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Recent advances in prebiotics: Classification, mechanisms, and health applications

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ABSTRACT

Background: Prebiotics are non-digestible food components that selectively stimulate the growth and activity of beneficial gut microbes, offering a range of health benefits.
Findings: This review highlights recent advancements in prebiotic research, focusing on their classification, mechanisms of action, and health applications. It covers traditional prebiotics, such as inulin and oligosaccharides, as well as emerging prebiotics like polyphenols. The review also explores innovations in formulation technologies, including microencapsulation and synbiotics. Clinical evidence supporting the roles of prebiotics in digestive, metabolic, immune, and mental health is presented. Additionally, regulatory considerations and safety profiles are examined, emphasizing the current regulatory frameworks and the need for standardized guidelines.
Conclusion: Future research should prioritize personalized nutrition and precision medicine to fully harness the potential of prebiotics. This review lays the groundwork for continued innovation in prebiotic research and application, advancing our understanding of their evolving role and their impact on health.

1. Introduction

Prebiotics are non-digestible food components that selectively stimulate the growth and activity of beneficial gut bacteria, conferring various health benefits (Bisht et al., 2024). The International Scientific Association for Probiotics and Prebiotics (ISAPP) defines prebiotics as "a substrate that is selectively utilized by host microorganisms, conferring a health benefit" (Yoo et al., 2024). Unlike probiotics, which are live microorganisms, prebiotics serve as food for beneficial bacteria, supporting a healthy gut microbiome (Bevilacqua et al., 2024). Over the past few decades, the importance of prebiotics in human health has gained increasing recognition (Vallianou et al., 2020). By promoting the growth of beneficial bacteria, such as *Bifidobacteria* and *Lactobacilli*, prebiotics help maintain a balanced gut microbiota, which is crucial for overall health (Singh and Shaida, 2023). The benefits of prebiotics are extensive, spanning digestive health, metabolic health, immune function, and mental well-being (Selvamani et al., 2023). They enhance gut health by improving bowel regularity and alleviating symptoms of gastrointestinal disorders like irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD) (Ji et al., 2023). Prebiotics also play a role in metabolic regulation, aiding in weight management and improving glucose metabolism, which can help manage and prevent conditions like obesity and diabetes (Chaudhari and Dwivedi, 2022). Additionally, prebiotics support immune function by modulating gut-associated lymphoid tissue (GALT) and boosting the body's immune response (Chettri et al., 2022). Through the gut-brain axis, prebiotics can influence brain function and mental health, potentially alleviating symptoms of anxiety and depression (Chudzik et al., 2021; Kumar et al., 2023). Emerging research also suggests benefits in areas like cardiovascular health and allergy prevention (Mousavi Ghahfarrokhi et al.,

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2024; Romero and Duarte, 2023).

The concept of prebiotics began to take shape in the early 20th century, with researchers noting the beneficial effects of certain non-digestible food components on bowel function and the prevention of constipation (Arruda et al., 2022; Yoo et al., 2024). However, the term "prebiotic" was not coined until the 1990s, when Glenn Gibson and Marcel Roberfroid introduced it in 1995, defining prebiotics as “non--digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, thus improving host health” (Daliri and Lee, 2015; Maftei et al., 2024). This definition marked a significant shift from the broader category of dietary fibers, emphasizing the selective stimulation of beneficial gut bacteria (Chavan et al., 2023). Early research focused on identifying specific carbohydrates with prebiotic properties (Enam and Mansell, 2019), such as inulin and fructooligosaccharides (FOS) (Annapure and Jadhav, 2023; Younis et al., 2015), which were shown to promote the growth of *Bifidobacteria* and *Lactobacilli* in the gut, improving digestive health and enhancing immune function (Chakraborty et al., 2025).

Since the introduction of the term, the understanding of prebiotics has expanded (Chavan et al., 2023). While early research centered on inulin and FOS, other prebiotics, such as galactooligosaccharides (GOS), human milk oligosaccharides (HMOs), and resistant starches, have since been identified (Michalak, 2014; Raman et al., 2019). These compounds have similar beneficial effects on gut microbiota, further supporting the prebiotic concept. As research progressed, scientists began exploring the broader health implications of prebiotics (Cecchi et al., 2024), revealing that prebiotics influence not only gut health but also metabolic processes, immune function, and even mental health (Adithya et al., 2021). This expanded understanding led to a more comprehensive definition of prebiotics, encompassing a wider range of non-digestible food ingredients and their diverse health benefits (Diaz, 2023; Fouhy, 2014). Moreover, advancements in microbiome research have provided deeper insights into the mechanisms by which prebiotics exert their effects. The development of high-throughput sequencing technologies has enabled more detailed characterization of gut microbiota and their interactions with prebiotics (Bedu-Ferrari et al., 2022; You et al., 2022). These technological advances have been instrumental in demonstrating the selective nature of prebiotics and their ability to modulate gut microbiota composition and activity (Adak and Khan, 2019).

Several key milestones have shaped the progression of prebiotic research, marking significant discoveries and advancements in the field. In 1995, Gibson and Roberfroid formally introduced the term “prebiotic” and provided an initial definition that laid the foundation for future research (Cunningham et al., 2021a). By the late 1990s and early 2000s, inulin and FOS were identified and characterized as the first recognized prebiotics, with studies demonstrating their ability to selectively promote beneficial gut bacteria and improve digestive health (Vieira et al., 2013). In the early 2000s, prebiotic research expanded to include other oligosaccharides, such as GOS and HMOs, highlighting their unique prebiotic properties and potential health benefits (Shah et al., 2020). In 2004, the establishment of the ISAPP played a crucial role in standardizing definitions and advancing research in the field (Hill et al., 2014; Scott et al., 2020). The 2010s ushered in significant advancements in microbiome research and high-throughput sequencing technologies, providing a deeper understanding of the interactions between prebiotics and gut microbiota and enabling more comprehensive studies on their health effects (Cunningham et al., 2021b). In 2017, ISAPP refined the definition of prebiotics, emphasizing their selective utilization by host microorganisms and broader health benefits beyond gut health, reflecting the growing understanding of the diverse roles of prebiotics in human health (Sampaio et al., 2022). More recently, the focus of prebiotic research has shifted toward personalized nutrition, with efforts aimed at tailoring prebiotics to individual microbiome profiles (Ballini et al., 2023). Emerging studies emphasize the development of novel prebiotic compounds, their synergistic interactions with probiotics (synbiotics), and their applications in precision medicine (Butt et al., 2021). The evolution of the prebiotic concept reflects the dynamic and interdisciplinary nature of this field, propelled by continuous scientific discovery and technological innovation (Pires et al., 2024). From the early recognition of the health benefits of dietary fibers to the current, nuanced understanding of prebiotics’ mechanisms and health implications, the journey of prebiotic research reflects the broader trends in nutritional science and microbiome research (He and Shi, 2017). This review builds on this foundation by offering a comprehensive analysis of recent advancements and identifying future directions in prebiotic research.

Prebiotics are categorized based on their chemical structure and their ability to selectively stimulate the growth of beneficial gut bacteria (Patra et al., 2022; Teferra, 2021). Traditional prebiotics, such as inulin and FOS, are well-established for promoting digestive health and supporting immune function. Inulin—found in chicory root and garlic—and FOS—present in bananas and onions—resist digestion in the upper gastrointestinal tract and are fermented in the colon (Guarino et al., 2020). More recently, attention has shifted to emerging prebiotics like GOS and HMOs. GOS, found in milk, and HMOs, unique to human breast milk, promote the growth of beneficial bacteria and confer a range of health benefits (Liu et al., 2022). Other compounds under investigation for their prebiotic potential include resistant starches—present in foods like green bananas and whole grains—and polyphenols, which are abundant in fruits and vegetables (Althubiani et al., 2019). Classification criteria for prebiotics include resistance to digestion, fermentability by intestinal microbiota, selective stimulation of beneficial bacteria, and demonstrated health benefits to the host (Biswal et al., 2017). This structured framework enables the precise identification and classification of prebiotics, supporting the development of innovative dietary options for improving gut health and overall well-being (Franco-Robles et al., 2020).

While numerous reviews have explored prebiotics within specific contexts—such as their effects on gut health or metabolic outcomes—there remains a lack of comprehensive integration across key areas, including classification, mechanisms of action, clinical applications, and technological innovations. Notably, only a few reviews comprehensively address recent advances in novel prebiotic discovery, innovative delivery systems, regulatory considerations, and their relevance to personalized nutrition. This review addresses these gaps by providing a holistic and up-to-date analysis of prebiotic research, covering their classification, mechanisms of action, health applications, and technological innovations. Additionally, it examines safety, regulatory frameworks, and future directions, with a particular focus on their potential in advancing personalized health strategies.

2. Criteria for classification and categories of prebiotics

2.1. Criteria for classification

The classification of prebiotics depends on key functional and health-related criteria, ensuring that only substances with proven benefits are recognized as prebiotics. These criteria include:

2.1.1. Resistance to digestion and absorption

A prebiotic must resist digestion and absorption in the upper gastrointestinal tract to reach the colon, where it can be fermented by gut microbiota (Narsing Rao and Li, 2024).

2.1.2. Fermentation by intestinal microbiota

Prebiotics must be selectively fermented by beneficial gut bacteria (Jandhyala et al., 2015), leading to the production of health-promoting metabolites like short-chain fatty acids (SCFAs) (Грицинская, 2022).

2.1.3. Selective stimulation of beneficial bacteria

Prebiotics must selectively stimulate the growth and activity of beneficial bacteria (e.g., *Bifidobacteria* and *Lactobacilli*) without supporting the proliferation of pathogenic microbes—a key factor in sustaining a balanced and healthy gut microbiota (Gibson et al., 1995; Rastall and Gibson, 2015).

2.1.4. Health benefits to the host

Prebiotics must provide clear health benefits (Khangwal and Shukla, 2019), such as improved digestive function, enhanced immune response, better metabolic regulation, and other systemic health effects (Van Loo, 2006).

By adhering to these criteria, researchers can systematically identify and classify prebiotics (Kurian et al., 2022), supporting the discovery and development of new compounds that enhance gut health and overall well-being (Patra et al., 2022).

2.2. Categories of prebiotics

Prebiotics are categorized based on their chemical structure and their ability to selectively stimulate the growth and activity of beneficial gut microbiota (Davani-Davari et al., 2019; Gibson et al., 1999). Below are the traditional and emerging categories of prebiotics, along with their sources, mechanisms, and health benefits (as outlined in Table 1).

2.2.1. Traditional prebiotics

Traditional prebiotics have been extensively studied and are well-established for their health benefits, particularly for gut health (Cardoso et al., 2021). These include:

2.2.1.1. Inulin. Inulin is a type of fructan—a carbohydrate consisting of a chain of fructose molecules ending in a glucose unit (Akram et al., 2019; Moreira and Ponce, 2024). It occurs naturally in plants such as chicory root, Jerusalem artichoke, and garlic. Inulin resists digestion in the upper gastrointestinal tract and reaches the colon, where it is fermented by beneficial bacteria such as *Bifidobacteria* and *Lactobacilli* (Bevilacqua et al., 2024; Goutchtat, 2023). Studies have shown that inulin can improve bowel regularity, enhance calcium absorption, and support immune function (Abed et al., 2016; de Souza Oliveira et al., 2011).

