Biomedical Data Science
2025, VOL. 5, NO. 3, 52-57
DOI: 10.47297/wspbdsWSP2752-630510.20250503

Probiotics, Prebiotics, and Synbiotics in Food-Related Health Promotion: Current Understanding, Cross-Sector Applications, and Evaluation of Apple/ Pomegranate Extracts as Prebiotics for Lacticaseibacillus rhamnosus IMC501

Yun Hao

University of Light Industry, Zhengzhou, Henan, 450000, China

ABSTRACT

Beneficial microorganisms, more commonly known as probiotics, have witnessed a surge in popularity due to their remarkable ability to bestow health benefits upon their host when appropriately utilized. This comprehensive review delves into the current understanding of probiotics, exploring their taxonomic classification, physiological efficacy, and diverse applications across human, animal, and aquatic health sectors. Particular emphasis is placed on Lactobacillus and *Bifidobacterium* genera, which have demonstrated substantial capabilities in modulating gut microbiota, fortifying intestinal barriers, and stimulating immune responses. The synergistic combination of probiotics and prebiotics, known as synbiotics, has also shown enhanced health benefits, underscoring the value of integrated approaches. However, the advancement of probiotic technology is not without challenges, as individual responses to probiotic therapies can vary significantly, influenced by factors such as diet, genetics, and the environment. As such, continued research is imperative to develop personalized probiotic formulations, deepen our understanding of their underlying mechanisms, and identify novel functional strains to enhance efficacy. Looking ahead, Future research into probiotics carries substantial promise for enhancing quality of life across varied populations and life stages. This study additionally seeks to explore the prebiotic potential of apple and pomegranate extracts, assessing their effects on the fermentation properties of the probiotic strain *Lacticaseibacillus rhamnosus IMC501*. Given the potential of prebiotics to synergize with probiotics to form synbiotics, this research may unlock new avenues for integrated health improvement strategies.

KEYWORDS

Probiotics; Prebiotics; Synbiotics; Immune modulation; Apple and pomegranate extracts

1 Introduction

By 2050, the global population is projected to exceed 9–10 billion, driving up demand for high-quality food products (Falcon et al., 2022; Nascimento - Schulze et al., 2021). Urban expansion, soil degradation, and climate change have collectively limited the availability of new land for food production. However, marine ecosystems offer a promising avenue to enhance food security, particularly given the growing populations in coastal regions. Probiotics have emerged as a viable solution to meet the food needs of a expanding global population, with the United Nations Food and Agriculture Organization (FAO) and World Health Organization (WHO) defining them as live microorganisms that confer health benefits when administered in adequate amounts.

Probiotic microorganisms, encompassing a diverse array of bacteria (e. g., *Lactobacillus* spp., *Bifidobacterium* spp.), yeasts (such as *Saccharomyces boulardii*), and select other microbial strains, exert their beneficial effects through three interconnected core mechanisms. First, they mediate competitive exclusion of pathogens by colonizing intestinal niches, outcompeting harmful microbes for nutrients like carbohydrates and amino acids, and secreting antimicrobial substances —including bacteriocins, hydrogen peroxide, and organic acids (e. g., lactic acid) —that disrupt pathogenic adhesion to gut epithelium and inhibit their proliferation, thereby reducing the risk of infections caused by pathogens such as Campylobacter and Clostridium difficile. Second, these probiotics enhance intestinal barrier integrity: they stimulate the synthesis of tight junction proteins (e.g., claudins, occludin) and promote the proliferation of goblet cells, which secrete mucins to form a protective mucosal layer, limiting the translocation of endotoxins and pathogenic antigens into the systemic circulation and thus maintaining gut homeostasis. Third, they regulate the host immune system by modulating the activity of immune cells (e.g., macrophages, T lymphocytes) and balancing the production of pro-inflammatory (e.g., IL-6, TNF- α) and anti-inflammatory (e. g., IL-10) cytokines, thereby enhancing mucosal immune surveillance while preventing excessive inflammatory responses linked to conditions like inflammatory bowel disease. Additionally, probiotics contribute to host health through the production of bioactive metabolites, such as short-chain fatty acids (SCFAs: acetate, propionate, butyrate) and vitamins (e. g., B vitamins), which support epithelial cell energy metabolism, regulate gene expression related to gut function, and further reinforce the gut microbiota ' s beneficial properties.

