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Mechanisms and Application of Medicine-Food Homologous Substances in Regulating Intestinal Microecology: A Review

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Abstract. With the development of biotechnology and multi-omics approaches and the rising demand for public health, the role of the intestinal microecology in the occurrence, progression and intervention of diseases has received sustained attention. Epidemiological studies indicate that the incidence of inflammatory bowel disease (IBD) is on the rise in many countries, and thus the maintenance of intestinal microecological homeostasis is regarded as an important foundation for the prevention and treatment of such diseases. The intestinal microecological system is jointly composed of the host, intestinal microbiota and their metabolic networks, with the intestinal microbiota participating in key physiological processes. Although therapeutic microecological preparations are commonly used, they face limitations such as individual differences in efficacy and insufficient product consistency. The concept of "homology of medicine and food" offers a promising alternative with advantages of sustainable intake and controllable safety. This paper reviews the potential mechanisms by which medicine-food homologous resources improve intestinal microecology through regulating microbial community composition and metabolic functions (e.g., SCFAs, bile acids), summarizes key evidence from the perspectives of the gut-immune axis, gut-metabolic axis and gut-brain axis, discusses application advantages and main challenges combined with multi-omics research progress, and provides a reference for subsequent mechanistic studies and product development.

Keywords: medicine-food homology, intestinal microecology, intestinal microbiota, short-chain fatty acids, physiological axes

1. Introduction

With the development of biotechnology and multi-omics approaches and the rising demand for public health, the role of the intestinal microecology in the occurrence, progression and intervention of diseases has received sustained attention. Epidemiological studies indicate that the incidence of inflammatory bowel disease (IBD) is on the rise in many countries, and thus the maintenance of intestinal microecological homeostasis is regarded as an important foundation for the prevention and treatment of such diseases.

The intestinal microecological system is jointly composed of the host, intestinal microbiota and their metabolic networks. The intestinal microbiota includes more than a thousand species with a quantity exceeding 10^14 [1], participating in key processes such as nutrient transformation, short-

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chain fatty acids (SCFAs) production, mucosal barrier maintenance and immune homeostasis regulation. In addition to chronic intestinal inflammations such as IBD, the imbalance of intestinal microbiota and the alteration of its metabolites are also associated with systemic physiological pathways such as the "gut-brain axis", providing a new mechanistic framework for the intervention of neurodegenerative diseases, immune disorders and adverse reactions related to tumor therapy. Therefore, targeted regulation of microbial community structure and metabolic functions is considered to have potential value in disease prevention and adjuvant therapy.

The commonly used strategies for improving microecology at this stage are therapeutic microecological preparations, mainly including probiotics, prebiotics and synbiotics [1]. Probiotics refer to live microorganisms that confer health benefits on the host when ingested in adequate amounts, and can improve the intestinal microenvironment through nutrient and adhesion site competition, production of bacteriocins/organic acids, enhancement of epithelial barrier and immune regulation. According to the ISAPP consensus definition, prebiotics are "substrates selectively utilized by the host microorganisms that confer a health benefit", which usually exert their effects by promoting the proliferation of beneficial bacteria and SCFAs production, and regulating mucosal immunity and inflammatory responses. Synbiotics are the synergistic combination of probiotics and prebiotics, emphasizing the "strain-substrate matching" and comprehensive effects. However, the clinical and industrial application of microecological preparations is still limited by problems such as individual differences in efficacy, insufficient product consistency and evidence for strain-specific efficacy, as well as limited verification of long-term safety and repeatability [2]. Based on this, there is an urgent need to explore more suitable microecological regulation strategies for long-term intake with more controllable risks.

The concept of "homology of medicine and food" originates from the theories of traditional Chinese dietary health preservation and herbal medicine, emphasizing that some food/medicinal and edible resources have both nutritional supply and health conditioning properties, and can be used for dietary intervention in "preventing disease" and chronic disease management. Compared with traditional drug therapy, its advantages lie in a more accessible intervention pathway in daily dietary scenarios, sustainable intake, relatively controllable safety, and translational potential for integration with the development of modern functional foods. Based on this, this paper intends to review the potential mechanisms by which medicine-food homologous resources improve intestinal microecology through regulating microbial community composition and metabolic functions (e.g., SCFAs, bile acids) starting from such resources. It further summarizes the key evidence from the perspectives of the gut-immune axis, gut-metabolic axis and gut-brain axis, discusses their application advantages and main challenges in combination with the progress of multi-omics research, and provides a reference for subsequent mechanistic studies and product development.

