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Modulation of Gut Microbiota Through Functional Foods to Reduce Low-Grade Chronic Inflammation

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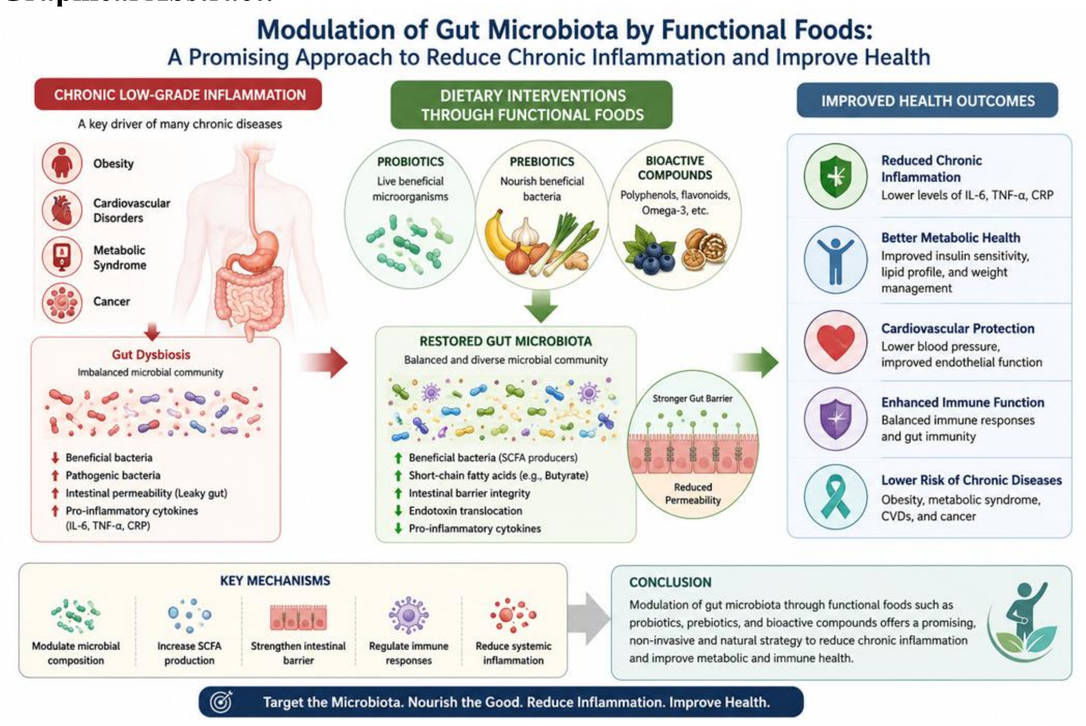
Abstract

Chronic low-grade inflammation is a condition that plays a significant role in the onset of and leads to many long-term diseases, including obesity, cardiovascular disorders, metabolic syndrome, and cancer. Emerging scientific evidence shows the role of the gut microbiota in regulating inflammatory responses and maintaining systemic health. The human gastrointestinal tract harbors a diverse and complex microbial community that plays a crucial role in regulating the immune system, metabolizing nutrients, protecting against pathogens, and maintaining intestinal barrier integrity. Changes in the makeup or function of this microbial community, known as dysbiosis, are linked to inflammation and metabolic issues. Dietary interventions have gained attention as an effective method for restoring microbial balance and controlling inflammation. Functional foods, such as probiotics, prebiotics, and bioactive compounds, can beneficially influence gut microbes by boosting the growth of health-supporting bacteria and overcoming harmful microbial activity. Probiotics enhance immune function and intestinal health, while prebiotics provide substrates that selectively nourish beneficial microbes. Advances in microbiome research and sequencing technologies have expanded understanding of host–microbe interactions, enabling the development of targeted nutritional strategies. Overall, modulation of gut microbiota through functional foods presents a promising, non-invasive approach to reducing chronic inflammation and improving metabolic and immune health.