2.2.1.2. Fructooligosaccharides (FOS). FOS are shorter chains of fructose molecules, also found in plants like bananas, onions, and asparagus (Mahalak et al., 2023). Like inulin, they are resistant to digestion in the upper gastrointestinal tract and undergo fermentation in the colon (de Paiva et al., 2023; Oku and Nakamura, 2017). FOS have been shown to promote the growth of beneficial gut bacteria, improve digestive health, and potentially lower the risk of certain infections (de la Rosa et al., 2019; Pengrattanachot et al., 2022; Rawat et al., 2024).

2.2.2. Emerging prebiotics

Emerging prebiotics are newly identified compounds gaining interest for their promising health benefits. These include various oligosaccharides and plant-derived substances.

2.2.2.1. Galactooligosaccharides (GOS). GOS are made of galactose units linked to a glucose molecule and are naturally present in human and cow milk (Cardoso et al., 2021; de Paulo Farias et al., 2019). GOS selectively promote the growth of *Bifidobacteria* and *Lactobacilli* and have been associated with improved bowel function, enhanced immune response, and reduced risk of infections in infants and adults (Balthazar et al., 2022; Patel et al., 2021).

2.2.2.2. Human milk oligosaccharides (HMOs). HMOs are complex carbohydrates unique to human breast milk (Wong et al., 2024) and represent its third-most abundant solid component after lactose and fat (Barile and Rastall, 2013). They play a key role in shaping the infant gut microbiota, promoting the growth of beneficial bacteria and defending against pathogens (Okburan and Kızıler, 2023; Wei et al., 2024). Studies are increasingly exploring the potential therapeutic applications of HMOs beyond infancy (Dinleyici et al., 2023).

2.2.2.3. Resistant starches. Resistant starches are starch molecules that resist digestion in the small intestine and reach the colon intact (Farooq and Dhital, 2024). Found in foods like green bananas, cooked and cooled potatoes, and whole grains, they act as fermentable fibers, producing SCFAs that promote colon health (Cereda and Andrade, 2023). They have been linked to benefits such as improved insulin sensitivity, enhanced satiety, and a reduced risk of colorectal cancer (Yan et al., 2024).

2.2.2.4. Polyphenols and other plant-based compounds. Polyphenols are bioactive compounds present in fruits, vegetables, tea, coffee, and wine (Bačić et al., 2023). Though not traditionally classified as prebiotics, growing evidence suggests they can modulate gut microbiota by promoting the growth of beneficial bacteria and inhibiting harmful ones

Table 1
Overview of Prebiotic Types, Their Sources, Mechanisms of Action, and Clinical Health Benefits.

Prebiotic Type	Source	Mechanism of Action	Health Benefits / Clinical Evidence	Ref*
Inulin	Chicory root, garlic, Jerusalem artichoke	Selective fermentation; short-chain fatty acid (SCFA) production; enhances gut barrier	Improves bowel regularity, enhances calcium absorption, and supports immune function	(Qin et al., 2023)
Fructooligosaccharides (FOS)	Bananas, onions, and asparagus	Promotes *Bifidobacteria*; SCFA production; immune modulation	Reduces the symptoms of irritable bowel syndrome, improves digestion, and supports allergy prevention	(Rahim et al., 2021)
Galactooligosaccharides (GOS)	Human and bovine milk	Selective fermentation promotes neurochemical signaling via the gut–brain axis	Enhances immune response, reduces anxiety/ depression, and supports infant gut health	(Johnstone and Kadosh, 2025)
Human Milk Oligosaccharides (HMOs)	Human breast milk	Supports infant-specific microbiota; anti-pathogenic; mucosal immunity	Promotes gut development, protects against infections, and supports long-term metabolic and immune health	(Van den Abbeele et al., 2024)
Resistant Starches	Green bananas, cooled potatoes, legumes	SCFA production (butyrate); improves gut barrier; regulates metabolism	Improves insulin sensitivity, reduces the risk of colorectal cancer, and aids in weight management	(Chen et al., 2024)
Polyphenols	Berries, cocoa, tea, wine	Modulates gut microbiota; antioxidant activity; reduces inflammation	Supports cardiovascular health, lowers low-density lipoprotein, and improves skin health	(Rodriguez-Mateos et al., 2024)
Xylooligosaccharides (XOS)	Corn cobs, bamboo shoots	Selective fermentation; gut pH modulation; promotes microbial diversity	Enhances lipid metabolism and reduces gastrointestinal inflammation	(Zhao et al., 2024)
Lactulose	Synthesized from lactose	Fermented to SCFAs; lowers colon pH; inhibits pathogens	Treats constipation and supports calcium absorption	(Karakan et al., 2021)

(Fernandes et al., 2023). Other plant-based substances, such as certain fibers and polysaccharides, are also under investigation for their prebiotic potential (Zhang et al., 2024).

3. Mechanisms of action

Prebiotics are non-digestible food components that confer health benefits by selectively stimulating the growth and/or activity of beneficial gut bacteria (Manning and Gibson, 2004). They shape the gut microbiota by serving as substrates for advantageous microbes, promoting their proliferation while inhibiting harmful species (Slavin, 2013). Prebiotics like inulin, FOS, and GOS are preferentially fermented by beneficial bacteria like *Bifidobacteria* and *Lactobacilli*, thereby supporting a balanced gut ecosystem vital for health (Guarino, Michele Pier Luca et al., 2020). This fermentation process fosters the expansion of beneficial microbes, which in turn suppress pathogens through competition for nutrients and the production of antimicrobial substances (You et al., 2022). By enriching beneficial bacteria, prebiotics enhance microbial activity and diversity (Macfarlane, 2009), leading to improved gut function and broader physiological benefits (Zimmermann et al., 2001). Additionally, promoting beneficial bacteria helps outcompete harmful bacteria, reducing their prevalence and potential pathogenic effects (Simon et al., 2021).

A key outcome of prebiotic fermentation is the production of SCFAs, such as acetate, propionate, and butyrate, which exert numerous positive effects. SCFAs fuel colonocytes, lower colonic pH to deter pathogens (Elshaghabee and Rokana, 2021), and possess anti-inflammatory properties that support mucosal integrity (Piccioni et al., 2023). Additionally, upon entering the bloodstream, they contribute to systemic benefits, including improved glucose homeostasis and lipid metabolism (Khare et al., 2018).

Prebiotics also strengthen the gut barrier by stimulating mucin production and enhancing epithelial tight junctions (Megur et al., 2022). SCFAs play a pivotal role in forming the protective mucus layer and reinforcing barrier integrity, thus reducing translocation of harmful substances into the bloodstream (Rastall et al., 2022). A robust gut barrier mitigates the risk of leaky gut syndrome, which is linked to inflammatory and autoimmune disorders (Davani-Davari et al., 2019; Tomasik and Tomasik, 2020).

Additionally, prebiotics modulate immune responses through interactions with GALT and by influencing immune cell activity. SCFAs and other fermentation products affect the activity of macrophages, dendritic cells, and T cells, promoting anti-inflammatory cytokine production and regulating immune balance (Lockyer and Stanner, 2019).

The gut microbiota itself is central to maintaining mucosal homeostasis and the structural integrity of the intestinal barrier, preventing the entry of pathogens and toxins (Wang et al., 2024). This microbial network cooperates with immune cells like dendritic cells and B lymphocytes to support immune function, reinforce barrier defenses, and promote tissue repair (Surapsari et al., 2023). The intestinal barrier—comprising a mucus layer and epithelial lining—serves as a primary defense mechanism, bolstered by mucins and antimicrobial peptides (Fig. 1) (Di Sabatino et al., 2023). Microbial imbalance, or dysbiosis, can disrupt this system, contributing to systemic inflammation and various diseases (Di Vincenzo et al., 2024). Thus, the association between gut microbiota and the immune system is vital for sustaining intestinal health and preventing disease (Ishiguro et al., 2023).

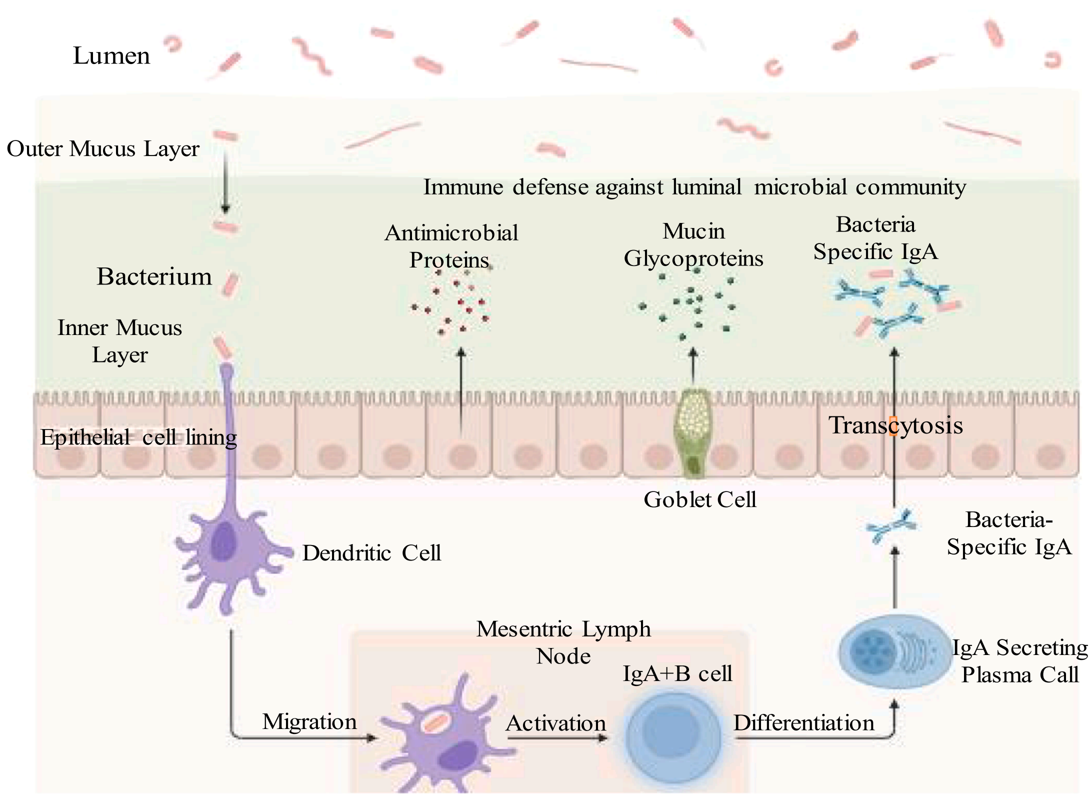

Fig. 1. Mucosal Homeostasis of the Gut Microbiota. This figure illustrates the structural and functional organization of the intestinal mucosal barrier and its interaction with the gut microbiota and host immune system. The outer mucus layer, enriched with mucins, antimicrobial proteins, and secretory immunoglobulin A (IgA), serves as the first line of defense against luminal microbes. Beneath it, the inner mucus layer offers additional protection to the epithelial surface. Dendritic cells within the lamina propria sample antigens and migrate to the mesenteric lymph nodes, where they activate B cells to differentiate into IgA-secreting plasma cells. These IgA molecules are then translocated to the gut lumen via transcytosis, where they contribute to microbiota regulation and mucosal immune defense. This dynamic interplay sustains mucosal homeostasis by maintaining a balance between microbial colonization and host immune responses (Created using Biorander.com).

