Vol. 5 No. 2 (2026)

Pakistan Journal of Medical & Cardiological Review

https://pakjmcr.com/index.php/1/about

Online ISSN 3007-2387

Print ISSN 3007-2379

Gut Microbiota Modulation Through Functional Foods and Its Impact on Metabolic Health

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Keywords: Gut Microbiota; Functional Foods; Metabolic Health; Probiotics; Prebiotics; Short-Chain Fatty Acids; Polyphenols; Precision Nutrition; Type 2 Diabetes; Obesity

Received on 15 Apr 2026

Accepted on 12 May 2026

Published on 23 May 2026

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Abstract

The human gut microbiota plays a crucial role in regulating metabolic health through its interaction with diet, host physiology, and immune responses. Recent research has highlighted that the gut microbiome functions as a dynamic metabolic organ capable of converting dietary components into bioactive molecules that influence systemic metabolism. This study examines how functional foods including probiotics, prebiotics, synbiotics, postbiotics, and polyphenol-rich foods modulate gut microbiota composition and metabolic activity. Functional foods promote the growth of beneficial microbial taxa, enhance microbial diversity, and stimulate the production of key metabolites such as short-chain fatty acids (SCFAs) and secondary bile acids. These metabolites improve intestinal barrier integrity, regulate immune responses, and influence metabolic pathways associated with obesity, type 2 diabetes mellitus, and metabolic dysfunction-associated steatotic liver disease (MASLD). The review also explores emerging approaches such as precision nutrition, artificial intelligence–based dietary personalization, and digital health technologies for targeted microbiota modulation. Furthermore, current regulatory developments and scientific consensus on functional foods and gut health are discussed. Overall, dietary modulation of the gut microbiome represents a promising strategy for improving metabolic health and preventing chronic metabolic disorders.

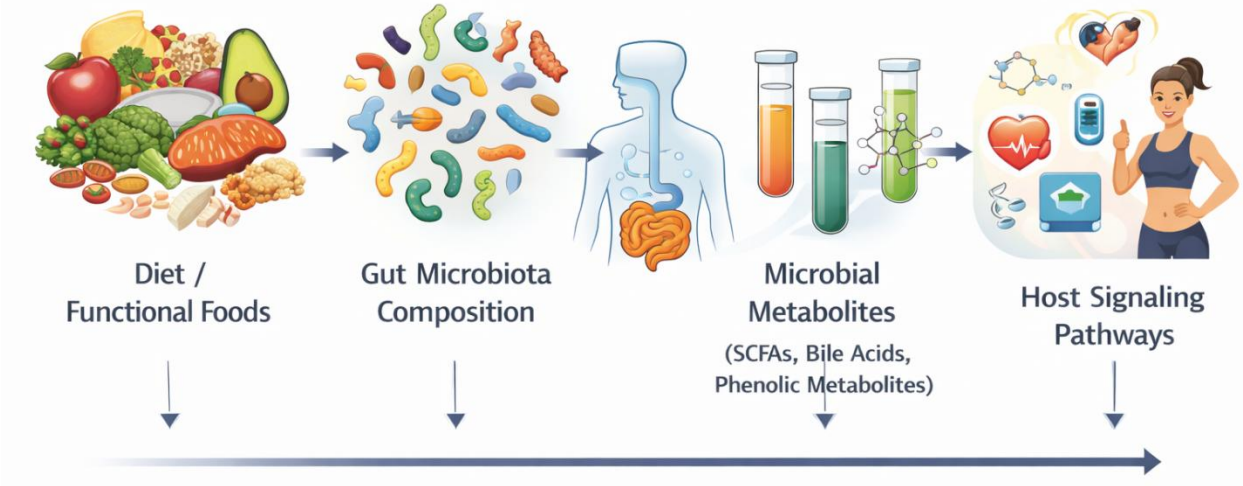
Introduction

The human gastrointestinal tract serves as the primary interface between the external environment and the internal physiological milieu, housing a complex and dynamic consortium of microorganisms collectively known as the gut microbiota (Vignesh et al., 2024). This microbial ecosystem, which includes bacteria, archaea, viruses, and fungi, has co-evolved with the human host to perform essential metabolic, immunological, and neurological functions (Beyer, 2025). Recent scientific advancements have transitioned the understanding of the gut microbiota from a

passive collection of commensals to a highly active "metabolic organ" that acts as a central interpreter of dietary intake, translating food components into molecular signals that regulate the host's neuro-endocrine-immune network (Dugas et al., 2018). As the global prevalence of metabolic disorders including obesity, type 2 diabetes mellitus (T2DM), and metabolic dysfunction-associated steatotic liver disease (MASLD) continues to escalate, the strategic modulation of this microbial community through functional foods has emerged as a transformative therapeutic and preventive paradigm (Pu et al., 2025).

