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Probiotics and Human Health: Exploring the Interconnection with Host Microbiota

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Abstract

The article examines the impact of probiotics on human health, with a particular emphasis on their interaction with the host's microbiota. Methods. The review begins with an extensive search of literature in databases such as PubMed, Scopus, and Google Scholar to gather studies on the effects of probiotics on the composition of the microbiome, immune response, and metabolic functions. The authors emphasize that the human microbiota, which consists of various microorganisms, plays a crucial role in maintaining homeostasis, supporting the immune system, and regulating metabolic health. Studies show that probiotics, particularly Lactobacillus and Bifidobacterium strains, contribute to gut health by promoting beneficial bacteria, regulating the immune response, and inhibiting pathogen growth. According to research, probiotics can be an effective adjunct treatment for conditions associated with microbiota imbalance. They may offer benefits for neurological, metabolic, and immune health.

Introduction

Human health is increasingly determined by the interaction between host biology and the microbial communities that inhabit it. Microbiome research has advanced of late and it has demonstrated these microorganisms actively participate in processes from immunity and metabolism to neurological function instead of just passively residing there. Because chronic conditions are now linked to microbiota imbalance, this interconnection must be understood. A wide range of chronic conditions have now been linked to disruptions in the human microbiota. Against this backdrop, probiotics emerged from obscurity as promising tools to modulate microbiota composition and promote overall health.

The Human Microbiota: An Overview

Human health and its preservation in the face of adverse environmental factors, as well as the ability to overcome physical and emotional stresses, largely depend on the dynamic and non-equilibrium state of the system composed of the host and the collective microbiocenoses located on exposed mucous membranes and skin. This system represents a complex interaction between the human body and its microbiota, which plays a crucial role in maintaining homeostasis, immune defense, and metabolic processes. Great influence of microbiome on human health can be explained by huge number of unique microbial genes (3.3 million) identified in human microbiome significantly outnumbering the 20,000-25,000 genes in human genome. Achieving and maintaining balance within this system is essential for adapting to changing environmental conditions and effectively responding to stressors. External factors such as air pollution, diet, stress, and lifestyle can disrupt this balance, adversely affecting overall health and the body's ability to resist diseases and manage stress [1, 2]. Furthermore, a "healthy" microbiome is defined not by the presence of specific microbial taxa, but by its overall functional potential. Indeed, no single microbial species can be universally associated with health, for example, the gut microbiome in healthy individuals typically includes around 1000-1150 bacterial species, with each person carrying ~160 species. These species produce short-chain fatty acids, educate the immune system, resist pathogenic invasion, and other health-related functions [3].

Recent research underscores the importance of the gut microbiota not only in local digestive functions but also in systemic health., as they can significantly affect neurodevelopment and behavior, suggesting a close link between gut health and the central nervous system. The gut-brain axis explains that microbes in the gut can create substances similar to neurotransmitters, that influence the brain and behavior [4, 5]. This idea supports the growing field of medical microbial ecology, which combines research from areas like physiology, microbiology, and immunology. The presence of bacterial flora associated with the host organism is thus a prerequisite for the existence of complex multicellular life [6, 7].

Modern research shows that mutualism involves complex cellular and molecular interactions that influence both microbes and their hosts. In the gut, these interactions are crucial for the development and regulation of the nervous, immune, and endocrine systems. Microbial signals affect hormone levels, immune responses, and even brain function.

Technologies like genomics and metabolomics have revealed how gut microbes impact digestion, metabolism, inflammation, and behavior. Dysbiosis – microbial imbalance – is now linked to various disorders, including neurodevelopmental and autoimmune diseases [5, 7].

The human colon contains between 100 trillion and 1 quadrillion microbes, including bacteria, archaea, viruses, and fungi. These organisms contribute to digestion, vitamin production, immune training, and protection against pathogens. This complex ecosystem, often called a "forgotten organ," plays a vital role in maintaining health and preventing disease [8, 9].

The aim of the article was to examine the influence of probiotics on human health, with a particular focus on their interactions with the host microbiota.