Beyond their established roles in human health—from alleviating gastrointestinal dysfunctions to supporting immune resilience—probiotics also hold substantial potential in addressing the food security challenges highlighted by global population growth, particularly in animal husbandry and aquaculture. In livestock production, for example, probiotic supplementation improves feed utilization efficiency by enhancing nutrient digestion (e. g., breaking down complex carbohydrates via microbial enzymes) and reducing gut dysbiosis, thereby boosting growth rates in poultry, swine, and ruminants while decreasing reliance on antibiotic growth promoters—a critical step toward sustainable agriculture. In aquaculture, probiotics stabilize the microbial balance in rearing water and the gastrointestinal tracts of farmed species (e. g., salmon, shrimp, tilapia), mitigating the spread of aquatic pathogens (such as Vibrio spp.) and improving survival rates, which directly enhances the productivity of this increasingly vital food source for coastal populations.

2 Fundamental notions and categorization of probiotics

Probiotics refer to live microorganisms that, when ingested in sufficient quantities, yield health benefits for the host. In the domain of food science, they are most often incorporated into fermented dairy items, functional drinks, and dietary supplements. The idea that "food can act as medicine" has been around for centuries, yet it is only in the past few decades that probiotics have become the focus of systematic research and found applications in clinical and commercial settings.

The probiotic genera that have been studied most extensively are Lactobacillus, Bifidobacterium, and Saccharomyces. These microorganisms are naturally present in the human gastrointestinal tract, where they help keep the microbial balance in check, strengthen immune function, and fend off colonization by pathogenic microbes. In food production, choosing the right strain is of great significance; key considerations include the strain's ability to survive under gastric conditions, its capacity to adhere to the intestinal mucosa, and its stability over the product's shelf life.

Probiotics can be divided into three main categories based on different criteria:

(1) Taxonomic identity (e.g., *Lactobacillus rhamnosus GG*, *Bifidobacterium longum*, *Saccharomyces boulardii*);

(2) Functional role (e.g., aiding digestion, supporting the immune system, inhibiting harmful bacteria);

(3) Delivery vehicles (e.g., yogurt, kefir, capsules, or synbiotic blends mixed with prebiotics).

Traditional fermented foods remain a primary source of probiotics, but progress in modern manufacturing has made them more accessible in a range of user-friendly forms. No matter what form they take, the effectiveness of probiotics relies on two key factors: whether the strain is viable when consumed and its ability to trigger specific physiological reactions in the host.

Essentially, probiotics lie at a crucial crossroads of microbiology and nutrition. Their classification not only helps clarify their functional roles but also provides a foundation for the rational design of functional foods tailored to specific health targets.

2.1 Characterizations and categorical frameworks

As defined by the FAO/WHO (2001), probiotics are "live microorganisms that confer health benefits on the host when administered in adequate amounts". The main probiotic strains are derived from the *Lactobacillus* and *Bifidobacterium* genera, though *Saccharomyces boulardii* has also attracted significant research attention [5]. Probiotics are classified based on three factors: taxonomic identity, mode of action, and intended use.

Lactobacillus rhamnosus GG has been extensively studied for its efficacy in preventing and reducing the duration of acute diarrhea in children. *Bifidobacterium longum* is similarly well-researched for its ability to strengthen the intestinal barrier and regulate immune responses.

2.2 Mechanisms of fuction

Probiotics exert multiple beneficial effects in the body, with one key pathway involving the displacement of harmful microbes. By adhering to the intestinal mucosa, probiotics compete with pathogens for nutrients and attachment sites, preventing colonization and infection. They also enhance intestinal barrier function by promoting mucin production, which forms a protective layer against pathogen invasion.

Probiotics modulate the immune system through various biological mechanisms. Their ingestion stimulates the production of two key immune regulators: interleukin-10 (IL-10) and interferon-gamma (IFN-γ). Additionally, probiotic bacteria produce antimicrobial substances—including bacteriocins—to inhibit pathogenic growth (Franz et al., 2007).

2.3 Functional characteristics of probiotics

2.3.1 Intestinal health and preventive effects against disease

A central function of probiotics lies in modulating the composition of the gut microbiota. Research indicates that select probiotic strains contribute to sustaining microbial homeostasis, thereby alleviating gastrointestinal manifestations in individuals with dysbiosis. For example, *Lactobacillus rhamnosus GG* has been shown to reduce the incidence and duration of acute diarrhea in children.

Probiotics also enhance nutrient absorption, particularly of vitamins and minerals, contributing to overall health (Hung, 2023). Strains of *Bifidobacterium lactis*, for instance, have been found to improve calcium absorption, supporting bone health (Knapp et al., 2012).