Graphical Abstract:



Low-grade chronic inflammation

Inflammation is a natural biological response that helps the body maintain balance when exposed to harmful or pathogenic factors [1]. However, when the triggering stimulus persists or the inflammatory response fails to resolve properly, it can progress into a state known as chronic low-grade inflammation [2]. This condition is closely related to the rising incidence of serious long-term diseases, including obesity, cancer, and cardiovascular disorders, thereby increasing global morbidity and mortality rates. The growing burden of chronic diseases highlights the urgent need to better understand persistent inflammation, its underlying mechanisms, and effective preventive strategies [3]. Evidence now clearly shows that unresolved low-grade inflammation leads to the early stages of many age-related conditions [4]. Recent scientific contributions, including work supported by the International Life Sciences Institute Europe, have brought together current findings on acute and chronic inflammation and their connections with cardiometabolic, gut, and cognitive health [5]. Research also emphasizes the influence of dietary patterns and early-life nutrition on inflammatory status. Traditional reliance on circulating inflammatory markers, particularly fasting cytokines, has limitations due to their variability and low sensitivity [6]. As a result, innovative and integrated assessment methods are being explored. Advances in sequencing technologies have also transformed gut microbiome research, revealing a complex microbial ecosystem influenced by genetics, lifestyle, diet, and medical interventions [7][8]. *As shown below in Figure 1.* Alterations in microbial composition, known as dysbiosis, are associated with inflammatory and metabolic disorders, although causal relationships remain under investigation [9].

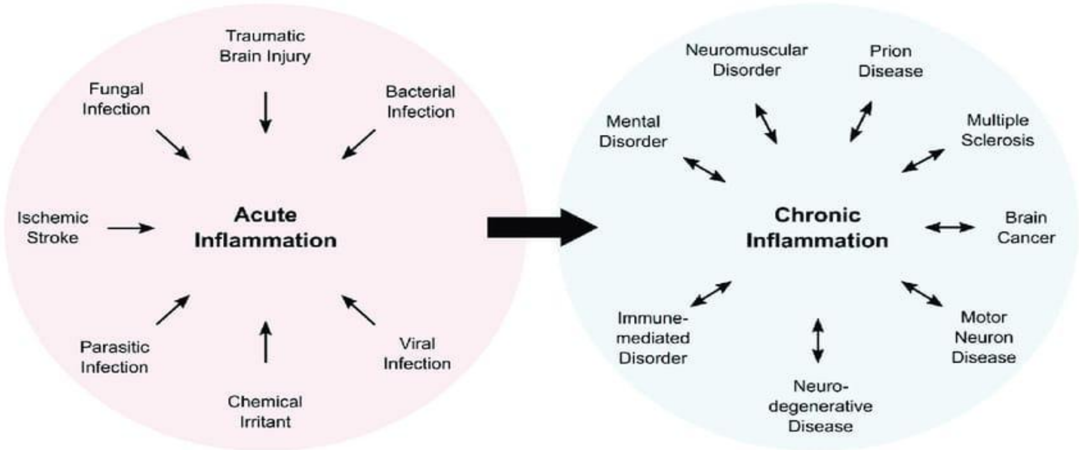


Figure 1: Schematic representation showing how acute inflammatory triggers can evolve into chronic inflammation, which is associated with persistent immune activation and diverse chronic neurological diseases.