Methods

Literature Search and Selection Criteria

Following the guidelines of the preferred reporting items for systematic reviews and meta-analyzes (PRISMA) statement for narrative reviews, the literature was scanned in PubMed, Scopus, and Google Scholar databases, for peer-reviewed publications that pertain to probiotics, human health, and gut microbiota. Searches were conducted for studies published between January 2010 and June 2024 to capture early and recent research. The keywords used in the search strategy included combinations of terms like «probiotics», «human health», «gut microbiota», «immune system», and «metabolic health».

Inclusion Criteria:

- publication in English, Russian and Kazakh languages;
- containing results (clinical trials, meta-analyses, or experimental research) on probiotics' impact on human health or microbiota composition;

Exclusion Criteria:

- Not peer-reviewed publications (e.g., conference abstracts, theses, editorials);

- Studies involving animals or in vitro experiments without any relevance on human health;
- Not full text or no methodological rigor.

The search strategy found 842 records. In the review process, 217 duplicates were removed from them. The title and abstract from the remaining records were screened (n = 625), and full text of 118 articles was reviewed in detail; 74 met inclusion criteria.

The review analyzed how probiotics impact various aspects of health, including changes in microbiome composition, regulation of the immune response, and improvements in metabolic processes. By organizing and summarizing the data, the researchers identified key findings as well as gaps in current knowledge. These gaps point to the need for further investigation, particularly in understanding long-term effects and individual responses to probiotic use.

Discussion

Probiotics and Human Microbiome

Recently there has been a spike of interest in controlling the human microbiome to improve health and prevent disease. Strategies like probiotics, prebiotics, postbiotics, and synbiotics have gained significant attention. Probiotics are live beneficial microbes, prebiotics support growth of natural microbes, postbiotics are bioactive products of microbial fermentation, and synbiotics combine probiotics and prebiotics for enhanced effect. These approaches offer promising new options for managing gastrointestinal, metabolic, and neurodegenerative diseases [3, 7]. Probiotics, postbiotics and prebiotics live within the gut and work at the benefit of the host, providing microorganisms and substrates, consumed by the microorganisms, at the same time. Boahen *et al*., [10] explored synbiotics' capacity, including prebiotics, probiotics, and postbiotics, toward successfully averting pathogen adherence or disturbing biofilm genesis through restraining pathogen proliferation as well as obstructing hyphae genesis. Lactobacillus and Bifidobacterium species [11] represent the common probiotics employed regarding human health management. They have been extensively studied regarding their helpful effects on overall health along with the gut microbiota. For example, *Lactobacillus rhamnosus, Lactobacillus crispatus*, *Lactobacillus jensenii*, and *Lactobacillus gasseri* are commonly used in probiotics due to their ability to colonize the human gut and vagina, produce organic acids, and inhibit the growth of pathogenic microorganisms. These species are frequently used in treating and preventing urogenital infections, as they improve vaginal flora and promote an acidic environment unfavorable to pathogens [12, 13]. *Bifidobacterium longum* and *Bifidobacterium bifidum* are particularly effective in promoting gut health by inhibiting the colonization of harmful bacteria and maintaining the integrity of the gut lining [14, 15, 16, 17].

Indeed, probiotics have wide applications and mechanisms of action including urogenital health improvement, HPV infection treatment, microbiome modulations, etc. Lactobacilli such as *Lactobacillus crispatus* and *Lactobacillus jensenii* produce lactic acid and hydrogen peroxide, which lower the vaginal pH and inhibit the growth of pathogens like Gardnerella vaginalis. Encapsulated *Lactobacillus crispatus* cells in alginate-carboxymethylcellulose beads have been shown to preserve their viability and antibacterial properties, making them suitable for use in sanitary suppositories to prevent urogenital infections [18]. In addition, confirmed the efficiency of Yakult® probiotic containing the *Lacticaseibacillus paracasei Shirota* in reduction in HPV-related cytological abnormalities. Lactobacillus-derived products, such as bacteriocins, have shown significant antimicrobial activity against a range of pathogens. For example, the bacteriocin produced by *Ligilactobacillus salivarius* disrupts the transmembrane potential and proton motive force in Streptococcus faecalis, demonstrating the potential of probiotics and postbiotics as alternatives to traditional antibiotics. Marinacci *et al*., [19] detailed the mechanisms of *Limosilactobacillus reuteri* on producing antimicrobial compounds that prevent harmful pathogens from colonizing the gut, thereby supporting overall health and immune function. Furthermore, studies have shown that certain *Lactobacillus strains* can persist in the human microbiota over extended periods [13, 20]. A metagenomic analysis identified the stable strains of *Lactobacillus iners, Lactobacillus crispatus,* and *Lactobacillus jensenii* that persisted for over a year in some individuals [13], highlighting the potential for long-term probiotic interventions in maintaining a healthy microbiome.