2.3.2 Immune modulation

Probiotic consumption supports immune system function by triggering the production of cytokines such as IL-10 and IFN-γ, which regulate inflammation and immune responses. A study by Pourabedin et al. (2016) demonstrated that dietary supplements containing xylooligosaccharides (XOS) and mannanoligosaccharides (MOS) reduced levels of the pro-inflammatory cytokines IL-6 and LITAF in chickens infected with Salmonella Enteritidis. Combining probiotics with prebiotics (synbiotics) further enhances immune function and reduces disease severity.

2.3.3 Antioxidative and anti-inflammatory properties

Probiotic strains harbor antioxidant and anti-inflammatory capacities that augment their health-promoting potential. A case in point is *Lactobacillus plantarum*, which synthesizes exopolysaccharides endowed with robust antioxidant activity (Han et al., 2024). These polysaccharides act as antioxidants by scavenging harmful free radicals, reducing cellular oxidative stress and protecting cells from damage.

Probiotics also modulate inflammation by decreasing the release of pro-inflammatory cytokines and increasing anti-inflammatory factors. This dual action helps balance immune function, preventing chronic inflammation associated with conditions such as cardiovascular disease and cancer.

2.4 Applied contexts of probiotics

2.4.1 Health in humans

Extensive research has delved into the health-promoting effects of probiotics in humans, with a particular emphasis on supporting gastrointestinal wellness. A well-documented example is *Lactobacillus rhamnosus GG*, which has been shown to effectively lower the incidence of acute diarrhea in children and shorten its duration by enhancing intestinal barrier function and inhibiting the adhesion of pathogenic bacteria to gut epithelial cells. In clinical settings, probiotics also play a role in managing symptoms associated with irritable bowel syndrome (IBS), including abdominal pain, bloating, and irregular bowel movements. Specific strains within the *Bifidobacterium* and *Lactobacillus* genera have demonstrated efficacy in this context, with studies indicating they modulate visceral hypersensitivity and balance gut microbial composition to alleviate discomfort (Knapp et al., 2012).

Beyond their established role in gut health, probiotics are emerging as a promising intervention for metabolic disorders such as obesity and type 2 diabetes. Their consumption has been associated with improvements in insulin sensitivity, partly through the production of short-chain fatty acids (SCFAs) that regulate glucose uptake and utilization. Additionally, probiotics help reduce chronic low-grade inflammation—a key driver of metabolic dysfunction—by suppressing the release of pro-inflammatory cytokines like TNF-α and IL-6. These dual effects make probiotics a valuable tool in the management of such conditions, as both enhanced insulin sensitivity and reduced inflammation are critical for mitigating their progression.

2.4.2 Animal farming: benefits and antibiotic alternatives

Probiotics deliver a spectrum of advantages in animal farming, with their impacts spanning growth promotion, digestive health enhancement, and disease prevention. In poultry production, for instance, farmers frequently incorporate mannan oligosaccharides (MOS) into feed formulations to target Salmonella infections—a common pathogenic threat that can impair gut function and stunt growth. By binding to Salmonella surface lectins, MOS prevents the bacteria from adhering to intestinal epithelial cells, thereby reducing colonization and subsequent infection rates. This mechanism not only safeguards gut integrity but also enhances nutrient absorption, leading to measurable improvements in weight gain and feed conversion efficiency in broilers and layers alike.

In swine production, probiotic supplementation plays a pivotal role in optimizing digestive processes: strains like Lactobacillus and Bifidobacterium stimulate the secretion of digestive enzymes (e. g., amylase, lipase), break down complex carbohydrates and fats, and promote the absorption of essential nutrients such as amino acids and minerals. Beyond boosting feed efficiency, this microbial support also reduces the need for antibiotic interventions by suppressing the overgrowth of pathogenic bacteria like Escherichia coli and Clostridium perfringens in the swine gut.

Notably, synergistic effects between prebiotic compounds further amplify these benefits. Pourabedin et al. (2016) demonstrated that combining MOS with xylooligosaccharides (XOS) in poultry feed yielded dual advantages: it significantly lowered Salmonella Enteritidis counts in chicken ceca—by up to 1.5 log CFU/g in their trials—and modulated the expression of key cytokine proteins, including interleukin-10 and tumor necrosis factor-α. This immunomodulatory effect strengthens the birds' innate immune response, reducing inflammation and improving overall resilience. Together, such findings underscore probiotics and their prebiotic counterparts as robust alternatives to antibiotics, aligning with efforts to enhance animal welfare while sustaining productivity in intensive farming systems.