Functional foods are defined as dietary products that provide health benefits beyond basic nutritional value due to the presence of bioactive compounds such as probiotics, prebiotics, and phytochemicals (Rezagholizade-shirvan et al., 2024). These components exert their effects by selectively shaping the microbial landscape, fortifying the intestinal barrier, and regulating the production of bioactive metabolites like short-chain fatty acids (SCFAs) and secondary bile acids (BAs) (Martin-Gallausiaux et al., 2021). The interplay between diet, the microbiome, and host metabolism is bidirectional; while dietary patterns are the primary determinants of microbial composition, the microbiota itself determines the bioavailability and metabolic impact of many dietary constituents (Sindhushree, 2025). This comprehensive report synthesizes cutting-edge evidence from 2024 to 2026, elucidating the biochemical mechanisms, clinical implications, and regulatory frameworks surrounding gut microbiota modulation through functional foods for the enhancement of metabolic health (Li et al., 2020). The interaction between diet, gut microbiota, and host metabolism represents a complex regulatory network influencing metabolic health. The conceptual framework of this diet–microbiome–metabolism axis is illustrated in Figure 1.

Figure 1: Conceptual Framework of the Gut Microbiota–Diet–Metabolic Health Axis



The Human Holobiont: Structural and Functional Foundations of the Gut Microbiota

The human body is increasingly viewed as a "holobiont," a biological entity comprised of the host and its symbiotic microbial communities. The adult gut microbiota contains between 10 and 100 trillion microorganisms, representing a genetic diversity that exceeds the human genome by at least 150-fold (Schippa & Conte, 2014). This diversity is essential for metabolic robustness, providing the host with enzymatic pathways that human cells lack, particularly for the degradation of complex polysaccharides and the synthesis of essential vitamins (Jelku, 2024).

Taxonomic Distribution and Ecological Metrics

The gut microbial landscape is dominated by two major bacterial phyla, Firmicutes and Bacteroidetes, which typically constitute over 90% of the total community. Other significant phyla include Actinobacteria, Verrucomicrobia, and Proteobacteria (Marco et al., 2022). In a state of eubiosis, or microbial balance, high levels of alpha-diversity (richness and evenness) and stable beta-diversity (compositional consistency) are hallmarks of health (Chen et al., 2024). Conversely, metabolic dysfunction is characterized by dysbiosis a loss of diversity and a shift toward pro-inflammatory or pathogenic taxa (GMFH Editing Team, 2025).

Table 1. Common Gut Microbiota Phyla and Their Metabolic Contributions

Phylum	Predominant Genera	Principal Metabolic Contributions	Metabolic Health Association
Firmicutes	Lactobacillus, Ruminococcus, Roseburia, Clostridium	Fiber fermentation; Butyrate production via various pathways	Often increased in obesity; critical for gut barrier integrity (Chen et al., 2024; Goni et al., 2016; Loi et al., 2017; Marco et al., 2022)
Bacteroidetes	Bacteroides, Prevotella	Complex carbohydrate degradation; Propionate synthesis	Essential for weight regulation and insulin sensitivity (Chen et al., 2024; Loi et al., 2017; Marco et al., 2022)
Actinobacteria	Bifidobacterium	Cross-feeding with butyrate producers; Vitamin B synthesis	Generally beneficial; reduced in T2DM and elderly populations (Guan et al., 2024; Lam et al., 2023; Marco et al., 2022)
Verrucomicrobia	Akkermansia	Mucin degradation; Signaling via Amuc_1100 protein	High levels associated with lean phenotypes and metabolic health (Beyer, 2025; Gopal et al., 2024; Marco et al., 2022)
Proteobacteria	Escherichia, Enterobacter	Pro-inflammatory signaling (LPS); Potential pathobionts	Elevated in MetS, T2DM, and chronic inflammation states (Marco et al., 2022; Ng et al., 2022; Universitas Diponegoro, 2024)

Beyond the bacterial component, emerging research in 2025 has highlighted the importance of the "non-bacterial" microbiome, including the virome (primarily bacteriophages) and the mycobiota (fungi) (Ritz, 2023). Reductions in virome diversity and altered phage-bacteria interactions are now understood to amplify bacterial dysbiosis, promoting inflammatory signaling and impairing metabolic homeostasis (Antohi et al., 2025). This ecological complexity necessitates a shift toward functional metagenomics rather than simple taxonomic profiling to understand the true metabolic capacity of the gut community (Garcia-Bonete et al., 2023).