Role of the normal gut microbiota

The connection between gut microbiota and human health has gained increasing scientific attention, with strong evidence indicating that a balanced intestinal microbial community is essential for maintaining overall well-being [10][11]. In healthy individuals, the gut microbiota is primarily dominated by two major bacterial groups, Bacteroidetes and Firmicutes [12]. Although microbial colonization in early infancy appears irregular, it gradually matures and becomes similar to the adult microbial profile by approximately three years of age [13]. Throughout life, microbial populations vary across different regions of the gastrointestinal tract, from the esophagus to the rectum [14]. Advances in genomic sequencing and bioinformatics have significantly enhanced the ability to analyze gut microorganisms, their functions, and their interactions with the host under both healthy and disease conditions [15]. A stable gut microbiota supports key physiological processes, including nutrient absorption, metabolism of drugs and foreign compounds, reinforcement of the intestinal barrier, immune system regulation, and defense against harmful pathogens [16][17]. Multiple factors influence microbial composition, such as mode of birth, dietary patterns during infancy and adulthood, and exposure to antibiotics [18]. Excessive or prolonged antibiotic use raises concerns due to long-term disruption of beneficial microbes and the spread of antimicrobial resistance [19][20]. Growing research also highlights that individual differences in microbial composition influence disease susceptibility. Functional classification of microbes based on host interactions offers valuable insight into microbiota-related health outcomes and may advance future therapeutic strategies [21].

Bacteria and the gastrointestinal tract: beneficial and harmful effects

Bacteria are distinctive microorganisms that perform numerous beneficial physiological functions within the human body [19]. Nevertheless, they can also become harmful when they move from the gastrointestinal tract to surrounding tissues, particularly following surgical procedures. Such bacterial translocation may result in contamination of surgical sites by intestinal microbes, including species such as *Escherichia coli*, *Proteus*, and *Klebsiella*. In addition, the consumption of contaminated food can lead to serious gastrointestinal infections, sometimes causing severe health complications [22]. Healthcare professionals, especially those caring for surgical patients, elderly individuals, infants, and immunocompromised patients, must understand both the protective and harmful roles of bacteria [23]. The human gastrointestinal tract contains an estimated 10^{14} microorganisms, greatly exceeding the total number of human cells. Recent research showed the essential role of gut microbiota composition in normal growth, immune system development, and central nervous system function [24]. Dysbiosis, or an imbalance in microbial harmony, is linked to various issues like digestive problems, obesity, heart disease, allergies, and brain disorders [25]. The intestinal microbiota, which has co-evolved with the host, plays a key role in preventing pathogen colonization through immune regulation and nutrient competition. Breakdown of this protective community increases susceptibility to infection and inflammation, highlighting the potential of microbiota-based therapies in disease prevention and treatment [26].

The impact of gut microbes on metabolic health

The worldwide rise in NCDs (non-communicable diseases), e.g., diabetes, heart disease, and cancer, has become a major public health concern over recent decades [27]. Besides overeating and lack of exercise, growing evidence shows gut microbes heavily influence obesity and metabolic issues. The composition of intestinal microorganisms varies widely both within the same individual over time and among different individuals [28]. Unfavorable alterations in this microbial balance may increase susceptibility to metabolic diseases. Experimental studies involving germ-free animals, antibiotic-treated models, and microbiota transfer have provided evidence that disruptions in gut microbial communities can influence metabolic outcomes [29]. Multiple biological pathways have been proposed to explain how gut microorganisms affect energy regulation, fat storage, and insulin sensitivity. This body of research highlights the potential link between gut microbiota and metabolic health, although definitive cause-and-effect relationships remain to be fully established [30]. More experimental and clinical research is needed to validate these links. Establishing a clear causal link would support the development of targeted dietary strategies aimed at modifying gut microbial composition for the prevention and management of metabolic disorders [31]. *As shown in figure 2.*

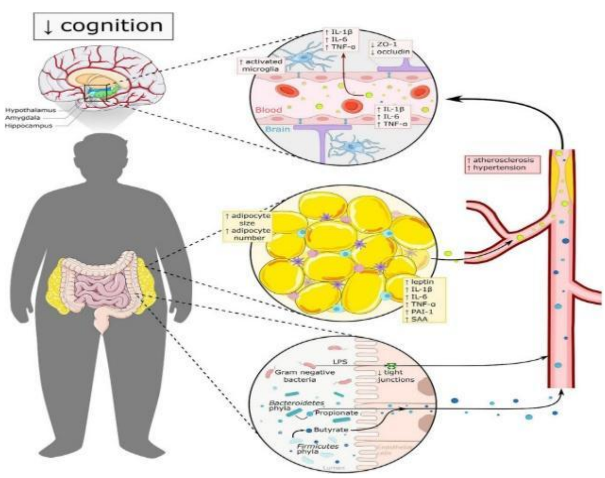


Figure 02: Integrated representation of gut microbiota, adipose tissue inflammation, and vascular pathways contributing to systemic inflammatory signaling that affects the brain and is associated with impaired cognitive function.

