiotic strains and their interactions with the host microbiome. Emerging concepts like next-generation probiotics (e.g., *Akkermansia muciniphila* and *Faecalibacterium prausnitzii*) and engineered probiotics are being explored for targeted therapeutic applications. In addition, the development of synbiotic and postbiotics has opened new avenues for enhancing probiotic efficacy and stability. Advances in microencapsulation and delivery systems have improved the survival and shelf life of probiotics in food and pharmaceutical products. Furthermore, growing interest in personalized probiotics based on individual microbiome profiles is paving the way for precision medicine. These developments highlight the evolving potential of probiotics in improving human health and disease management.

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