The Pathophysiology of Metabolic Dysregulation and Meta-inflammation

The transition from health to metabolic disease is frequently described through the "multi-hit" theory, where environmental triggers, genetic predisposition, and microbial shifts converge to disrupt the host's metabolic balance (Hein et al., 2026). A primary driver is the consumption of a chronic high-fat diet (HFD) or Western-style diet, which functions as a detrimental "dietary sensor" that reshapes the microbial landscape (Universitas Diponegoro, 2024).

In this context, dysbiosis leads to several interconnected pathological pathways:

Enhanced Energy Extraction: Certain microbial profiles are more efficient at harvesting calories from the diet, particularly from otherwise indigestible fibers, contributing to positive energy balance and weight gain (Hsu & Tain, 2026).

Compromised Barrier Integrity: Disruptions in the intestinal epithelium allow the translocation of bacterial by-products most notably lipopolysaccharide (LPS) into the systemic circulation (Vignesh et al., 2024).

Metabolic Endotoxemia: Elevated systemic LPS levels trigger a state of chronic, low-grade "meta-inflammation" by activating Toll-like receptor 4 (TLR4) on immune cells and metabolic tissues such as the liver, adipose tissue, and the vascular endothelium (Mohammad & Thiemermann, 2021).

Incretin Dysfunction: Dysbiosis alters the secretion of gut-derived hormones like glucagon-like peptide-1 (GLP-1), which is essential for glucose-stimulated insulin secretion and satiety signaling (Eslam et al., 2020).

These mechanisms underscore why the gut microbiota is now targeted as a central therapeutic node in metabolic management (Ng et al., 2022).

Biochemical Mechanisms of Microbial Modulation

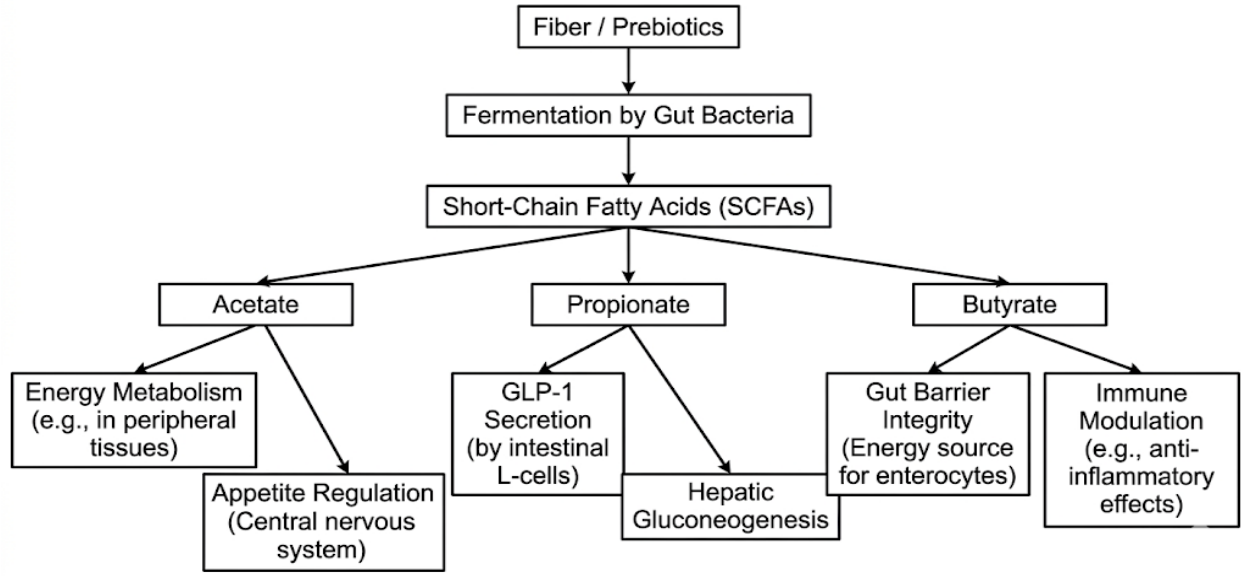
Functional foods exert their influence on metabolic health through several distinct but overlapping biochemical pathways. These pathways primarily involve the modulation of microbial metabolites that act as ligands for host receptors (Zhang et al., 2025)