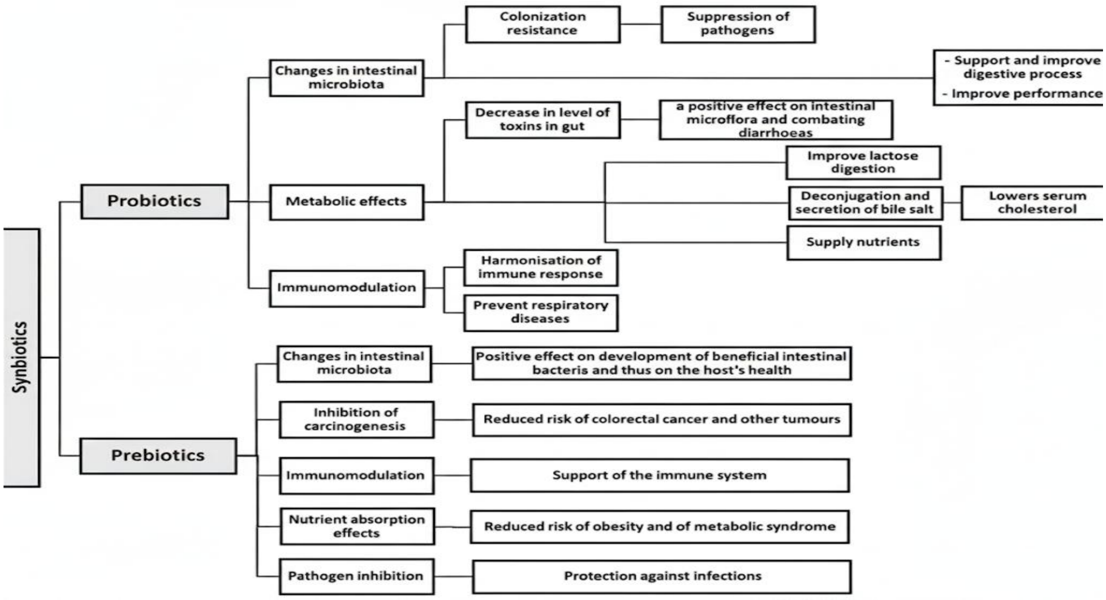
Development of functional foods:

Recent developments in the research of intestinal microbes have smoothed the way for functional foods. Functional foods often include lactic fermentation products and can be categorized into three groups on the basis of their action mechanism: probiotics, prebiotics, and biogenics [32][33]. Probiotics are live microorganisms, i.e., lactobacilli and bifidobacteria, that provide health benefits by improving the balance of intestinal bacteria. Prebiotics are indigestible food parts (like oligosaccharides and fibers) that boost beneficial gut bacteria, improving host health. Biogenics are bioactive compounds (e.g., immune peptides, plant flavonoids) that benefit health directly/indirectly by tweaking gut microbes. Functional foods contribute to bioregulation, including stress management, appetite control, and nutrient absorption; enhance biodefense by boosting immunity and reducing allergic responses; prevent diseases, i.e., diarrhea, constipation, cancer, high cholesterol, and diabetes; and slow aging by stimulating immunity and reducing mutagenesis, carcinogenesis, oxidative stress, intestinal putrefaction, and cholesterol accumulation [15][33]. The concept of probiotics was first proposed by Elie Metchnikoff in the early 1900s, who observed that consuming live microbes like *Lactobacillus bulgaricus* in yogurt or fermented milk improved gastrointestinal health [34]. Today, the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) define probiotics as "live microorganisms that, when administered in adequate amounts, confer a health benefit to the host" [35]. According to the International Scientific Association for Probiotics and Prebiotics (ISAPP). Probiotics must meet specific criteria, which include precise genus, species, and strain identification and proper nomenclature deposition in international culture collections. At least one human study demonstrates health benefits. Additionally, functional food products containing probiotics should provide sufficient live microorganisms to exert health benefits throughout the product's shelf life. Probiotics must also tolerate harsh gastrointestinal conditions, inhibit pathogenic microbes, support the host's immune system, and maintain viability under food processing conditions [36]. Bifidobacteria and lactic acid bacteria are the most widely researched and utilized probiotics, although other genera such as *Streptococcus*, *Enterococcus*, *Saccharomyces,* and *Bacillus* have also been commercialized [37]. *Lactobacillus* is one of the most studied genera, and recent taxonomic updates have introduced 23 new *Lactobacillus* genera, opening new avenues for research into their probiotic potential [38]. Colon-resident microflora perform several vital functions, making the gut a natural target for functional food development. For dairy applications, the best probiotic should resist acid and bile, modulate the immune system, adhere to epithelial cells, produce antimicrobial compounds, grow efficiently, and provide measurable health benefits. The specific mechanisms of probiotics vary between strains, while certain prebiotics (i.e., lactitol, inulin, lactulose, and xylitol) can enhance probiotic activity in the gut [39].

Impact of probiotics, prebiotics & synbiotics on human wellness

A complex community of microorganisms lives in the human gastrointestinal tract. Intestinal bacteria have co-evolved synergistically with their host, making them more than just commensal. Beneficial gut microbes perform multiple critical functions, including nutrient production, protection against pathogenic infections, and modulation of normal immune responses [40]. Therefore, maintaining or restoring a favorable balance in the intestinal microbiota is essential for host health. Introducing probiotics, prebiotics, or synbiotics into the diet supports gut microbiota balance and may be achieved through raw fruits and vegetables, fermented foods, dairy products, pharmaceutical formulations, or functional foods [41]. This review summarizes the current knowledge about the effects of probiotics, prebiotics, and synbiotics on human health. Highlighting action mechanisms and evidence from verified studies as shown in *figure-3*. The human gut contains thousands of bacterial species acquired during the co-evolution of humans and microbes [42]. Gut microorganisms outnumber human tissue cells by approximately tenfold, and metagenomics analyses reveal around 3.3 million microbial genes compared to about 23,000 human genes [43]. The role of gut microbiota in health and disease is increasingly recognized, with imbalances in conditions (i.e., autoimmune disorders, colon cancer, gastric ulcers, cardiovascular disease, functional bowel disorders, and obesity) [44]. Probiotics have shown promising results in clinical studies, and advances in microbiomes have sparked growing scientific, industrial, and public interest in their use. Genomics and bioinformatics may allow for personalized approaches to gut microbiota management [45]. Fermented foods, consumed for nearly 10,000 years, host unique microbial populations and provide bioactive peptides and metabolites beneficial to human health. These foods can influence the gut microbiome both transiently and long-term, either through metabolites or viable microorganisms [46]. Polyphenols, abundant in plant foods, are another class of bioactive compounds with potential health benefits, including cardiovascular protection, anti-inflammatory effects, and neuroprotection [45] [47]. Despite decades of research, human studies show variable responses due to interindividual differences, and mechanisms of action remain complex, involving gene regulation and protein activity at multiple body sites [48]. Future research should focus on identifying individuals who benefit most from polyphenols and elucidating the underlying molecular mechanisms. Clinical trials have investigated polyphenol-rich foods, such as chokeberry juice, for cardiovascular and metabolic outcomes, showing mixed results on traditional biomarkers.