By supporting a healthy gut microbiota, prebiotics enhance immune resilience and protect intestinal integrity (Blaut, 2002). Prebiotics play a crucial role in maintaining gut health and overall well-being through various mechanisms. Through modulation of microbial composition, SCFA production, barrier reinforcement, and immune regulation, prebiotics play a vital role in gut and systemic health (Fehlbaum et al., 2018). Understanding these mechanisms provides valuable insight into the potential health benefits of dietary prebiotics and supports their therapeutic use in managing gastrointestinal and systemic conditions.

4. Recent advances in prebiotic research

Recent advances in prebiotic research have significantly deepened our understanding of how these non-digestible food components support health (Shaikh and Sreeja, 2017). One key development is the identification and characterization of novel prebiotics beyond conventional types, such as inulin and FOS (Biswas and Mohapatra, 2023). Compounds like HMOs and resistant starches have emerged as promising candidates, demonstrating unique effects on gut microbiota composition and activity (Goel et al., 2006; Yadav et al., 2022). These newer prebiotics are being investigated for their specific roles in promoting beneficial bacteria, strengthening the gut barrier, and modulating immune function (Aghebati-Maleki et al., 2021).

Another major breakthrough is the development of synbiotics—combinations of prebiotics and probiotics designed to act synergistically to enhance gut health (Polanía et al., 2023). Studies indicate that specific pairings of prebiotics with compatible probiotic strains can produce enhanced benefits, surpassing those of either component alone (Panesar et al., 2022; Tripathy et al., 2023a). Tailored synbiotics are being formulated to address specific health conditions, such as IBS, obesity, and IBD (Monteagudo-Mera and Charalampopoulos, 2018; Simon et al., 2021), aiming to optimize therapeutic outcomes through complementary mechanisms.

The field is also moving toward personalized nutrition, acknowledging that individual responses to prebiotics are influenced by variations in gut microbiota composition and genetic background (Hathi et al., 2021). Ongoing research is identifying biomarkers to predict responsiveness, paving the way for customized dietary strategies (Gibbons et al., 2022). Such personalized interventions may enhance the efficacy of prebiotics in maintaining gut health and managing disease risk (Kok et al., 2023; Kviatcovsky et al., 2021).

These advancements have been greatly supported by progress in analytical technologies. Techniques such as high-throughput sequencing, metagenomics, and metabolomics now enable comprehensive profiling of microbial communities and their metabolic interactions (Misheva et al., 2021; Wu et al., 2022). These tools provide deeper insights into how prebiotics influence host physiology and microbiome dynamics (Puig-Castellví et al., 2023; Stincone et al., 2022), facilitating the identification of new compounds and the elucidation of their mechanisms of action (Bedu-Ferrari et al., 2022). As the field evolves, these technological innovations are expected to accelerate the development of more precise and effective prebiotic-based interventions (Sadeghi et al., 2023).

4.1. Advances in identification and synthesis

4.1.1. Novel sources and extraction methods

Recent progress in the identification and synthesis of prebiotics has underscored the importance of discovering novel sources and developing innovative extraction techniques. While traditional prebiotics, such as inulin and FOS, are well-known for their health-promoting properties (Pressley et al., 2024), the exploration of unconventional sources revealed new prebiotic compounds. HMOs, for example, have attracted considerable interest for their unique role in modulating infant gut microbiota and supporting immune function (Gan et al., 2023). Additionally, marine algae, fungi, and agro-industrial by-products are emerging as rich sources of prebiotic polysaccharides (Pérez-Escalante et al., 2022).

Extraction methods have also evolved significantly (Lefebvre et al., 2021). Conventional techniques often rely on chemical solvents, which can be inefficient and environmentally harmful (Yiping et al., 2024). In contrast, recent advances favor more sustainable approaches, such as enzyme-assisted extraction, ultrasonic extraction, and supercritical fluid extraction (Herzyk et al., 2024). These techniques improve both the yield and purity of extracted compounds while minimizing ecological impact. For instance, enzyme-assisted extraction employs specific enzymes to break down complex plant materials, releasing prebiotics more efficiently and selectively (Gao et al., 2023). Ultrasonic and supercritical fluid extraction techniques employ physical processes that reduce or eliminate the need for harsh chemicals, offering scalable and eco-friendly alternatives for industrial applications (Tang et al., 2024).

4.1.2. Synthetic and engineered prebiotics

The development of synthetic and engineered prebiotics is rapidly advancing, enabling the creation of tailored compounds with specific health benefits (Ma et al., 2022). Synthetic prebiotics are chemically designed to replicate or enhance the functions of their natural counterparts (Yadav and Shukla, 2020). Advances in carbohydrate chemistry and glycoscience have facilitated the accurate synthesis of compounds like GOS and xylooligosaccharides (XOS), which are engineered to selectively stimulate beneficial gut bacteria (Kang et al., 2020).

Engineered prebiotics represent a new frontier in prebiotic research, where biotechnology and genetic engineering are employed to create novel compounds (Fang et al., 2022). For example, microbial engineering enables the development of modified microorganisms (Du et al., 2021) capable of synthesizing complex oligosaccharides that are otherwise difficult to obtain through traditional means (Zhantlessova et al., 2022). Advances in metabolic engineering have also led to prebiotics with improved functional properties, such as greater resistance to digestion or enhanced microbiota-modulating activity (Jain et al., 2021; Murali and Mansell, 2024).

These breakthroughs in the identification and synthesis of prebiotics are expanding the toolkit for improving gut health and overall well-being (Shen et al., 2022). Whether derived from novel natural sources or synthesized through engineered methods, next-generation prebiotics offer promising potential for more effective, sustainable, and personalized dietary supplements and therapeutic strategies (Kerry et al., 2022). These innovations are paving the way for more targeted approaches to utilizing prebiotics in nutrition and medicine.

4.2. Technological developments

4.2.1. Microencapsulation techniques

Recent advancements in microencapsulation techniques have significantly enhanced the stability, bioavailability, and targeted delivery of prebiotics (Khandbahale, 2020). Microencapsulation involves enclosing prebiotic compounds in a protective coating, which shields them from adverse environmental conditions and allows for their controlled release in the gastrointestinal tract (Rokkam and Vadaga, 2024). Common microencapsulation methods include spray drying, freeze-drying, coacervation, and emulsion techniques (Ibraheem et al., 2024).

Spray drying, one of the most widely used techniques, involves spraying a liquid prebiotic solution into a hot chamber (Akbarbaglu et al., 2021), where it rapidly dries into fine particles encapsulated within a protective matrix (Piñón-Balderrama et al., 2020). This cost-effective method is suitable for large-scale production (Srivastava et al., 2022).

Freeze-drying (or lyophilization) involves freezing the prebiotic solution and then sublimating the ice under low pressure, resulting in a porous structure that preserves the integrity and activity of prebiotics (Ge et al., 2024; Küçükata et al., 2023). Coacervation and emulsion techniques use polymers to form a shell around the prebiotic particles, providing additional protection and enabling controlled release (Razavi et al., 2021).

These microencapsulation techniques extend the shelf life of prebiotics by protecting them from moisture, heat, and oxidation (Rodrigues et al., 2020). Additionally, they enhance the prebiotics' ability to reach the colon intact, where they selectively stimulate the growth of beneficial gut bacteria (Xie et al., 2023). By improving the stability and delivery of prebiotics, these technologies play a pivotal role in the development of effective prebiotic products (Zhang et al., 2020).

4.2.2. Delivery systems and formulations

Innovative delivery systems and formulations are pivotal to the technological advancement of prebiotics, ensuring effective administration and maximizing health benefits (Cunningham et al., 2021b). Traditional forms of prebiotic delivery, such as powders, capsules, and tablets, are increasingly supplemented by more advanced and versatile delivery methods (Gao et al., 2023). Functional foods and beverages are now being fortified with prebiotics, providing a convenient and enjoyable way to incorporate these beneficial compounds into daily diets (Hurtado-Romero et al., 2020). Prebiotic-enriched foods are being developed to address specific health concerns (Green et al., 2020; Mollakhalili-Meybodi et al., 2021), such as gastrointestinal disorders, immune dysregulation, and metabolic imbalances (Green et al., 2020). These products, including dairy items, cereals, and snack bars, are designed to appeal to a wide range of consumers, including those with dietary restrictions or specific health goals (Fabiano et al., 2021).

Additionally, prebiotic delivery systems are being tailored to enhance the synergistic effects of prebiotics and probiotics, collectively known as synbiotics (García-Montero et al., 2023). Synbiotic formulations combine specific prebiotics with compatible probiotic strains to promote the growth and activity of beneficial gut bacteria (Jiménez-Villeda et al., 2023). These formulations are available in various forms, including capsules, powders, and fortified foods, providing versatile options for consumers (Edwards et al., 2020).

Nanotechnology represents another innovative approach for prebiotic delivery. Nanoparticles and nanocapsules can encapsulate prebiotics, enhancing their solubility, stability, and bioavailability (Rostamabadi et al., 2021). This enables targeted and controlled release of prebiotics in the gut, optimizing their efficacy (Sun et al., 2023). Nanotechnology also offers the potential to create multifunctional delivery systems that simultaneously deliver prebiotics, probiotics, and other bioactive compounds (Sing et al., 2023).

Technological advancements in microencapsulation and delivery systems are revolutionizing the field of prebiotics (Neekhra et al., 2022), enhancing stability, bioavailability, and targeted delivery, thus improving accessibility and effectiveness for consumers (Tripathy et al., 2023b). As research and technology progress, these innovations will likely lead to more sophisticated and personalized prebiotic products, further enhancing their role in promoting gut health and overall well-being.

4.2.3. Limitations of current technological approaches

Despite the promising advances in microencapsulation and innovative delivery systems for prebiotics, several challenges remain. One of the major limitations is the stability of encapsulated prebiotics during processing, storage, and gastrointestinal transit (Singh et al., 2022). Environmental factors, such as temperature, humidity, and oxygen exposure, can compromise the protective coatings, leading to premature degradation or release of prebiotic compounds before reaching the colon (Camilleri, 2021).

Scalability is another concern, particularly with techniques such as coacervation and nanoencapsulation, which face high production costs and complex processing requirements, limiting their commercial feasibility (Ayyaril et al., 2023). Variability in release profiles also poses significant challenges. Achieving consistent, targeted release in the colon is difficult due to inter-individual differences in gut pH and microbiota composition (García et al., 2022). Moreover, the lack of standardization in encapsulation materials and techniques complicates comparisons between studies and may delay regulatory approval (Giordani et al., 2023).