Short-Chain Fatty Acids (SCFAs): The Metabolic Currency of the Gut

SCFAs primarily acetate, propionate, and butyrate are the metabolic end-products of the anaerobic fermentation of dietary fibers and resistant starches. These molecules represent a critical link between host nutrition and systemic homeostasis, serving as signaling molecules that regulate energy expenditure and immune function (Loi et al., 2017).

Acetate is the most abundant SCFA and is produced by a wide variety of gut bacteria. It can cross the blood-brain barrier and has been implicated in central appetite regulation, though its peripheral effects include serving as a substrate for lipogenesis and cholesterol synthesis (Fusco et al., 2023). Propionate is primarily produced by Bacteroides and Prevotella via the succinate pathway and is a significant substrate for hepatic gluconeogenesis. More importantly, propionate acts as a potent signaling molecule that inhibits fatty acid synthesis in the liver and promotes satiety (Schippa & Conte, 2014). Short-chain fatty acids serve as key mediators linking dietary fiber intake to host metabolic regulation. Their production pathways and physiological effects are summarized in Figure 2.

Figure 2: Production and Physiological Roles of Short-Chain Fatty Acids (SCFAs)



Butyrate, largely synthesized by the Firmicutes phyla (e.g., Faecalibacterium prausnitzii and Roseburia), is perhaps the most physiologically significant SCFA for metabolic health. It serves as the primary energy source for colonocytes and acts as a histone deacetylase (HDAC) inhibitor (Kase, 2022). This epigenetic modulation leads to several beneficial outcomes:

Barrier Fortification: Butyrate promotes the expression of tight junction proteins (occludin, ZO-1) and mucins, which are essential for maintaining the physical integrity of the gut barrier (Marco et al., 2026).

Immune Regulation: By inhibiting HDACs in T cells, butyrate promotes the differentiation of regulatory T cells (Tregs), thereby suppressing mucosal inflammation (Singh et al., 2023).

Hormone Induction: SCFAs activate G-protein coupled receptors, specifically GPR41 (FFAR3) and GPR43 (FFAR2), on enteroendocrine L-cells. This activation triggers the release of GLP-1 and PYY, enhancing insulin sensitivity and reducing food intake (Wen et al., 2023).

Table 2. Short-Chain Fatty Acids and Their Metabolic Impact

SCFA	Predominant Producers	Targeted Receptors	Metabolic Impact
Butyrate	Faecalibacterium, Roseburia, Eubacterium	GPR41, GPR109A	Colonocyte energy; Gut barrier integrity; HDAC inhibition; Treg activation (Kase, 2022; Loi et al., 2017; Marco et al., 2026)
Propionate	Bacteroides, Dialister, Phascolarctobacterium	GPR41, GPR43	Satiety signaling via PYY; Gluconeogenesis regulation; Hepatic lipid inhibition (Kase, 2022; Loi et al., 2017)
Acetate	Bifidobacterium, Akkermansia, Lactobacillus	GPR43	Lipid metabolism; Central appetite control; Anti-inflammatory signaling (Kase et al., 2024; Loi et al., 2017)

Bile Acid Biotransformation and Signaling

Bile acids (BAs) have been elevated from simple biological detergents to sophisticated endocrine signaling molecules. Primary BAs, such as cholic acid (CA)

and chenodeoxycholic acid (CDCA), are synthesized from cholesterol in the liver and secreted into the duodenum (Houten et al., 2006). While 95% of BAs are recycled through the enterohepatic circulation, the remaining 5% reach the colon, where they undergo extensive microbial transformation (Hou et al., 2022).

Microbial modulation of BAs involves two critical enzymatic processes:

Deconjugation: Bacterial bile salt hydrolases (BSH) cleave the glycine or taurine conjugates from primary BAs. BSH activity is widespread among phyla such as Firmicutes (e.g., Lactobacillus) and Actinobacteria (e.g., Bifidobacterium) (Wang, 2021).