Figure 03: Schematic representation of synbiotic action demonstrating how probiotics and prebiotics interact to modulate gut microbiota, promote metabolic



balance, regulate immune responses, and reduce the risk of infectious, inflammatory, and metabolic diseases.

Future direction

Functional food is the subject of extensive scientific research. Governments, academic institutions, and private research organizations worldwide are putting in significant efforts to understand how food ingredients and functional foods may help prevent disease and infection, improve health, reduce healthcare costs, and raise the standard of health for individuals. Nutrigenomics is an emerging field that examines the relationship between diet and disease development based on a person's genetic profile [49]. This allows for the prescription of a personalized functional diet tailored to an individual's specific genetic makeup. This approach is expected to greatly influence the future of new probiotic functional food products aimed at disease prevention. Next-generation probiotics will focus on population-level strategies or personalized nutrition strategies [50]. These will involve creating new probiotic formulations that include indigenous gut bacteria effective for humans. Future research should also focus on identifying functional lipids with superior antioxidant and hepatoprotective properties, such as olive oil- and flaxseed-derived bioactive compounds, and incorporating these ingredients into next-generation functional foods designed to prevent oxidative stress-related metabolic disorders and liver diseases [51]. The development of novel fermented functional foods using probiotic adjunct cultures, including *Lactobacillus rhamnosus*, is expected to expand the diversity of probiotic products while improving their nutritional value, microbial stability, and health-promoting potential [52]. Simultaneously, future functional meat products should emphasize improved quality, biosafety, and nutritional attributes through advanced processing technologies and stringent food safety strategies to enhance consumer confidence [53].

Innovative protein engineering approaches involving soy–whey hybrid proteins, sustainable whey–corn protein formulations, and microbial transglutaminase crosslinking are anticipated to generate functional protein ingredients with enhanced digestibility, biological value, and technological functionality for use in personalized nutrition [54,55]. Furthermore, the continued development of plant-based meat analogues with improved physicochemical, microbial, sensory, and nutritional characteristics will accelerate the transition toward sustainable dietary patterns while satisfying increasing consumer demand for alternative protein sources [56]. The incorporation of probiotic yogurt into personalized dietary interventions for weight management and metabolic health is also expected to become an important component of future functional nutrition programs targeting obesity and metabolic syndrome [57].

Artificial intelligence will increasingly facilitate the formulation of personalized functional foods by integrating dietary records, nutrigenomic profiles, metabolomic biomarkers, and predictive computational models to optimize nutritional recommendations for individual consumers [58]. Future functional foods should also be specifically designed for different physiological groups, including athletes, by incorporating targeted micronutrients such as zinc and other performance-enhancing bioactive compounds capable of improving endocrine regulation, muscle development, recovery, and overall physical performance [59]. Likewise, phytochemical-rich functional diets capable of modulating epigenetic mechanisms, including DNA methylation, may offer innovative nutritional approaches for reducing obesity, insulin resistance, and associated metabolic disorders [60].

The convergence of functional foods with modern biotechnology is expected to enable the production of nutritionally enhanced crops through advanced genome editing approaches, including CRISPR-based technologies, allowing the development of plant varieties possessing superior nutritional quality, enhanced bioactive compounds, and improved resistance to environmental stresses and diseases [61,62,63]. Alongside these innovations, ensuring microbiological safety, preventing food adulteration, and minimizing heavy metal contamination throughout food production systems will remain essential priorities for maintaining consumer confidence in future functional foods [64]. Moreover, continued advances in plant-based functional foods will contribute to sustainable nutrition by providing nutrient-dense alternatives with scientifically validated health benefits while reducing dependence on conventional animal-derived food products [65].

Artificial intelligence-assisted decision-support systems are expected to accelerate functional food innovation by improving ingredient selection, formulation optimization, supply-chain management, and commercialization strategies, thereby reducing development costs and enhancing market competitiveness [66]. Personalized nutrition will further benefit from AI-assisted healthcare platforms capable of integrating clinical information, wearable devices, and dietary monitoring systems to generate individualized nutritional recommendations that continuously adapt to changing physiological conditions [67]. Such intelligent nutritional platforms may also facilitate personalized rehabilitation strategies for patients recovering from musculoskeletal disorders by integrating functional foods with individualized physical recovery programs [68].