Future research should focus on optimizing the stability, scalability, and precision targeting of encapsulated prebiotics to maximize their clinical efficacy and commercial viability.

5. Integration with other therapies

5.1. Synbiotics (Prebiotics + probiotics)

The integration of prebiotics with probiotics to form synbiotics marks a significant advancement in gut health therapies (Simon et al., 2021). Synbiotics combine prebiotics and probiotics in a synergistic manner to enhance the survival, colonization, and activity of beneficial gut bacteria (da Silva et al., 2021). By serving as a nutrient source, prebiotics promote the growth and function of probiotics, amplifying their positive effects on the host (Bisht et al., 2024). Thus, synbiotics support the nutritional needs of beneficial bacteria while promoting a balanced and optimized gut microbiota composition (Zheng et al., 2021). This dual-action strategy supports improved digestive health, enhanced immune function, and the management of gastrointestinal disorders.

Synbiotic formulations have demonstrated efficacy in relieving symptoms of IBS, reducing inflammation in IBD, and restoring gut microbiota balance (Zhang et al., 2021). Recent studies emphasizes tailoring synbiotic combinations to target specific conditions or populations—such as infants, older adults, or individuals with chronic diseases—to maximize therapeutic outcomes (Lee et al., 2024). These personalized formulations ensure optimal synergy between prebiotics and probiotics, advancing the potential for more effective and individualized interventions (Cunningham et al., 2021a).

5.2. Postbiotics and their synergy with prebiotics

Postbiotics—metabolic byproducts of probiotic bacteria—represent a growing area of interest in gut health therapeutics. These bioactive compounds, including SCFAs, enzymes, peptides, polysaccharides, and cell wall components, have demonstrated various health-promoting effects (Li et al., 2021). When paired with prebiotics, they form a synergistic relationship that further enhances gut health and systemic well-being (Vallianou et al., 2020). Prebiotics foster the growth of probiotic bacteria, which in turn produce postbiotics (Martyniak et al., 2021), creating a continuous supply of beneficial metabolites. SCFAs, for example, play key roles in reducing inflammation, strengthening gut barrier integrity, and supplying energy to colonocytes (Chaudhari and Dwivedi, 2022). The combined action of prebiotics and postbiotics contributes to a more stable and resilient gut environment (Shi et al., 2024).

Moreover, this synergy can improve the effectiveness of other therapeutic strategies (Mohd Fuad et al., 2023). In metabolic disorders such as diabetes and obesity (Vallianou et al., 2020), prebiotics enhance gut microbiota composition, while postbiotics influence metabolic pathways and mitigate inflammation (Shi et al., 2024). Together, they can produce better clinical outcomes than either component alone (Gurunathan et al., 2023).

Functional foods and supplements incorporating both prebiotics and postbiotics are under active development (Martyniak et al., 2021). These products aim to deliver a comprehensive set of bioactive compounds that work together to support gut and overall health. Innovations in formulation and delivery technologies are also being pursued to enhance the stability, bioavailability, and targeted release of these compounds (Salminen et al., 2021).

The integration of prebiotics with probiotics (synbiotics) and with postbiotics exemplifies the expanding frontier of microbiota-based therapies (Boyajian et al., 2024; Thorakkattu et al., 2022). These approaches leverage synergistic interactions to improve microbiota composition, strengthen gut barrier function, and modulate immune responses (Chiu et al., 2023). As research progresses, these strategies hold significant promise for the development of more effective and personalized treatments for a wide range of health conditions (Lê et al., 2022).

6. Health benefits and applications of prebiotics

6.1. The influence of prebiotics on digestive health and nutrition

Prebiotics are non-digestible food ingredients that confer health benefits by selectively stimulating the growth and activity of beneficial gut bacteria (Franco-Robles et al., 2020). They play a pivotal role in digestive health (Ribeiro et al., 2022), with a balanced gut microbiota linked to reduced inflammation, improved lipid metabolism, enhanced antioxidant production, and better insulin sensitivity—factors that collectively lower the risk of infections and chronic diseases (Chaudhary, 2024). Conversely, gut dysbiosis contributes to heightened inflammation, elevated lipopolysaccharide (LPS) levels, and disrupted short-chain fatty acid (SCFA) production. These changes are associated with insulin resistance and an increased risk of cardiovascular disease (Goyat and Bhatnagar, 2024). The gut–brain axis further underscores the connection between gut and systemic health, as microbial metabolites can influence neuroinflammation and metabolic regulation, linking microbial balance to neurological outcomes (Ashique et al., 2024). Therefore, maintaining healthy gut microbiota is essential for optimal health, highlighting the need for dietary interventions and therapeutic strategies to restore microbial homeostasis and mitigate disease risk (Fig. 2) (Chen et al., 2022).

6.1.1. Alleviation of gastrointestinal disorders

Prebiotics are effective in alleviating various gastrointestinal disorders (Guarino et al., 2020), including IBS (Ghoshal et al., 2022), IBD (Gandhi et al., 2021), and small intestinal bacterial overgrowth (SIBO) (Shah and Holtmann, 2022). By promoting the proliferation of beneficial bacteria like *Bifidobacteria* and *Lactobacilli*, prebiotics help maintain microbial balance, which is key to digestive health (Rodríguez-Pastén et al., 2022). This balance can reduce IBS symptoms like bloating, pain, and irregular bowel movements. In cases of IBD, prebiotics enhance the production of anti-inflammatory SCFAs—particularly butyrate—which support mucosal healing and reduce intestinal inflammation (Shin et al., 2023; Zhang et al., 2022). In cases of SIBO, prebiotics help restore a healthier microbial balance in the small intestine, thereby alleviating associated symptoms (Guilliams and Drake, 2021).

6.1.2. Improvement of bowel regularity

Prebiotics also play a vital role in promoting bowel regularity (De Fraia et al., 2023). Prebiotics such as inulin, FOS, and GOS are fermented by gut microbes to produce SCFAs, which stimulate peristalsis— the coordinated muscle contractions that move food through the intestines (Zhou et al., 2024). This fermentation process increases stool bulk and water content, easing stool passage and helping to prevent constipation (Araújo and Botelho, 2022). Regular intake of prebiotics has been associated with increased stool frequency and improved bowel function, contributing to a more consistent and comfortable digestive process (Sant'Anna and Ferreira, 2014). By alleviating gastrointestinal disorders and improving bowel regularity, prebiotics contribute significantly to maintaining a healthy and functional digestive system (Naseer et al., 2020; Rau et al., 2024; Yu et al., 2017). These benefits underscore the importance of integrating prebiotics into the diet—either through whole foods or supplements—to support gut health and overall well-being.

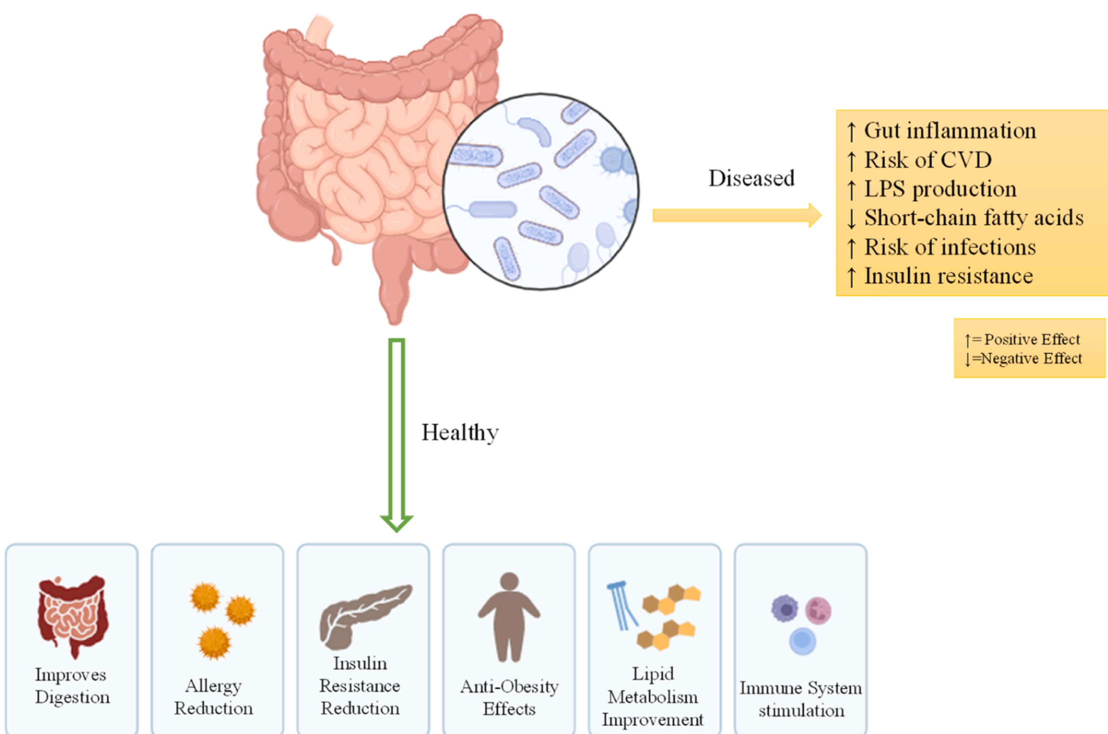

Fig. 2. Impact of Gut Microbiota Dysbiosis on Host Health and the Benefits of a Healthy Microbiota. This figure illustrates the physiological and pathological implications of gut microbiota composition. A balanced gut microbiota is associated with multiple health benefits, including improved digestion, reduced allergy symptoms, decreased insulin resistance, anti-obesity effects, improved lipid metabolism, and enhanced immune system stimulation. Conversely, dysbiosis or microbial imbalance is linked to negative outcomes, including increased gut inflammation, heightened risk of cardiovascular diseases (CVD), elevated lipopolysaccharide (LPS) production, reduced short-chain fatty acid (SCFA) production, increased infection risk, and worsened insulin resistance (Created using Biorander.com).

6.2. The influence of prebiotics on metabolic health

6.2.1. Impact on obesity and weight management

Prebiotics contribute to weight regulation by modifying gut microbiota composition and function (Khosravi et al., 2024). Obese individuals typically have a less diverse gut microbiome compared to lean individuals (Delzenne et al., 2011). Prebiotics such as inulin, FOS, and GOS selectively stimulate the growth of beneficial bacteria like *Bifidobacteria* and *Lactobacilli*, which support metabolic health and contribute to weight regulation (Hassan et al., 2024a). These microbes enhance the production of SCFAs, including acetate, propionate, and butyrate, which influence host metabolism. SCFAs serve as energy substrates and stimulate the release of appetite-regulating hormones such as glucagon-like peptide-1 (GLP-1) and peptide YY (PYY), promoting satiety and reducing overall energy intake (Alhabeeb et al., 2021).