7-alpha-dehydroxylation: A specialized subset of anaerobic bacteria (e.g., Clostridium scindens) removes the 7-alpha-hydroxyl group, converting primary BAs into secondary BAs like deoxycholic acid (DCA) and lithocholic acid (LCA) (Zhang et al., 2024).

BAs exert their systemic effects by activating two key receptors: the farnesoid X receptor (FXR) and the Takeda G protein-coupled receptor 5 (TGR5). Activation of FXR in the ileum induces the secretion of FGF15 (in mice) or FGF19 (in humans), which travels to the liver to inhibit de novo bile acid synthesis via the repression of CYP7A1, the rate-limiting enzyme (Caballero-Flores et al., 2023).

The composition of the BA pool is highly sensitive to diet. For instance, tea polyphenols and soluble fibers have been shown to inhibit 7-alpha-dehydroxylating bacteria, thereby reducing the levels of hydrophobic and potentially cytotoxic secondary BAs like DCA (Wang et al., 2022). Shifting the BA pool toward a more hydrophilic profile is associated with reduced systemic inflammation and improved metabolic markers (Lippolis et al., 2023).

Categorization of Functional Foods and Their Bioactive Components

Functional foods represent a diverse array of dietary products, categorized by their bioactive constituents and their specific interactions with the gut ecosystem (Mondal et al., 2021).

Probiotics and Next-Generation Probiotics (NGPs)

Probiotics are defined by the International Scientific Association for Probiotics and Prebiotics (ISAPP) as live microorganisms that, when administered in adequate amounts, confer a health benefit (Salminen et al., 2021). While traditional probiotics often involve Lactobacillus and Bifidobacterium species found in fermented dairy products like yogurt and kefir, the field is rapidly advancing toward Next-Generation Probiotics (NGPs) (Rezagholizade-shirvan et al., 2024).

NGPs are commensal bacteria identified through comparative metagenomic studies that exhibit specific metabolic functions (Marco et al., 2022). Akkermansia muciniphila is a prime example; it resides in the mucus layer and promotes gut barrier integrity. Levels of Akkermansia are consistently inversely associated with obesity, T2DM, and MASLD (Gopal et al., 2024). Other emerging NGPs include:

Faecalibacterium prausnitzii: Recognized for its high butyrate production and potent anti-inflammatory properties (Chen et al., 2024).

Research in 2025 has also explored the use of "engineered microbial consortia," where specific strains are combined to occupy distinct nutritional niches, providing a more stable and robust modulation of the gut environment (Joshi et al., 2023).

Prebiotics, Synbiotics, and Postbiotics

Prebiotics are non-digestible food components, primarily oligosaccharides (e.g., inulin, fructo-oligosaccharides/FOS, and galacto-oligosaccharides/GOS), that serve as substrates for beneficial bacteria (Guan et al., 2024). By selectively stimulating the growth of Bifidobacterium and other fermentative taxa, prebiotics enhance SCFA

production and lower colonic pH, which inhibits the proliferation of pathobionts (Bashiardes et al., 2018).

Synbiotics are formulations that combine probiotics and prebiotics to create a synergistic effect, enhancing the survival and colonization of the probiotic strain within the host. Clinical trials in 2025 have demonstrated that synbiotic supplementation can significantly reduce liver fibrosis markers and improve insulin sensitivity in MAFLD patients (Lam et al., 2023).

Postbiotics are a relatively new category, defined as inanimate microorganisms and/or their components (e.g., cell wall fragments, enzymes, or metabolites) that provide health benefits (Arslan et al., 2022). Postbiotics offer several logistical advantages, including greater shelf-life stability and safety for immunocompromised individuals, while still being able to trigger beneficial immune and metabolic responses (Drabsch & Holzapfel, 2019).

Phytochemicals and Secondary Metabolites: The Polyphenol Paradox

Polyphenols, found in fruits, vegetables, coffee, and tea, present a "bioavailability paradox". While these compounds have potent antioxidant and anti-inflammatory properties, most are poorly absorbed in the small intestine (Xie et al., 2026). Consequently, they reach the colon intact, where the gut microbiota acts as a pivotal vector, metabolizing complex polyphenols into simpler, more bioavailable phenolic acids (Harasym et al., 2025).

This interaction is bidirectional: polyphenols act as "prebiotic-like" agents, promoting the growth of beneficial taxa (e.g., Akkermansia and Bifidobacterium) while inhibiting pathogens like Clostridium and Enterococcus. For example, green tea catechins like EGCG are converted by the microbiota into simple phenolic acids that can enter the systemic circulation to exert metabolic effects (Wu et al., 2021).