Future functional food development should increasingly incorporate sustainability principles that extend beyond environmental protection to include social wellbeing, responsible production systems, ethical ingredient sourcing, and equitable access to nutritionally enhanced foods across different populations [69]. In addition, functional foods specifically formulated for physically active individuals may optimize post-exercise recovery, bone mineral metabolism, hormonal stability, lean muscle preservation, and long-term athletic performance through evidence-based nutritional interventions [70].

The application of advanced risk assessment and governance frameworks throughout functional food production will strengthen quality assurance, traceability, regulatory compliance, and consumer safety while supporting global commercialization of innovative food products [71]. Emerging processing technologies, particularly ultrasonication-assisted microbial transglutaminase crosslinking and high-moisture extrusion, are expected to improve the structural integrity, digestibility, functional properties, and sensory acceptability of plant-derived protein ingredients and next-generation meat analogues [72].

Artificial intelligence will further transform functional food research through predictive modeling of nutrient–gene–microbiome interactions, enabling highly personalized dietary interventions capable of optimizing butyrate production, insulin sensitivity, glucose homeostasis, and gut microbial balance in individuals with metabolic disorders such as type 2 diabetes mellitus [75,77]. Similarly, precision fermentation integrated with artificial intelligence is anticipated to enable the efficient production of customized bioactive compounds, peptides, vitamins, probiotics, and postbiotics for individualized functional food formulations with enhanced therapeutic efficacy [75].

Future precision nutrition approaches will increasingly incorporate multi-omics technologies, including genomics, metabolomics, proteomics, transcriptomics, and microbiome analyses, to improve the understanding of host–diet interactions and facilitate the identification of reliable biomarkers for personalized nutritional interventions [78]. Polyphenol-rich nutraceuticals derived from agricultural by-products, including pomegranate peel, are expected to become valuable ingredients for future functional foods owing to their potential roles in improving glycemic regulation, enhancing insulin sensitivity, and reducing oxidative stress associated with metabolic diseases [79].

As environmental pollution continues to influence food quality, future investigations should evaluate the effects of microplastics, nanoplastics, and emerging contaminants on food safety, nutrient bioavailability, aquatic food resources, and overall human health to ensure the long-term sustainability of functional food systems [80,78]. Artificial intelligence-driven automation and machine learning technologies are also expected to improve food manufacturing, quality control, predictive maintenance, consumer behavior analysis, and intelligent decision-making throughout the functional food industry, resulting in greater production efficiency and product consistency [81,82].

Future public health strategies should integrate functional foods into nutritional programs designed for nutritionally vulnerable populations, including displaced communities, socioeconomically disadvantaged groups, and university students experiencing inadequate dietary intake, thereby addressing nutrition-related health inequities on a broader population scale [83,84]. Finally, successful implementation of next-generation functional foods will require multidisciplinary collaboration among nutrition scientists, food technologists, clinicians, public health professionals, policymakers, and industry stakeholders to promote sustainable food systems, improve workforce wellbeing, strengthen healthcare outcomes, and maximize the societal benefits of personalized nutrition worldwide [85].

Conclusion

The gut microbe has an important role in immune function maintenance and metabolic stability, while disturbances in its composition are strongly related to chronic low-grade inflammation and the development of long-term diseases. Evidence suggests that a food-based approach, particularly the use of functional foods, i.e., probiotics and prebiotics, can beneficially modulate intestinal microbial balance and reduce inflammatory responses. Advances in microbiome research have enhanced understanding of host–microbe interactions and their impact on health. Targeted nutritional strategies, therefore, offer a promising, non-invasive approach for improving gut health. Continued research is essential to optimize functional food applications for effective disease prevention.

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