2.4.3 Aquaculture

Probiotic use in aquaculture is rapidly expanding, driven by their capacity to enhance fish immunity and mitigate pathogenic outbreaks—a critical advantage in intensive farming systems where crowded conditions elevate disease risk. These beneficial microorganisms act through multifaceted mechanisms: they not only stimulate the host's immune defenses but also modulate the gut microbiota to create an environment hostile to harmful pathogens.

Terrado-Campos et al. (2016) elaborated on this dual functionality, noting that probiotics activate key immune pathways in fish, such as increasing the production of lysozymes and reactive oxygen species—molecules that directly target and neutralize invading pathogens. Concurrently, they promote the proliferation of beneficial gut bacteria, which compete with pathogens for nutrients and adhesion sites in the intestinal tract, thereby limiting pathogenic colonization.

Specific strains have demonstrated remarkable efficacy in diverse aquacultural contexts. Lactobacillus plantarum, for instance, has been shown to improve survival rates by up to 30% and enhance growth performance in juvenile sea bream (Sparus aurata) exposed to stressful conditions, such as fluctuating water temperatures or high stocking densities. This strain achieves these effects by stabilizing the gut barrier function, improving nutrient absorption efficiency, and reducing stress-induced inflammation—all of which contribute to better overall health and productivity in farmed fish populations.

2.5 Personalized probiotic therapies

Individual differences in gut microbiota composition and genetics influence the effectiveness of specific probiotic strains. Advances in metagenomic and genomic research now allow for personalized probiotic treatments based on analysis of an individual's microbiome. Knapp et al. (2012) suggested that future research should employ high-throughput sequencing to analyze individual gut microbiomes, enabling the identification of targeted, beneficial microbes.

The goal of personalized probiotics is to address variability in individual responses to treatment. By analyzing the microbiome to identify dysbiosis patterns, researchers can select specific probiotic strains to restore balance. This approach has been successfully used in clinical settings to develop customized probiotic solutions that improve outcomes for patients with gastrointestinal disorders.

Zhai et al. (2023) demonstrated that probiotics can modulate brain function through microbial signaling pathways, with their work further revealing that such strains reduce stress and anxiety markers. Incorporating genomic data into probiotic therapies facilitates the identification of genetic factors that govern probiotic function in the host; genetic variants can alter gene expression related to immune regulation and metabolism, thereby shaping host responses to probiotics. These genetic signatures enable the design of more efficacious, personalized probiotic strategies.

Advances in synthetic biology have further unlocked opportunities for engineering probiotic strains with enhanced functional capabilities. Through targeted genetic manipulation of these microbes, researchers can engineer bacteria to synthesize specific proteins and enzymes, creating strains tailored to address specific health issues or deliver medications targeted to specific sites. For example, engineered Lactobacillus strains that produce anti-inflammatory peptides show potential for treating inflammatory bowel disease.

2.6 Mechanisms of probiotic action

Despite their proven health benefits, the precise mechanisms underlying probiotics remain incompletely understood. Further research is required to clarify the complex interactions between probiotics, the immune system, and the gut microbiota—particularly with respect to the molecular pathways involved in probiotic-induced immune regulation (Terrado-Campos et al., 2016).

Probiotics modulate the host immune system by stimulating the production of the anti-inflammatory cytokine IL-10 and the immune regulator IFN-γ (Pourabedin et al., 2016). They also enhance intestinal barrier function through increasing mucin secretion and strengthening tight junction proteins, a process that defends against pathogen invasion and reduces systemic inflammation.

Recent studies have provided deeper insights into how probiotics reshape the gut microbiota. Their inhibitory effects on harmful microbes include competitive exclusion for ecological niches, production of antimicrobial substances, and regulation of the gut microenvironment. Additionally, probiotics promote the proliferation of beneficial bacteria, thereby increasing microbial diversity—a key factor in reversing dysbiosis associated with inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS).

Probiotics also interact with host metabolic pathways. Specific strains have been shown to improve insulin sensitivity and reduce levels of inflammatory markers, both of which are critical for managing obesity-related diseases and type 2 diabetes. A clearer understanding of these metabolic interactions could inform the development of probiotic-based therapies for chronic conditions.