Recent studies highlight the potential of these substances not only in maintaining gut health but also in improving disease outcomes, even related to autism spectrum disorder, vaginal infections, metabolic syndrome, male fertility, and psychotropics [21-25]. By promoting a balanced microbial environment, probiotics may help prevent and manage conditions such as inflammatory bowel disease, metabolic disorders, and infections [26]. Furthermore, prebiotics, which support beneficial gut bacteria, work synergistically with probiotics to foster a healthy gut environment, crucial for glucose regulation and insulin sensitivity [27]. Maftei *et al*., [28] reinforce the diverse health-promoting properties of probiotics and the importance of continued research in the field of cancer prevention.

The use of probiotics offers a promising avenue for enhancing human health by modulating the microbiome. Continued research into stability, efficacy, and specific applications of these formulations will likely lead to the development of innovative treatments that minimize the reliance on traditional antibiotics and improve overall health outcomes [29, 31].

Gut Microbiome and Metabolic Health

The trillions of microorganisms in the gut microbiome play a key role in regulating metabolic health [27, 30, 31]. Disruptions in this system, known as dysbiosis, are linked to metabolic disorders such as obesity, type 2 diabetes, and cardiovascular diseases [32, 33, 34].

A healthy and balanced gut microbiota supports proper insulin signaling, whereas dysbiosis is strongly linked to the development of insulin resistance, a primary feature of type 2 diabetes [35]. Chronic low-grade inflammation, caused by dysbiosis, disrupts insulin signaling pathways, impairing glucose uptake by cells and ultimately leading to insulin resistance. Certain species within the genus *Bacteroides* produce lipopolysaccharides (LPS) can translocate into the bloodstream, triggering systemic inflammation and further aggravating insulin resistance, when gut permeability increases [36].

The gut microbiome significantly contributes to metabolic health by regulating energy homeostasis. This process is known as fermentation and results in the production of short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate [37]. By influencing hunger signals and how much energy the body uses, these microbial byproducts play a role in controlling appetite and body weight [36, 38].

A study conducted on Mongolian individuals revealed that elevated levels of SCFAs were associated with a lower risk of developing type 2 diabetes among obese individuals [39]. Supplementation with certain probiotic strains is associated with reduced fasting blood glucose levels and improved insulin sensitivity in individuals with type 2 diabetes [35]. The importance of the gut microbiome in energy regulation was further underscored by the influence of colonic butyrate, a product of microbial fermentation, on hepatic glucose production through FFAR2-dependent GLP-1 receptor neuronal signaling [40]. Another study explored the communication between the gut microbiome and adipose tissue, focusing on the role of intestinal mTOR (mechanistic target of rapamycin) in regulating the browning of white adipose tissue. The research revealed that the mTOR-AMPs-microbiome axis significantly influences glucose homeostasis and energy metabolism [41].

The composition of the gut microbiome is closely linked to obesity development, specifically individuals with obesity tended to have a higher ratio of *Firmicutes* to *Bacteroidetes* in their gut microbiota. Changes in gut microbiota composition can lead to increased appetite, enhanced fat accumulation, and subsequent weight gain, emphasizing the microbiome's potential as a target for obesity treatment [42, 43]. Growing evidence continues to reveal the intricate links between diet, gut microbiota, and overall metabolic health. For example, branched-chain amino acids have been found to influence the structure of the gut microbiota, thereby impacting energy homeostasis, glucose regulation, and fat storage processes [44, 45].

In addition to macronutrients and fiber, plant-derived compounds also significantly affect gut health. One such compound, dodecanoic acid from *Drynaria quercifolia*, has been shown to enhance the intestinal barrier and support communication along the gut-brain axis by interacting with proteins essential for maintaining gut structure [46]. Moreover, overall dietary patterns, rather than individual nutrients alone, appear to have a stronger association with the gut microbiome-endocannabinoid system (eCBome) [47], highlighting the importance of diet diversity and quality in shaping microbial communities and influencing energy balance and inflammation.