Table 3. Bioactive Phytochemicals and Their Impact on the Gut-Metabolic Axis

Bioactive Compound	Primary Food Source	Microbial/Metabolic Effect	Health Benefit
Resveratrol	Grapes, Berries, Red Wine	Promotes Lactobacillus and Bifidobacterium; activates AMPK pathway	Improved insulin sensitivity; reduced liver steatosis (Beyer, 2025; Lam et al., 2023; Li et al., 2020)
EGCG (Catechins)	Green Tea	Inhibits 7-alpha-dehydroxylase; modulates FXR/TGR5 signaling	Reduced systemic inflammation; improved lipid profiles (Wen et al., 2023)
Quercetin	Onions, Apples, Kale	Exhibits probiotic-like activity; regulates NF-kappaB signaling	Mitigation of oxidative stress; anti-obesity effects (Beyer, 2025; Lam et al., 2023)
Curcumin	Turmeric	Modulates bile acid homeostasis via FXR and TGR5	Anti-inflammatory; neuroprotective effects (Li et al.,

			2020; Wen et al., 2023)
Ellagitannins	Pomegranates, Berries, Nuts	Converted to urolithins; promotes Akkermansia growth	Protection against obesity and T2DM (Beyer, 2025)

Strategic Targets in Metabolic Disease Management

The modulation of the gut microbiota has shown profound implications across a spectrum of metabolic disorders (Fan & Pedersen, 2021).

Obesity and Adipose Tissue Dysfunction

Obesity is characterized by a "low-diversity" microbiome often linked to an increased Firmicutes/Bacteroidetes ratio, which is associated with a greater capacity for energy harvest from the diet (Tilg et al., 2022). Dietary interventions utilizing functional foods high in fiber and specific probiotics (e.g., Lactobacillus gasseri) have been shown to reduce visceral fat, decrease adipocyte size, and downregulate adipogenic markers like PPAR-gamma (Lam et al., 2023).

Microbial metabolites like butyrate and propionate play a central role by:

Stimulating the release of satiety hormones (GLP-1 and PYY), thereby reducing caloric intake

Upregulating thermogenic genes in brown adipose tissue (BAT), increasing energy expenditure

Reducing the expression of pro-inflammatory cytokines in white adipose tissue (WAT), mitigating the chronic inflammation that drives insulin resistance (Loi et al., 2017).

Type 2 Diabetes Mellitus (T2DM) and Glycemic Control

In T2DM, dysbiosis is frequently characterized by a depletion of butyrate-producing bacteria and an increase in pro-inflammatory Proteobacteria. Functional foods address this imbalance by promoting a more eubiotic state. Clinical studies have shown that probiotic yogurt and multi-strain supplements can significantly reduce fasting blood glucose and HbA1c levels (Matusheski et al., 2021).

A critical discovery in 2025 revealed that the gut microbiota can influence the efficacy of common antidiabetic drugs. For instance, Metformin has been found to exert part of its glucose-lowering effect by promoting the growth of Akkermansia muciniphila and increasing SCFA production (Eslam et al., 2020). Furthermore, specific microbial metabolites like imidazole propionate have been identified as markers of early cardiovascular and diabetic risk, providing a new target for precision interventions (Ng et al., 2022).

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD/MAFLD)

MASLD, affecting over 25% of the global population, is fundamentally a disease of the gut-liver axis. Dysbiosis-induced intestinal barrier dysfunction allows the translocation of LPS and other pathogen-associated molecular patterns (PAMPs) to the liver via the portal vein, where they trigger the activation of Kupffer cells and the subsequent development of steatohepatitis and fibrosis (Joshi et al., 2023).

Functional foods, particularly fermented products and polyphenol-rich diets, have shown promise as adjunctive strategies for MASLD. The newly proposed "Dietary Index of Gut Microbiota" (DI-GM) provides a scoring system to evaluate how dietary components impact microbial diversity and MASLD risk (Pu et al., 2025).