Additionally, prebiotics help lower systemic inflammation, which is often elevated in individuals with obesity (Han et al., 2021). Chronic low-grade inflammation is closely linked to metabolic disorders, including insulin resistance and fat accumulation (Cheng et al., 2022). By restoring microbial balance, prebiotics help mitigate this inflammation, thereby supporting healthier weight management (Tokarek et al., 2021). Furthermore, they may reduce dietary fat absorption by binding to bile acids—compounds essential for fat digestion—and promoting their excretion (Liu et al., 2021).

6.2.2. Impact on glucose metabolism and diabetes management

Prebiotics positively influence glucose metabolism and diabetes management by improving gut health and metabolic function (Byndloss et al., 2024; Kumar et al., 2024). The production of SCFAs, such as acetate, propionate, and butyrate, during the fermentation of prebiotics by gut bacteria has been shown to improve insulin sensitivity, an essential aspect of effective glucose regulation (Huda et al., 2021). SCFAs activate receptors like G-protein-coupled receptor 41 (GPR41) and GPR43, which play critical roles in energy homeostasis and glucose metabolism (Nishida et al., 2022).

Prebiotics also interact with the gut–brain axis to influence the release of incretin hormones, such as GLP-1, which enhance insulin secretion and help lower blood glucose levels. This mechanism is particularly beneficial for individuals with type 2 diabetes (Cunningham et al., 2021), where insulin resistance and impaired insulin secretion are primary concerns (Beteri et al., 2024). Studies have demonstrated that regular prebiotic intake can result in lower fasting blood glucose levels and improved glycemic control (Guo et al., 2024).

In addition to their direct effects on glucose metabolism, prebiotics also contribute to reductions in body weight and adiposity, both of which are critical factors in diabetes management (Liu and Lou, 2020). By reducing inflammation and improving gut microbiota composition, prebiotics contribute to better metabolic health (Byndloss et al., 2024), leading to improved outcomes for individuals with diabetes, including reduced reliance on medication and a lower risk of diabetes-related complications (Li et al., 2020). Thus, prebiotics play a pivotal role in improving metabolic health by supporting obesity and weight management while positively influencing glucose metabolism and diabetes (Cani et al., 2021). Their ability to modulate gut microbiota, boost the production of beneficial metabolites such as SCFAs, and influence key metabolic hormones positions them as an essential element in dietary strategies aimed at improving metabolic function and promoting overall health (Vezza et al., 2020).

6.3. The influence of prebiotics on immune health

6.3.1. Modulation of immune responses

Prebiotics play a pivotal role in immune regulation by modulating the gut microbiota, a key player in immune system function (Liu et al., 2022). The GALT (Yeşilyurt et al., 2021), which includes structures such as Peyer's patches and intestinal lymphoid follicles, acts as a critical interface between the gut microbiota and the host immune system, orchestrating immune surveillance and response (Pujari and Banerjee, 2021). Prebiotics selectively stimulate the growth of beneficial bacteria such as *Bifidobacteria* and *Lactobacilli*, which interact with the GALT to enhance immune function (Ashaolu, 2020). One of the primary mechanisms underlying this modulation is the microbial fermentation of prebiotics into SCFAs, such as acetate, propionate, and butyrate (Yahfoufi et al., 2018). These SCFAs exert profound immunomodulatory effects. For example, butyrate has anti-inflammatory properties and helps maintain the integrity of the gut barrier, reducing the risk of systemic inflammation and immune activation (Peters et al., 2019). Moreover, SCFAs promote the differentiation and function of regulatory T cells, which play a key role in controlling immune responses and preventing autoimmune reactions (Rousseaux et al., 2023). Prebiotics also enhance the production of antimicrobial peptides and immunoglobulins (Lyu et al., 2023), reinforcing mucosal immunity and reducing pathogen load (Ashaolu, 2020). They also support the overall balance of the gut microbiota, which is essential for maintaining a well-regulated immune system. A balanced microbiota helps prevent the overgrowth of pathogenic microorganisms and reduces the incidence of infections and inflammatory conditions (Yeşilyurt et al., 2021).

6.3.2. Potential in allergy prevention

Prebiotics have demonstrated potential in the prevention and management of allergic conditions by modulating immune function and gut microbiota composition. Allergies arise from an exaggerated immune response to otherwise harmless substances, and early-life exposure to prebiotics may help shape immune development in a manner that reduces the risk of allergic diseases (Selle et al., 2024). It has been suggested that prebiotics support allergy prevention by promoting the growth of beneficial gut bacteria that support a well-regulated immune response (Bouchaud et al., 2014). For example, prebiotics can increase the abundance of *Bifidobacteria* and *Lactobacilli*, genera that have been correlated with healthier immune profiles and a lower incidence of allergic conditions. These microbes may help shift the immune balance from a pro-inflammatory T-helper 2 (Th2) profile—commonly linked to allergies—to a more regulated T-helper 1 (Th1) response, which is less reactive to allergens (Forouhandeh et al., 2024). Moreover, prebiotics modulate the production of specific cytokines and immunoglobulins that mediate allergic responses (Sharma and Im, 2018). By enhancing the production of regulatory cytokines and reducing the levels of pro-inflammatory cytokines, prebiotics help attenuate hypersensitivity to allergens (Akelma and Topçu, 2016). Some studies report that prebiotic supplementation in early childhood correlates with a lower incidence of eczema and food allergies, underscoring their potential in allergy prevention (Drago and Toscano, 2015). Thus, prebiotics support immune health by modulating immune pathways and contributing to the maintenance of a balanced gut microbiota, which is essential for reducing the risk of allergic diseases (Lopez-Santamarina et al., 2021).

6.4. The influence of prebiotics in mental health

6.4.1. Impact on the gut–brain axis and cognitive function

The gut–brain axis represents the bidirectional communication between the gastrointestinal tract and the central nervous system, emphasizing the influence of gut health on mental and cognitive functions (Fig. 3) (Chowdhury, 2024). Prebiotics contribute significantly to this connection by modulating the gut microbiota's composition and activity, thereby affecting brain health (Casertano et al., 2022). Prebiotics such as inulin, FOS, and GOS promote the proliferation of beneficial gut bacteria that ferment dietary fibers to produce SCFAs, including acetate, propionate, and butyrate. These SCFAs are pivotal in maintaining gut barrier integrity and mitigating systemic inflammation (Ashique et al., 2024). Notably, butyrate can cross the blood–brain barrier, exerting neuroprotective effects by enhancing neuronal health, reducing oxidative stress, and modulating neurotransmitter systems

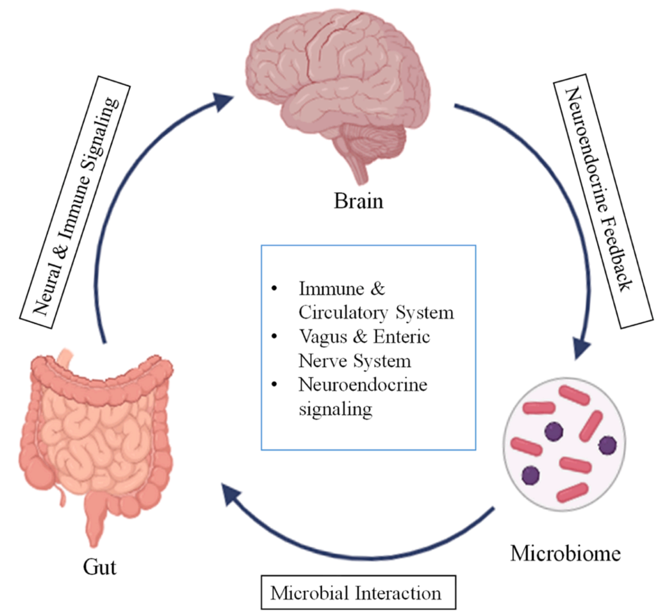

Fig. 3. The Gut–Brain–Microbiota Axis and Its Communication. This figure illustrates the intricate relationship between the brain and the gut, known as the gut–brain axis, which is mediated by the microbiome. This dynamic connection involves a complex network of systems, including the immune system, vagus nerve, circulatory system, enteric nerve system, and neuroendocrine system. The brain and gut communicate through these interconnected pathways, influencing various aspects of health and well-being (Created using Biorander.com).

(Kim et al., 2018). Additionally, prebiotics influence the gut–brain axis by affecting the production of neuroactive substances and signaling molecules (You et al., 2024). Beneficial gut bacteria can synthesize neurotransmitters such as serotonin and gamma-aminobutyric acid (GABA), which are crucial for mood regulation and cognitive processes (Chen et al., 2021). Thus, maintaining a balanced gut microbiota can positively influence cognitive functions such as memory, learning, and overall mental clarity (Liwinski et al., 2023).

6.4.2. *Impact on mood disorders*

Emerging research indicates that prebiotics may positively affect mood disorders such as depression and anxiety. These conditions are often linked to dysbiosis—an imbalance in the gut microbiota—which can lead to increased inflammation and altered neurotransmitter levels (Kosyra et al., 2024). Prebiotics can help restore a healthy gut microbiota balance, thereby addressing some of the factors contributing to mood disorders (Luqman et al., 2024). The modulation of gut microbiota by prebiotics can help reduce systemic inflammation—a common feature of mood disorders (Morán, 2023). By promoting the growth of beneficial bacteria that produce anti-inflammatory SCFAs, prebiotics may lower the levels of pro-inflammatory cytokines and contribute to improving mood (Kumar et al., 2023).

Additionally, prebiotics enhance the production and activity of key neurotransmitters (e.g., serotonin), which play a vital role in mood regulation and emotional well-being (Bogusz et al., 2023). Clinical studies have shown that prebiotic supplementation may alleviate symptoms of anxiety and depression by altering gut microbiota composition and enhancing the production of neuroactive compounds (Barkhidarian et al., 2021). While these findings are promising, further research is needed to fully understand the underlying mechanisms and validate the efficacy of prebiotics in managing mood disorders (Luqman et al., 2024).

Overall, prebiotics contribute significantly to mental health by influencing the gut–brain axis, supporting cognitive function, and alleviating mood disorders (Chen and Clark, 2021). By fostering a balanced gut microbiota, stimulating the production of beneficial SCFAs, and modulating neurotransmitter systems, prebiotics help promote overall mental and cognitive well-being (Souza et al., 2023). As research in this area evolves, prebiotics may present new opportunities for enhancing mental health and addressing mood-related conditions.

6.5. *Other emerging applications of prebiotics*

Prebiotics are increasingly recognized for their potential benefits beyond traditional digestive health applications (da Cruz et al., 2021). Emerging scientific evidence underscores their versatility and suggests that they may contribute to various domains of human health and wellness (Durazzo et al., 2020).