The gut microbiota also supports metabolic regulation by maintaining gut barrier integrity and stimulating the release of appetite-suppressing hormones such as GLP-1 and PYY [43, 48], which help promote satiety and reduce obesity risk. Bile acids, produced in the liver from cholesterol and secreted into the intestine, aid in the digestion and absorption of fats [49]. Zhang *et al.*, [50] examined the correlations between bile acids and the gut microbiome in dairy cows with different glucose and lipid metabolism statuses, revealing a complex relationship between bile acids, gut microbiota, and host plasma concentrations of glucose and lipid metabolites. In addition, gut microbiota influences the expression of genes involved in lipid metabolism. For example, certain bacterial species regulate the expression of fibroblast growth factor 15/19 (FGF15/19), a hormone that inhibits bile acid synthesis in the liver, thereby affecting cholesterol levels in the host [51]. Dysbiosis can disrupt these regulatory mechanisms, leading to dyslipidemia, a condition characterized by abnormal levels of lipids in the blood, which is a major risk factor for cardiovascular diseases [42]. Indeed, several studies aimed at modulating gut microbiome in order to accelerate the host lipid metabolism. For instance, *Limosilactobacillus fermentum* HNU312 supplementation was found to enhance lipid metabolism pathways, reduce fat accumulation, and increase short-chain fatty acids in the gut microbiome, effectively mitigating the effects of a high-fat diet and

supporting lipid metabolism homeostasis by reducing lipid accumulation and inflammation [52]. A ketogenic diet was also shown to significantly alter glucose tolerance, lipid metabolism, peripheral tissue phenotype, and gut microbiome composition in healthy adults. The study highlighted the distinct impact of the ketogenic diet on lipid metabolism, contrasting with the effects of free-sugar restriction, particularly in terms of glucose tolerance and lipoprotein profiles [53]. Probiotic mixture Prohep was found to regulate hepatic lipid metabolism and the gut microbiome in diet-induced metabolic associated steatohepatitis (MASH) in mice, thereby controlling the progression from metabolic associated steatosis liver disease to MASH [54]. Indeed, combined with fecal microbiota transplants, probiotics show promise in restoring microbial balance and enhancing health outcomes. Urolithin A derived from pomegranate extract was studied for its impact on gut microbial metabolism of bile acids and cholesterol in overweight and obese individuals with positive results observed for individuals with mild dyslipidemia [55]. An intervention using resistant dextrin demonstrated enhanced glucose homeostasis and reduced lipid metabolism and inflammation levels compared to a high-fat, high-sugar diet group [56]. Furthermore, fungi- and algae-derived polysaccharides were found to modulate the gut microbiome, contributing to intestinal homeostasis and offering protective effects against metabolic associated fatty liver disease [57]. Indeed, heat-moisture-treated high-amylose rice flour can serve as a functional food ingredient for managing obesity and cholesterol-related disorders [58]. Whereas the negative impact on lipid metabolism homeostasis were observed in HTNV-infected and morphine-induced microbiome modulations [59, 60]. Surprisingly, the interplay between mitochondria and the gut microbiota, examined in the content of aging and brain homeostasis, was detected to potential contribution to the aging process [61].

Gut-Brain Axis

The relationship between the gut microbiome and host metabolism is bidirectional, meaning that the microbiome influences metabolic processes, and the host's metabolic state affects the composition and function of the gut microbiota [26].

Such bi-directional communication linking the gastrointestinal tract with the central nervous system means the enteric nervous system constitutes the gut-brain axis. Gut motility, intestinal permeability, enteroendocrine signaling, coupled with mucosal immune activity, which are intimately related to gut functions independently of the central nervous system [26], are eased via the enteric nervous system located within the gastrointestinal tract. The aforementioned nerve systems may be stimulated as a result. Certain signal compounds or neurotransmitters get fabricated via gut microbiota for such activation. Several investigations have probed the connection between neurological conditions and alterations within the gut microbiome.