Table 4. Dietary Index of Gut Microbiota (DI-GM) Components and Liver Health Impact

DI-GM Component	Classification	Effect on Gut Microbiota	Impact on MASLD/MAFLD
Fermented Dairy	Beneficial	Increases probiotic abundance; reduces pathobionts	Lowered risk of hepatic steatosis (Kase et al., 2022; Pu et al., 2025)
Whole Grains / Fiber	Beneficial	Enhances SCFA production; maintains gut barrier	Reduced systemic inflammation (hs-CRP) (Kase et al., 2022; Loi et al., 2017)
Coffee / Green Tea	Beneficial	Modulates bile acid pool; antioxidant effects	Inhibition of liver fibrosis progression (Kase et al., 2022; Wen et al., 2023)
Processed / Red Meat	Unfavorable	Promotes pro-inflammatory taxa; reduces diversity	Increased risk of liver inflammation and BMI (Kase et al., 2022)
High-Fat Diet (at least 40%)	Unfavorable	Induces dysbiosis; compromises gut barrier	Direct driver of hepatic lipid accumulation (Kase et al., 2022; Sindhushree, 2025)

Clinical evidence from 2025 suggests that a 7-10% weight reduction achieved through microbiota-targeted dietary patterns can lead to the resolution of steatohepatitis and the improvement of liver fibrosis (Tilg et al., 2022).

Precision Nutrition: AI and the Future of Individualized Modulation

The "one-size-fits-all" approach to nutrition is rapidly being replaced by precision nutrition, which accounts for the vast inter-individual variability in microbial composition, host genetics, and environmental factors (Dugas et al., 2018).

Multi-omics Integration and AI Algorithms

Advances in artificial intelligence (AI) and machine learning (ML) have enabled the integration of massive biological datasets to generate personalized dietary recommendations (Sempionatto et al., 2022). By analyzing gut microbiome sequencing, genetic traits (e.g., FTO and TCF7L2 polymorphisms), and real-time metabolic data from continuous glucose monitors (CGMs), AI models can predict how an individual will respond to specific functional foods (Moore, 2020).

For example, research in 2025 has highlighted "digital twin" systems that can accurately calculate post-meal blood sugar levels and cardiometabolic risk by learning non-linear associations between nutrients and physiological responses (Ahmed et al., 2024). This personalized approach is particularly effective for managing carbohydrate intolerance and IBS, with some studies reporting a 39% reduction in symptom severity when using AI-generated dietary plans (Qasrawi et al., 2025).

Digital Health and Real-Time Monitoring

The integration of digital health technologies including wearable sensors and AI-powered mobile apps allows for the real-time monitoring of food intake and its immediate impact on metabolic biomarkers. This instant feedback loop improves

patient adherence and empowers consumers to take a proactive role in managing their gut-metabolic health (Gopal et al., 2024).

Regulatory Frameworks and Scientific Consensus (2025-2026)

As the market for functional foods and biotics grows, regulatory agencies and scientific organizations have established clearer definitions and safety standards (Abdul Manan, 2025).

FDA: Modernizing Labels and Nutrient Claims

In 2025, the U.S. Food and Drug Administration (FDA) finalized the updated "healthy" nutrient content claim for food labeling. This update aligns the term "healthy" with current nutritional science, emphasizing the inclusion of foundational food groups like fruits, vegetables, and whole grains, while setting strict limits on added sugars, sodium, and saturated fats (FDA, 2024). Furthermore, the FDA's "Closer to Zero" initiative and new proposed regulations for Generally Recognized as Safe (GRAS) substances ensure that functional ingredients undergo rigorous safety assessments before reaching consumers (Arnold & Porter, 2025).

EFSA: Stringent Standards for Novel Foods

The European Food Safety Authority (EFSA) introduced significant changes to its novel food regulations in 2025. These updates impose stricter toxicology and allergenicity requirements for "next-generation" ingredients, such as precision-fermented proteins and nanomaterials (EFSA, 2025

ISAPP: The 2026 Consensus on Gut Health

A landmark event in 2026 was the publication of the ISAPP consensus statement on the definition and scope of "gut health". The expert panel proposed a definition of gut health as "a state of normal gastrointestinal function without active gastrointestinal disease and gut-related symptoms that affect quality of life" (Bischoff, 2024). This definition is structured around six domains, providing a comprehensive metric for evaluating the efficacy of functional foods in clinical research (Marco et al., 2026).