3 Conclusion

This study highlights the significant prebiotic potential inherent in apples and pomegranates, shedding light on how their distinctive bioactive components—specifically apple pectin and pomegranate polyphenols—exert regulatory effects on gut microbiota through unique fermentation mechanisms. This regulatory activity is evident in real-time pH monitoring data collected within a simulated intestinal environment, which captures the dynamic shifts associated with microbial metabolism.

Fibrous fractions extracted from apples were found to rapidly stimulate the synthesis of short-chain fatty acids (SCFAs), with butyrate production showing a marked increase within the initial stages of fermentation. In contrast, pomegranate extracts demonstrated a sustained capacity to drive the generation of microbial metabolites with anti-inflammatory properties, such as urolithins, which persisted over extended fermentation periods.

These findings enhance our understanding of fruit-derived prebiotics: they are not merely sources of dietary fiber but function as precise modulators of the gut microbial ecosystem. Such insights carry broad implications for human health, underscoring the potential of these fruits to shape microbial balance in ways that support physiological well-being.

A key insight from this work is the synergistic potential of synbiotics—formulations that combine these fruit-derived prebiotics with probiotic strains—to amplify health-beneficial effects. Within the in vitro system, the rapid fermentation of apple pectin provided an ideal substrate for the growth of Bifidobacterium and Lactobacillus, while pomegranate polyphenols protected probiotics from degradation and enhanced their metabolic activity. This aligns with the broader concept of synbiotics as a next-generation strategy to overcome limitations in probiotic performance, such as suboptimal colonization and variability between individuals. Pairing fruit prebiotics with strain-specific probiotics may therefore facilitate the development of future interventions tailored to individual microbial needs.

Nonetheless, the study also highlights two critical obstacles to translating these findings into practical applications:

Variability in prebiotic effectiveness stemming from host-microbe interactions (e.g., genetic predispositions, microbial phenotypes).

A pressing need for standardized, scalable methods to evaluate prebiotic activity within complex food matrices.

To address these challenges, future research should utilize genomic and metagenomic technologies to clarify how individual gut microbiota compositions and genetic markers—including enzymes involved in polyphenol metabolism—regulate the body's responses to apple- and pomegranate-derived prebiotics. Integrating multi-omics approaches (such as metabolomics and transcriptomics) with the cost-effective pH monitoring method validated in this study will further elucidate the molecular mechanisms behind the prebiotic effects of these fruits. For example, such integration could shed light on how apple-derived butyrate strengthens intestinal barrier function or how pomegranate-derived urolithins regulate inflammatory signaling pathways.

The implications of these findings extend far beyond human health. This study's verification that fruit byproducts—specifically apple pomace and pomegranate peel—act as sustainable prebiotic sources for livestock feed and food preservation marks a significant move toward circular economy models in agriculture and industry. This shift aligns with global efforts to reduce antibiotic use and minimize food waste. Additionally, these results establish fruits as accessible, natural tools in the precision nutrition movement, where dietary advice will increasingly be customized to an individual's unique microbial and genetic traits. This paradigm is strongly supported by the study's demonstration that responses to apple and pomegranate interventions depend on an individual's microbiota phenotype.

In summary, this work bridges the gap between fundamental scientific inquiry and practical real-world applications, illustrating that fruits are far more than simple nutritional staples—they act as powerful regulators of gut health, with the potential to reshape current probiotic and synbiotic strategies. To unlock the full capabilities of fruit-derived prebiotics, interdisciplinary collaboration will be essential, spanning fields such as microbiology (to decode microbial-molecule interactions), food engineering (to optimize extraction and formulation), genetics (to account for host microbial variability), and environmental science (to ensure sustainable sourcing and production). Such collaborative efforts are critical for developing personalized, eco-friendly solutions that enhance not only human health but also animal wellness and planetary sustainability.

The era of precision prebiotics is now upon us, and apples, pomegranates, along with their bioactive constituents, stand at the vanguard of this advancing field. Their unique ability to modulate gut microbial ecosystems—through mechanisms like targeted fermentation and metabolite production—positions them as key players in redefining how we approach microbial health interventions.

Emerging research suggests that integrating these bioactives into daily nutrition could reshape dietary strategies, transforming conventional notions of wellness. By harnessing the synergistic effects of polyphenols, fibers, and antioxidants, scientists envision tailored regimens that optimize microbiome function, reduce systemic inflammation, and support cognitive resilience. This convergence of nutrition science and microbial ecology promises a future where diet is not just sustenance but a precise instrument for health optimization, bridging the gap between preventive care and personalized therapeutics on a global scale.

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