Study of Vilela *et al.*, [62] explores the potential of gut microbiota as a therapeutic opportunity for managing Parkinson's Disease allowing to mitigate the disease progression or improve patient outcomes. Moreover, fecal microbiota transplantation and stem cell therapy were suggested as a promising approach to modulate gut-brain axis to address the root causes of Parkinson's Disease rather than just alleviating symptoms [63]. Leszek [64] confirmed the link between gut dysbiosis, inflammation, and the development of Alzheimer's Disease, suggesting that modulation of gut-brain axis can serve as a viable strategy for treating or preventing this neurodegenerative disorder. Whereas, Marrizoni *et al.*, [65] investigated markers of the microbiota-gut-brain axis, such as lipopolysaccharide and cytokines (IL1β, IL6, TNFα, and IL10), associated with Alzheimer's disease and identified specific gut microbiota signatures, specifically patients with cognitive impairment had significantly higher level of lipopolysaccharide and pro-inflammatory cytokines, suggesting potential biomarkers for early diagnosis. Another study underscored the complex relationship between gut microbiota and sleep disorders, revealing that certain bacterial populations, such as *Prevotella copri* and *Bacteroides fragilis*, were significantly linked to an increased risk of insomnia [66]. Cheng *et al.*, [67] delved into the biological mechanisms of gut microbiota-derived short-chain fatty acids in the context of depression and confirmed the significant influence of short-chain fatty acids on microbiota-gut-brain axis. Whilst in the study of Zhao *et al.*, [68] pre-administration of *Lacticaseibacillus rhamnosus* Fmb14 improved behavioral outcomes demonstrating protective capabilities against depression-like behaviors, through the modulation of the gut-brain axis. Bertossi *et al.* (Bertossi, 2024) examined the impact of *Akkermansia muciniphila* on mitigating weight gain and metabolic impairment induced by the antipsychotic drug olanzapine. The administration of *A. muciniphila* reduced weight gain by ~30% and improved glucose metabolism by 25%, suggesting the probiotic as adjunct therapy to counteract the metabolic side effects of olanzapine, offering a promising approach to managing antipsychotic-induced weight gain [69]. Similarly, supplementation of obese mice with butyrate-producing bacteria led to a reduction in body weight by ~15% and a 20%

improvement in glucose tolerance, highlighting their potential to modulate gut-axis brain and protect against obesity-related complications [70]. Study on the role of gut microbiota in neurodevelopmental disorders revealed a 50% reduction in total bacterial mass and a 40% decrease in key microbiota representatives such as *Bifidobacterium* and *Lactobacillus* in children with autism spectrum disorder [71, 72].

Conclusion

Summarizing the discussion, the human microbiome plays an important role in a wide range of biochemical and metabolic processes that sustain overall health. Indeed, the gut microbiome is closely associated to a range of functions as well as organs of host, even the brain, also it develops the gut-brain axis. Since discrete microbial factions with respective metabolites collaborate sophisticatedly, they impact brain function, behavior, with overall health substantially, spanning neurological, psychiatric, with metabolic ailments. Ailments like Parkinson's disease, Alzheimer's disease, depression, insomnia, and neurodevelopmental disorders manifest large promise within the management of probiotic interventions, interventions that modulate the gut-brain axis in addition to target gut dysbiosis. These perceptions underscore the auspicious prospect of employing gut microbiota-centered therapies for improving metabolic health plus addressing a wide spectrum of disorders. The treatments postulate the gut-brain axis is a key goal for forthcoming medicinal tactics.

Conflict of Interest

The authors declare no conflict of interest.

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Author Contributions

Amankeldi Sadanov and Baiken Baimakhanova conceptualized the study and supervised the overall structure of the manuscript; Irina Ratnikova, Vladimir Berezin, and Olga Lakh contributed to the literature review, data interpretation, and drafting of core sections, including microbiota mechanisms and health impacts; Saltanat Orazymbet, Andrey Bogoyavlenskiy, and Erik Shorabaev worked on the integration of metabolic and neurological aspects, including the gut-brain axis and related discussions; Gul Baimakhanova and Zere Turlybaeva assisted in organizing the methodology section, keyword refinement, and editing for clarity and coherence; Alma Amangeldi, Anel Omirbekova, and Aigerim Mamirova contributed to manuscript proofreading, citation formatting, and ensuring adherence to journal guidelines; Aida Kistaubayeva performed the final review of the manuscript, verifying consistency, scientific integrity, and formatting compliance. All authors read and approved the final version of the manuscript.

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