Table 5. The Six Domains of Gut Health according to the ISAPP 2026 Consensus

Domain	Scope of Assessment	Clinical/Research Metric
Digestive Physiology	Nutrient assimilation; transit time; motility	Stool consistency (Bristol Scale); power output thresholds (Exermove Platform, 2025; Marco et al., 2026)
Gut Microbiome	Community structure; metabolic potential	alpha-diversity; SCFA levels; pathobiont presence (Chen et al., 2024; Marco et al., 2026)
Intestinal Epithelium	Physical/chemical barrier function	Permeability markers; tight junction protein levels (Marco et al., 2026; Vignesh et al., 2024)
Mucosal Immunity	Interface between microbiome and host immune cells	Cytokine profiles (IL-6, TNF-alpha, IL-10) (Ghanbari et al., 2024; Marco et al., 2026; Universitas Diponegoro, 2024)
Subjective Experience	Absence of distressing symptoms	Quality of Life (QOL) surveys; symptom diaries (Guan et al., 2024; Marco et al., 2026)
Extrinsic Factors	Influence of diet, stress, and lifestyle	Dietary Index of Gut Microbiota (DI-GM) (Kase et al., 2022; Marco et al., 2026)

Chrono-nutrition and Rhythmic Modulation of the Microbiota

Recent research in 2025 and 2026 has underscored that when we eat is as significant as what we eat. The gut microbiota exhibits diurnal rhythms that are tightly linked to the host's circadian clock (Guan et al., 2024).

Intermittent Fasting (IF) and Microbial Rhythms

Intermittent fasting and other eating rhythmicity strategies have gained attention for their ability to reshape microbial rhythms and improve metabolic health (Salminen et al., 2021). These patterns support health by:

Restoring the rhythmic fluctuations of beneficial taxa that regulate lipid and glucose metabolism

Enhancing gut hormone secretion and intestinal barrier function during fasting periods

Modulating the interaction between the circadian system and the hypothalamic-pituitary-adrenal (HPA) axis, thereby reducing stress-related metabolic dysfunction (Fan & Pedersen, 2021).

Studies have shown that aligning functional food intake with the host's natural biological rhythms can maximize the metabolic benefits of microbial modulation (Wu et al., 2021).

Developmental and Population-Specific Considerations

The impact of functional foods on the gut microbiota is not uniform across different life stages or specialized populations (Xie et al., 2024).

Pediatric and Early-Life Interventions

The gut microbiota begins to assemble at birth (or possibly in utero) and stabilizes between the ages of 2 and 5. This early developmental window represents a critical period for establishing a healthy "microbial blueprint" (Eslam et al., 2020). Disruptions in this process, often due to poor diet or antibiotic use, are strongly linked to the risk of childhood obesity and the early onset of T2DM. Research suggests that early intervention with prebiotics and probiotics can help alleviate metabolic complications during this critical period (Schippa & Conte, 2014).

The Athlete Microbiome

In contrast to sedentary individuals, elite athletes exhibit greater microbial diversity and higher concentrations of SCFAs, which support their high energy demands. However, extremely high exercise capacity has occasionally been associated with reduced diversity, raising questions about the optimal microbial ecosystem for host energy metabolism (Lippolis et al., 2023). Functional foods designed for athletes focus on maintaining intestinal permeability and supporting muscle glycogen storage through specific exercise-associated microbial signatures (Exermove Platform, 2025).

Conclusions

The growing body of evidence demonstrates that the gut microbiota plays a central role in maintaining metabolic homeostasis and influencing the development of metabolic disorders. Functional foods offer an effective and non-pharmacological approach to modulate the gut microbial ecosystem by promoting beneficial microorganisms and suppressing pathogenic taxa. Through the production of bioactive metabolites such as short-chain fatty acids and through the regulation of bile acid metabolism, these dietary components improve gut barrier integrity, reduce systemic inflammation, and enhance metabolic signaling pathways related to glucose and lipid metabolism. The integration of probiotics, prebiotics, synbiotics, and polyphenol-rich foods into daily diets has shown significant potential in managing conditions such as obesity, type 2 diabetes, and metabolic dysfunction-associated steatotic liver disease. Moreover, advancements in precision nutrition, multi-omics

technologies, and artificial intelligence are transforming the field by enabling personalized dietary interventions tailored to an individual's microbiome profile. Despite these promising developments, further long-term clinical trials and standardized regulatory frameworks are required to validate the therapeutic efficacy and safety of microbiota-targeted functional foods. Future research should focus on understanding complex host–microbe interactions and developing targeted nutritional strategies that maximize metabolic health benefits. Ultimately, dietary modulation of the gut microbiota represents a sustainable and innovative approach for preventing and managing metabolic diseases in modern healthcare systems.

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