6.5.1. *Skin health*

Recent investigations have highlighted the potential role of prebiotics in promoting skin health (Mourelle et al., 2024). Similar to the gut, the skin harbors a complex and dynamic microbiota that influences its physiological condition and responsiveness to environmental stimuli (De Almeida et al., 2023). Prebiotics can support skin health by selectively stimulating the growth of beneficial skin microbiota and reinforcing the integrity of the skin barrier (Shirkhan et al., 2024). These effects are associated with improved moisture retention and enhanced protection against pathogenic organisms. Additionally, prebiotics exert systemic anti-inflammatory effects, which are relevant to the pathophysiology of skin conditions such as acne, eczema, and psoriasis (Kianmehr et al., 2022). In light of these findings, both topical and oral prebiotic formulations are being developed to capitalize on their dermatological benefits (Pistone et al., 2021).

6.5.2. *Cardiovascular health*

The influence of prebiotics on cardiovascular health represents a promising area of ongoing research. Prebiotics may contribute to cardiovascular risk reduction through multiple mechanisms (Oniszczuk et al., 2021). Notably, they have been shown to improve lipid metabolism by decreasing total cholesterol and low-density lipoprotein (LDL) cholesterol levels, an effect partly mediated by SCFAs that inhibit bile acid reabsorption (Olas, 2020). Additionally, SCFAs may promote vasodilation and thereby support blood pressure regulation (Pavlidou et al., 2022). The anti-inflammatory and antioxidative properties of prebiotics further enhance their potential to support cardiovascular function (Romero and Duarte, 2023). As research progresses, prebiotics may become an important component of dietary strategies aimed at preventing and managing cardiovascular diseases.

6.5.3. *Bone health*

Bone health is another area where prebiotics are showing considerable promise (Castaneda et al., 2020). Emerging evidence indicates that prebiotics may enhance mineral absorption, particularly of calcium and magnesium, which are critical for maintaining bone density and structural integrity (Harahap and Suliburska, 2021). Moreover, SCFAs produced through the fermentation of prebiotics have been shown to influence bone metabolism by promoting the activity of osteoblasts (bone-forming cells) and suppressing osteoclasts (bone-resorbing cells) (Varvara and Vodnar, 2023). Thus, prebiotics may contribute to the prevention of osteoporosis and other bone-related disorders, particularly among aging populations (Behera et al., 2020).

6.5.4. *Cancer prevention*

Prebiotics are also being investigated for their potential role in cancer prevention and treatment (Śliżewska et al., 2020). The beneficial gut bacteria promoted by prebiotics can produce SCFAs that exhibit anti-cancer properties (Mahdavi et al., 2021), such as the ability to inhibit tumor growth and promote apoptosis (programmed cell death) in cancer cells (Samanta, 2022). Additionally, the modulation of the gut microbiota by prebiotics can influence systemic inflammation and immune responses, both of which are key factors in cancer development and progression (Alam et al., 2022). Although this remains an emerging area of research, existing findings point to promising opportunities for incorporating prebiotics into cancer prevention and treatment strategies (Gutiérrez Salmeán et al., 2024).

6.5.5. Metabolic syndrome management

Prebiotics are increasingly recognized for their potential in the management of metabolic syndrome—a cluster of conditions including obesity, hypertension, insulin resistance, and dyslipidemia (Koumpouli et al., 2024). By positively altering gut microbiota composition and stimulating SCFA production, prebiotics have been shown to improve insulin sensitivity, reduce systemic inflammation, and support healthy weight management (Singh et al., 2024). Their beneficial effects on glucose and lipid metabolism position them as a valuable component in dietary interventions aimed at mitigating the risks associated with metabolic syndrome (Ramadhan and Rosdiana, 2024).

In summary, prebiotics are emerging as versatile agents with potential applications beyond gastrointestinal health (Gao et al., 2024). Their contributions to skin health, cardiovascular and bone function, cancer prevention, and metabolic regulation underscore the broad therapeutic potential of prebiotics (Hassan et al., 2024b). Continued research and innovation in these domains are essential to further elucidate their mechanisms and expand their role in promoting overall health and preventing diseases (Secchiero et al., 2024).

7. Safety and regulatory aspects of prebiotics

7.1. Comprehensive safety evaluations and toxicity studies

Ensuring the safety of prebiotics is paramount in their development and approval as dietary supplements or functional foods (Boyte et al., 2024). Comprehensive evaluations are required to confirm that these compounds do not pose health risks when consumed within recommended limits (Nataraj et al., 2024).

Safety evaluations typically involve examining a prebiotic's digestibility, absorption, metabolic byproducts, and potential side effects (Cruz Neto et al., 2024). Although prebiotics are generally considered safe at recommended doses (Malih et al., 2024), safety evaluations also address possible adverse effects, particularly gastrointestinal discomfort, which is commonly reported at high intake levels (Bhori et al.). Key areas of assessment include:

7.1.1. Acute toxicity

Acute toxicity studies evaluate the short-term effects of high doses of prebiotics (Szymczak-Pajor et al., 2024; Wang et al., 2024). Evidence from clinical and preclinical studies suggests a favorable safety profile, though data specific to prebiotics remain limited. Some studies involving probiotics, which are often co-administered or studied alongside prebiotics, may offer useful insights. For instance, a study on a multi-strain probiotic showed only mild gastrointestinal symptoms without serious adverse events (Saadati et al., 2024). Similarly, a preclinical study on *Limosilactobacillus fermentum* NCDC 400 reported no observable adverse effects in mice, even at high doses (10^{10} CFU/mouse/day) administered over 14 to 90 days, supporting its potential safety for clinical use (Nataraj et al., 2024). In contrast, a study on high-dose probiotic supplementation with *Lactobacillus casei* showed no significant benefits and reported potential increases in endotoxins and cytokines, raising concerns about its efficacy and safety in certain contexts (Scrivin et al., 2024). While these findings pertain to probiotics, they highlight the need for continued research on prebiotics, especially regarding the effects of high doses and their safety in diverse populations (Deshmukh and Patole, 2024).

7.1.2. Subchronic and chronic toxicity

Long-term studies assess potential cumulative effects from extended periods of prebiotic consumption (Prior et al., 2024). These studies are essential for identifying delayed or chronic adverse effects and establishing safe intake limits for long-term use (Vijaya et al., 2024).

7.1.3. Allergenicity

Safety assessments include tests to ensure that prebiotics do not cause allergic reactions in sensitive individuals (Bai et al., 2024; Shi et al., 2024). While rare, allergenic responses must be carefully monitored, especially in high-risk groups.

7.1.4. Genotoxicity and carcinogenicity

Studies assessing the genotoxic and carcinogenic potential of prebiotics are conducted to ensure they do not induce genetic mutations or promote cancer development (Rowaiye et al., 2024). Although the risk of such effects is generally considered low for prebiotics (Zaoui et al., 2024), these evaluations remain an important component of comprehensive safety assessments.

7.1.5. General toxicity studies

Toxicity studies using both animal models and human trials (Nataraj et al., 2023) help establish the maximum tolerable intake and determine the safety margins across a range of doses (Wampers et al., 2024). Toxicity assessments help establish safety margins and guidelines for safe consumption (Nataraj et al., 2024). Overall, prebiotics have shown a strong safety record when consumed as directed (Floch and Kim, 2024), but ongoing monitoring and post-market surveillance remain essential (Liang et al., 2024).

7.2. Ethical considerations and commercial misuse

Despite their safety and health potential, the commercialization of prebiotics raises important ethical and regulatory concerns. Unsubstantiated health claims are frequently made by food and supplement manufacturers, often targeting vulnerable populations such as infants, the elderly, and individuals with chronic conditions. Many commercial products labeled as “prebiotic-rich” lack standardized dosages, validated efficacy, or scientific substantiation, leading to consumer misinformation and exploitation.

Regulatory bodies such as the United States (U.S.) Food and Drug Administration (FDA) and the European Food Safety Authority (EFSA) require scientific substantiation for health claims; however, enforcement of these regulations is often inconsistent across regions (Misra and Raghuwanshi, 2022). The lack of harmonized global standards further contributes to confusion and misuse in the marketplace.

Ethical concerns also extend to clinical research, particularly when industry sponsorships introduce bias in study design, execution, or reporting (Liang et al., 2024). Transparent disclosures, rigorous peer review, and strong regulatory oversight are critical to upholding scientific integrity, protecting public trust, and ensuring that prebiotic innovations are safe, evidence-based, and ethically marketed.

7.3. Regulatory frameworks and approvals

The regulation of prebiotics differs globally, with regional agencies establishing standards for safety, efficacy, and labeling (Saji et al., 2024). Understanding and adhering to these frameworks is essential for product approval and consumer protection (Liang et al., 2024).

7.3.1. Regional regulations

7.3.1.1. United states food and drug administration (FDA). In the U.S., prebiotics are primarily regulated as dietary supplements (Riar and Panesar, 2024). While the FDA does not require pre-market approval, manufacturers must ensure product safety and comply with good manufacturing practices (GMP) (Dar et al., 2024). The FDA may take enforcement action if products are deemed unsafe or if health claims are misleading or unsubstantiated (Suleria et al., 2022).

7.3.1.2. European food safety authority (EFSA). In the European Union, prebiotics are regulated as food ingredients or supplements, and their safety is evaluated by the EFSA (Yadav et al.). The EFSA conducts thorough safety and efficacy evaluations before providing approval (Ghosh and George, 2023). EFSA issues scientific opinions on health claims (Patel and Goyal, 2013) and requires detailed data to support the safety, functional benefits, and intended uses of prebiotics (Kimes and Barberio, 2024).

7.3.2. Standardization and labeling requirements

7.3.2.1. Standardization. To ensure product consistency and quality, prebiotic formulations must undergo standardization (Thatcher and Garcia Quesada, 2024). This includes defining the structure, concentration, and purity of active compounds (Roe et al., 2022). International organizations and regulatory bodies offer guidelines to support the standardization of ingredients used in prebiotic products (Grumet et al., 2020).

7.3.2.2. Labeling. Accurate and transparent labeling is essential to inform consumers about a product's contents, usage, and potential risks (Spatola et al., 2024). Regulatory agencies mandate that labels clearly display ingredient lists, nutritional information, recommended dosages, and any known allergens (Schulze et al., 2024). Health claims must be substantiated by scientific evidence and approved by the relevant authorities to prevent misinformation and protect consumers (Thanopoulos et al., 2024). Additionally, labels must comply with regional regulations to ensure claims are truthful, not misleading, and consistent with approved guidelines (Boncinelli et al., 2024).

Overall, the safety and regulatory landscape for prebiotics depends on rigorous safety assessments and strict adherence to established regulatory standards. These measures ensure that prebiotic products are not only safe but also consistently formulated, properly labeled, and supported by credible evidence (Morán and Kilasoniya, 2024). A clear understanding of these aspects is essential for both manufacturers and consumers to ensure the safe and effective use of prebiotics (Schebesta and Purnhagen, 2024).

8. Future directions and research needs

8.1. Identification of new prebiotics

The discovery of new prebiotics is a rapidly evolving field focused on identifying novel compounds that offer potential health benefits (Smith, 2018). While traditional prebiotics such as inulin, FOS, and GOS have been extensively studied, current research is exploring a broader array of sources (Panesar et al., 2013). This includes investigating natural sources, including plants, fruits, vegetables, grains, and other dietary components (Chavan et al., 2023). Researchers are delving into underutilized plant-based substances and exotic fruits that may harbor unique oligosaccharides or polysaccharides with prebiotic potential (da Silva, 2019). Additionally, traditional diets and indigenous foods offer promising avenues for uncovering prebiotic compounds that have yet to be fully characterized.

Advancements in biotechnology are instrumental in the discovery and synthesis of new prebiotics (Dominguez et al., 2014). Enzyme engineering techniques enable the modification of carbohydrate structures to create novel prebiotic compounds. For instance, enzymatic processes can transform simple sugars into complex oligosaccharides with potential prebiotic effects (Chavan et al., 2023). Fermentation technologies also play a role, utilizing various strains of bacteria or yeast to produce prebiotics with distinct properties (Bisht et al., 2024). Moreover, synthetic biology facilitates the design and production of prebiotics through genetically modified microorganisms, allowing for the creation of custom-designed prebiotics that may offer specific health benefits (Mande et al., 2023).

Following the identification of potential new prebiotics, comprehensive functional characterization is essential to validate their efficacy and safety (Fentie et al., 2024). This process involves conducting in vitro fermentation studies to assess the fermentability of prebiotics by gut microbiota and measuring the production of SCFAs, which serve as indicators of effectiveness (Ballini et al., 2023). Functional studies also evaluate the impact of new prebiotics on the composition and activity of gut microbiota, examining shifts in microbial populations and overall gut health (Zeng et al., 2023). Additionally, clinical trials and observational studies are conducted to assess specific health benefits, such as improved bowel regularity, enhanced immune function, or reduced inflammation (Haranahalli Nataraj et al., 2023).

Before new prebiotics can be marketed or incorporated into dietary recommendations, they must undergo rigorous safety evaluations and validation processes (Merenstein et al., 2023). This includes conducting toxicity studies to ensure the absence of acute and chronic adverse effects (Easson et al., 2024; Mitrea et al., 2023). Allergenicity assessments are also crucial to confirm that the new prebiotics do not trigger allergic reactions or sensitivities in consumers (Anagnostou et al., 2023; Ballini et al., 2023; Capobianco et al., 2024). Additionally, new prebiotics must comply with regulatory standards set by food safety authorities (Chugh et al., 2023), necessitating the submission of evidence related to safety, efficacy, and quality control measures for approval by agencies such as the FDA or EFSA (Spacova et al., 2023).

The process of identifying new prebiotics often requires interdisciplinary collaboration among scientists from microbiology, biochemistry, nutrition, and pharmacology fields (Coates et al., 2024), as well as partnerships with industry and academic institutions to accelerate discovery and development (Mills et al., 2023).

8.2. Long-Term clinical trials

Long-term clinical trials are essential for comprehensively assessing the efficacy and safety of prebiotics over extended periods of consumption (Hradicka et al., 2023). While short-term studies offer valuable insights into immediate physiological responses, they are insufficient for evaluating the sustained benefits and potential risks associated with prolonged prebiotic use (Liu et al., 2023). A long-term research approach enables a deeper understanding of how prebiotics influence diverse health outcomes and helps ensure that their advantages outweigh any long-term adverse effects (Ji et al., 2023).

A primary objective of long-term clinical trials is to investigate the enduring health benefits of prebiotics (Maldonado Galdeano et al., 2019). While prebiotics have been shown to positively modulate gut microbiota and improve digestive health in the short term, their long-term effects on chronic conditions remain underexplored (Martinez et al., 2015). Extended studies should evaluate how prebiotics influence the progression or prevention of chronic diseases such as obesity, metabolic syndrome, cardiovascular health, and autoimmune disorders (Kleerebezem et al., 2019). By monitoring participants over months or years, researchers can determine whether short-term benefits persist and assess the role of prebiotics in long-term disease management (Chambers et al., 2019).

Safety evaluation is another essential focus of long-term trials (Sikorska et al., 2023). While short-term studies may not reveal all potential adverse effects (Piccioni et al., 2023), extended use could uncover issues such as gastrointestinal discomfort, nutrient malabsorption, or shifts in microbial balance that could have broader health implications (Chan et al., 2023). It is also important to monitor possible interactions between prebiotics and medications or supplements, ensuring that these interactions do not compromise treatment efficacy or overall health (Ayesha et al., 2023).

Long-term clinical trials should include diverse participant populations to enhance the generalizability of findings. Differences in age, gender, ethnicity, and health status can significantly influence individual responses to prebiotic interventions (Paquette et al., 2023). Including a broad demographic spectrum allows for tailored recommendations and helps identify population-specific benefits or risks (Li et al., 2024). For instance, elderly individuals may respond differently to prebiotics due to age-related changes in microbiota composition and health conditions, warranting targeted investigation (Yau et al., 2024).

Moreover, long-term studies should incorporate a wide range of outcome measures to comprehensively assess the impact of prebiotics (Rapoport et al., 2022). Beyond gastrointestinal health, researchers should assess metabolic markers, immune responses, cognitive performance, and overall quality of life (Gao et al., 2024). These comprehensive assessments will better capture the full spectrum of potential benefits.

Another key objective is determining optimal dosage and formulation (Zeraattalab-Motlagh et al., 2024). Long-term trials should evaluate the safety and efficacy of various delivery forms—such as powders, capsules, or food-based supplements—and identify the most effective dosing strategies (Kruth et al., 2024). Comparative studies of different formulations and dosages will support evidence-based guidelines for clinical and public use (Deshpande et al., 2007).

Finally, integrating long-term clinical trials with technological advances and interdisciplinary collaboration will be vital for future progress. Tools such as metagenomics and metabolomics can offer deeper insights into how prebiotics modulate microbiota dynamics and metabolic pathways over time (Hradicka et al., 2023). Additionally, collaborating with experts across nutrition, microbiology, pharmacology, and clinical medicine will support the design of robust trials that address complex health interactions (Patton and Guandalini, 2013).

Long-term clinical trials are indispensable for establishing the sustained safety and effectiveness of prebiotics (Radke et al., 2017). These studies must address key research priorities, including prolonged health outcomes, safety monitoring, demographic inclusivity, comprehensive outcome measures, dosage optimization, and the integration of emerging technologies (Neumer et al., 2021; Zhao et al., 2023). By addressing these needs, future research can provide critical insights to advance the use of prebiotics in promoting long-term health and wellness (Brown et al., 2022).

8.3. Personalized nutrition approaches

Personalized nutrition is an emerging strategy that customizes dietary interventions based on individual characteristics such as genetic makeup, gut microbiota composition, metabolic profile, and health status (Kviatcovsky et al., 2021; Siddique et al., 2022). This tailored approach aims to optimize nutritional benefits by aligning diet with each person's unique physiological needs (Zaukuu et al., 2023; Zilbauer et al., 2023). The integration of prebiotics into personalized nutrition is particularly promising, as the effects of prebiotics can vary significantly between individuals (Saxena et al., 2024).

A central component of personalized nutrition is microbiome profiling. The gut microbiota, which varies substantially across individuals, plays a critical role in mediating the health effects of prebiotics (Abavisani et al., 2024). Advances in sequencing technologies now enable comprehensive analysis of gut microbiota composition, facilitating the identification of how specific prebiotics influence different microbial communities (Bianchetti et al., 2023). By identifying individual microbiome profiles, researchers and healthcare providers can tailor prebiotic recommendations to enhance their effectiveness (Ramos-Lopez et al., 2024). This information allows for more precise prebiotic recommendations to enhance the growth of beneficial bacteria and support both gut and overall health (Kallapura et al., 2024).

Genetic and metabolic differences further contribute to individual variability in response to prebiotics (Bedu-Ferrari et al., 2022; Li et al., 2021). Personalized nutrition approaches take into account genetic variations that impact carbohydrate metabolism, gut function, and immune regulation (Neri-Numa and Pastore, 2020). For instance, polymorphisms in genes related to fiber digestion or SCFA metabolism may influence the body's ability to process prebiotics (Gibbons et al., 2022; Jakobsdottir et al., 2014; Peluzio et al., 2021). Metabolomic profiling also provides insight into how prebiotics affect various biochemical pathways, offering potential benefits for managing metabolic disorders such as obesity and diabetes (Megur et al., 2022).

The development of personalized prebiotic formulations represents a key innovation in this field (Vandeputte, 2020). By combining data from microbiome and genetic assessments, customized prebiotic products can be created to meet specific health needs—such as boosting the abundance of underrepresented beneficial microbes or targeting specific metabolic dysfunctions (Yeşilyurt et al., 2022). This approach maximizes the effectiveness of prebiotics by aligning them with each individual's unique biological profile, leading to more precise and beneficial outcomes (Singh and Natraj, 2021).

However, significant individual variability remains a challenge in optimizing prebiotic interventions. Factors such as age, diet, health conditions, baseline microbiota, and genetic differences can all influence how individuals respond to prebiotics (Bianchetti et al., 2023; Ramos Meyers et al., 2022). In particular, polymorphisms in genes associated with carbohydrate metabolism or mucosal immunity can modulate host–microbiome interactions, further contributing to differences in prebiotic efficacy (Li, 2023). This biological complexity complicates the development of one-size-fits-all dietary recommendations. To address this, future research should prioritize stratified approaches using predictive biomarkers and integrate advanced tools such as systems biology, machine learning, and longitudinal clinical trials to design more precise, individualized prebiotic strategies.

The integration of personalized nutrition with precision medicine offers a promising, comprehensive strategy to advance health management (Gray et al., 2020). Precision medicine utilizes detailed individual health information, including genetic, environmental, and lifestyle data, to tailor medical treatments and interventions (Gupta and Kumar, 2023). When combined with personalized nutrition, this approach creates a more holistic framework in which prebiotics can be used alongside other individualized therapies to more effectively address specific health conditions (Meral et al., 2024).

Achieving this integration requires coordinated efforts among researchers, healthcare providers, and technology developers to design and implement comprehensive, personalized health strategies (Gurry et al., 2018). Bringing personalized nutrition into routine clinical practice also involves overcoming several practical challenges (Song and Shin, 2022). For instance, the development of standardized and validated tools for assessing individual microbiome profiles and genetic factors is essential (Hughes et al., 2019). Moreover, healthcare providers must receive proper training and access to resources that enable them to interpret personalized nutrition data and apply tailored prebiotic recommendations effectively. Public health initiatives should also prioritize education, equipping individuals with knowledge about the benefits of personalized nutrition and how to access such services (Narduzzi et al., 2022; Tom, 2024).

Personalized nutrition approaches in prebiotics specifically involve tailoring dietary interventions based on an individual's microbiome composition, genetic and metabolic characteristics, and unique health requirements (Yeşilyurt et al., 2022). When integrated with precision medicine, these strategies enable the development of targeted prebiotic formulations designed to maximize health benefits (Kok et al., 2023). By overcoming implementation barriers and advancing supportive infrastructure, personalized nutrition has the potential to significantly enhance the effectiveness of prebiotic interventions and deliver improved, individualized health outcomes (Hernández-Calderón et al., 2022).

8.4. Integration with precision medicine

The integration of prebiotics into precision medicine represents a cutting-edge approach to health optimization, combining personalized dietary interventions with detailed individual health profiles (Bianchetti et al., 2023). Precision medicine aims to tailor treatments and lifestyle recommendations based on genetic, environmental, and lifestyle data (Shah, 2024), and incorporating prebiotics into this framework enhances its nutritional dimension (Clemente-Suárez et al., 2023).

A fundamental element of this integration is the development of comprehensive individual health profiles, including genomic data, microbiome composition, and health history (Hood and Price, 2023; Huang and Hood, 2019). These profiles allow for precise dietary interventions. For example, genetic differences can affect fiber metabolism, while microbiome profiling identifies which bacterial populations may benefit most from specific prebiotics (Murga-Garrido et al., 2021). Together, these data enable the development of personalized prebiotic recommendations tailored to an individual's specific needs and health conditions (Yang and Zhao, 2021).

One of the most promising intersections between prebiotics and precision medicine lies in the management of chronic conditions such as obesity, diabetes, and cardiovascular diseases (Shi et al., 2024). Personalized prebiotic interventions can be designed to modulate specific metabolic pathways that are disrupted in these conditions, offering a more targeted and effective therapeutic strategy (Singh et al., 2023). By analyzing an individual's genetic predispositions and metabolic profile, it becomes possible to select or formulate prebiotics that enhance glycemic control, regulate lipid metabolism, and reduce systemic inflammation (Bilal et al., 2022). This tailored approach offers a significant advantage over generalized dietary recommendations, with the potential to improve health outcomes through more precise and individualized care (Corb Aron et al., 2021).

Another critical aspect of this integration involves combining prebiotics with targeted drug therapies, a core component of precision medicine (Feng et al., 2020). Prebiotics can complement pharmacological treatments by enhancing drug metabolism, improving bioavailability, and mitigating adverse gastrointestinal effects through modulation of the gut microbiota (Peng et al., 2020). Realizing these synergistic benefits requires coordinated collaboration among researchers, clinicians, and pharmacologists to develop and implement integrated intervention strategies (Rodriguez-Arrastia et al., 2021).

Despite its promise, the incorporation of prebiotics into precision medicine presents several practical challenges (Sharpton et al., 2021). A key obstacle is the need for reliable and accessible diagnostic tools to assess individual microbiome compositions and genetic traits (Moreno-Indias et al., 2021). Advances in technologies such as high-throughput sequencing and metabolomics are crucial for generating the detailed biological information needed to support personalized prebiotic recommendations (Wensel et al., 2022). Additionally, clear evidence-based guidelines and standardized clinical protocols must be developed to help healthcare professionals effectively translate this information into practice (Adams et al., 2020).

To support implementation, healthcare providers require appropriate training and resources to interpret personalized data and deliver tailored nutritional interventions (Mechanick et al., 2020). Equally important is patient engagement—educating individuals about the benefits of personalized nutrition can enhance acceptance, adherence, and outcomes (Bush et al., 2020). Public health efforts should also prioritize making personalized nutrition services more widely accessible and affordable, helping to close equity gaps and improve population health at scale (Belardo et al., 2022).

Ultimately, the integration of prebiotics with precision medicine offers a powerful approach to health optimization by aligning dietary strategies with an individual's genetic, microbial, and clinical profile (Kok et al., 2023). This model includes the development of detailed health profiles, targeted disease management, and synergistic use of prebiotics with other precision-based therapies (Salehi and Emami, 2023). Addressing the logistical and educational challenges associated with implementation is critical for success (Pincelli et al., 2020). By harnessing the full potential of personalized nutrition within the framework of precision medicine, we can move toward more effective, individualized, and sustainable health solutions (Green et al., 2020).

8.5. Addressing gaps in current knowledge

Addressing current gaps in the understanding of prebiotics is essential to advancing the field and optimizing their use in health promotion (Lakshmanan et al., 2024). Although substantial progress has been made in elucidating the mechanisms and benefits of prebiotics, several critical areas remain underexplored, limiting their integration into evidence-based health and nutrition strategies (Kiousi et al., 2019).

A major knowledge gap lies in the lack of a detailed understanding of the mechanisms through which prebiotics exert their effects (Cavalcante et al., 2023). While it is well-established that prebiotics influence gut microbiota composition and promote the production of SCFAs, the precise molecular and physiological pathways involved are not yet fully understood (Vitetta et al., 2013). Further research is needed to elucidate how prebiotics affect microbial diversity, interspecies interactions, and the downstream impacts on host metabolism, immunity, and signaling pathways (Wang et al., 2023). A clearer mechanistic understanding will support the development of targeted interventions and improve the predictability of clinical outcomes (Korotkyi et al., 2020).

Another important area requiring attention is the long-term impact of prebiotic consumption. Most current findings are based on short-term studies that demonstrate improvements in bowel regularity, immune modulation, and metabolic markers. However, the sustainability of these benefits over time and any potential adverse effects remain largely unknown (Turroni et al., 2020). Longitudinal clinical trials are needed to assess the effects of chronic prebiotic intake on gut microbiota stability, nutrient absorption, and overall health outcomes (Bedu-Ferrari et al., 2022).

The differential effects of prebiotics across population subgroups—such as children, older adults, and individuals with conditions like diabetes or cardiovascular disease—also represent a critical area for further study (Bock et al., 2021; Oniszczuk et al., 2021). These groups may exhibit unique physiological responses to prebiotic interventions, necessitating specific formulations or dosages tailored to their needs.

Furthermore, the interaction of prebiotics with other dietary components and medications remains poorly characterized (Vernocchi et al., 2020). Since prebiotics do not function in isolation, understanding their synergistic or antagonistic interactions with probiotics, other fibers, or pharmaceuticals is essential for ensuring safety and optimizing therapeutic efficacy (Green et al., 2020).

Individual variability in response to prebiotics presents another challenge (Piccioni et al., 2023). Differences in genetics, microbiome composition, and lifestyle factors can influence prebiotic metabolism and outcomes (Nogal et al., 2021). Studies leveraging advances in genomics, metabolomics, and microbiome science is needed to uncover these interindividual differences and facilitate the development of personalized prebiotic strategies (Kok et al., 2023; Mishra et al., 2022).

Additionally, there is a pressing need for improved standardization and regulation of prebiotic products. Variability in the quality, potency, and composition of commercial prebiotics can affect both their efficacy and safety (Cunningham et al., 2021b). Establishing standardized protocols for product formulation, labeling, and quality control will help ensure consistent and reliable health outcomes. Research into robust, validated methods for evaluating prebiotic efficacy and bioactivity is also critical for advancing the field (Hurtado-Romero et al., 2020).

Thus, addressing current gaps in prebiotic research necessitates a comprehensive approach, including the exploration of detailed mechanisms of action, long-term clinical studies, evaluation across diverse populations, investigation of interactions with other dietary components and medications, consideration of individual variability, and the development of standardized product quality measures (Cardoso et al., 2021). By systematically tackling these areas, researchers and healthcare professionals can improve the understanding and practical application of prebiotics, ultimately enabling more effective and personalized health interventions (Routier et al., 2021).

Notably, despite a strong body of evidence supporting the health benefits of prebiotics, the literature also contains conflicting findings that warrant critical consideration. Notably, despite a strong body of evidence supporting the health benefits of prebiotics, the literature also contains conflicting findings that warrant critical consideration. For instance, while some studies reported significant improvements in glycemic control, mental health, and immune function following prebiotic intervention, others noted minimal or no effects—likely due to variations in study design, sample size, baseline microbiota, dosage, and duration of intervention. For example, Teparak et al. (2025) demonstrated that inulin supplementation significantly improved fasting blood glucose and insulin sensitivity in patients with type 2 diabetes, whereas Rein et al. (2022) observed no significant glycemic changes after a similar intervention, potentially reflecting differences in baseline microbiota and intervention length . Likewise, Eltokhi et al. (2020) reported reductions in anxiety symptoms following galacto-oligosaccharide intake, but Patel et al. (2022) did not find corresponding mental health benefits in a larger cohort. These discrepancies underscore the need for standardized clinical protocols and more rigorous control of confounding variables.

Moreover, most existing data are derived from short-term trials, limiting insights into long-term safety and efficacy. The field is also subject to publication bias, with studies reporting positive outcomes more likely to be published than those with null or negative findings. Recognizing these limitations is essential for building a more balanced and realistic evidence base for prebiotic research.

To overcome these limitations, future research should prioritize well-powered, longitudinal studies with transparent methodologies and standardized outcome measures. Such efforts will build a robust, nuanced evidence base that supports the integration of prebiotics into personalized nutrition and precision health strategies.

9. Conclusion and future prospects

Prebiotics hold significant potential for improving health by modulating the gut microbiota and influencing a wide array of physiological functions. Although considerable progress has been made in understanding their mechanisms and benefits, the field remains in an evolving stage, with several critical knowledge gaps to address. Deeper insights into the molecular mechanisms of action, evaluation of long-term safety and efficacy, and the development of population-specific interventions are key areas requiring further research.

The future of prebiotics lies in their integration into personalized nutrition and precision medicine. Leveraging advances in genomics, microbiomics, and metabolomics will enable healthcare professionals to tailor prebiotic interventions to individual biological profiles, thereby enhancing therapeutic outcomes. This personalized approach not only improves the effectiveness of prebiotic therapies but also opens new avenues for the prevention and management of metabolic, immunological, and gastrointestinal disorders.

Additionally, a more nuanced understanding of prebiotic interactions with dietary components, medications, and host-specific factors is essential. Variability in individual responses to prebiotics underscores the need for precision strategies. In this context, developing standardized methodologies for evaluating and regulating prebiotic products will be critical to ensure their quality, consistency, and consumer trust.

Future research must prioritize long-term, large-scale clinical trials to validate the sustained health benefits and safety of prebiotics across diverse populations. Equally important is the need for interdisciplinary collaboration among researchers, clinicians, industry stakeholders, and policy-makers to translate scientific findings into practical, evidence-based applications. Advances in data analytics and health informatics will play a pivotal role in deciphering individual variability and guiding personalized dietary recommendations.

In conclusion, prebiotics represent a promising frontier in health and nutrition. Their incorporation into personalized dietary strategies has the potential to significantly enhance human health and well-being. Continued research, innovation, and collaboration will be key to fully realizing the transformative potential of prebiotics in promoting optimal health outcomes and improving quality of life.

Declarations

This article is not under consideration for publication elsewhere.

Ethical statement

This study did not involve any human or animal subjects, therefore no ethical approval was required.

CRediT authorship contribution statement

Sajid Ali: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Investigation, Data curation. **Muhammad Hamayun:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Muhammad Siraj:** Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Sumera Afzal Khan:** Writing – review & editing, Validation, Software, Project administration, Investigation, Conceptualization. **Ho-Youn Kim:** Writing – review & editing, Visualization, Validation, Resources, Project administration, Funding acquisition, Conceptualization. **Bokyung Lee:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare no competing interests.

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Data availability

No data was used for the research described in the article.

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