2. Types and functional components of medicine-food homologous substances

The regulation of intestinal microecology is significantly affected by polysaccharides. Multiple molecules are linked together via glycosidic bonds to constitute such compounds, which can be extensively found in plants, animals and microorganisms. Foods such as Tremella fuciformis, mushrooms and Astragalus membranaceus are common sources of polysaccharides. Tremella polysaccharide (TP) can significantly improve the structure of intestinal microecology by restoring the abundance of beneficial bacteria such as Lactobacillus, Helicobacter and Bifidobacterium, and inhibiting the growth of potential pathogenic bacteria such as Clostridium [3]. In addition, TP can be fermented by intestinal probiotics to produce SCFAs such as propionic acid and butyric acid, which help reduce intestinal pH and enhance immune activity. Astragalus polysaccharide (APS) has

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immunomodulatory, antioxidant and anti-inflammatory effects, and promotes the health of intestinal microorganisms by regulating the balance of Bacteroidetes. β-glucan in mushrooms enhances the activity of beneficial microbiota, promotes SCFAs production, further regulates the intestinal microenvironment and boosts the immune response.

Dietary fiber, especially that in oats and Amorphophallus konjac, has been proven to play an important role in improving intestinal microecology. Dietary fiber, a category of indigestible carbohydrates, can be utilized and fermented by intestinal microbes in the large intestine, thereby generating beneficial SCFAs including acetic acid, propionic acid and butyric acid. β-glucan in oats, due to its high viscosity, can slow down glucose absorption, thereby helping regulate blood glucose levels and reduce cholesterol. Konjac glucomannan (KGM) in Amorphophallus konjac has a significant prebiotic effect, which can promote the proliferation of Bifidobacterium and Lactobacillus, improve lipid metabolism disorders and alleviate constipation symptoms [4]. In addition, KGM further promotes bile acid metabolism by regulating the expression of the CYP7A1 gene, exerting a lipid-lowering effect.

Flavonoids are widely present in plants such as Crataegus pinnatifida, Pueraria lobata and Chrysanthemum morifolium, with multiple biological functions including lipid regulation, anti-inflammation and antioxidant activity. Crataegus pinnatifida flavonoids exhibit prominent anti-inflammatory effects, which can reduce intestinal inflammatory responses by inhibiting the gene expression of pro-inflammatory factors such as IL-1β, IL-6 and TNF-α [5]. Pueraria lobata flavonoids help alleviate hyperuricemia by regulating intestinal microbiota and improving intestinal function. Flavonoids in Chrysanthemum morifolium regulate immune function and promote intestinal health by exerting antioxidant and anti-inflammatory effects and modulating signaling pathways such as MAPKs and NF-κB. In addition, saponins are widely present in legumes, cereals and herbs, with various biological activities such as anti-inflammation, antioxidant and cholesterol-lowering effects. Saponins in Panax ginseng show strong antioxidant and immunomodulatory effects; its fibrous root saponin extract can increase the number of immune cells in mice and regulate immune function. Meanwhile, saponins have a prebiotic effect, promoting the growth of beneficial bacteria such as Lactobacillus lactis and Lactobacillus casei, thus improving the balance of intestinal microecology.

Table 1. Types and functional components of medicine-food homologous substances

Category	Example	Main Active Ingredients	Functions and Effects
Polysaccharides	Wolfberry	Lycium Barbarum Polysaccharides(LBP)	Enhance immunity, antioxidant activity
Dietary Fibers	Oats	β-Glucan, Insoluble Dietary Fibers	Promote intestinal peristalsis, regulate blood lipids
Flavonoids	Pueraria Lobata	Puerarin	Antioxidant, regulate endocrine system, improve microcirculation
Saponins	Ginseng	Ginsenosides	enhance immunity, regulate nervous system
Polyphenols	Green Tea	Catechins	Antioxidant, anti-inflammatory, protect cardiovascular system

In summary, medicine-food homologous substances can significantly improve intestinal microecology, enhance immune function, and exert various health benefits such as anti-inflammation and antioxidant activity through their abundant bioactive components. These

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substances show great potential in regulating intestinal microbiota, promoting intestinal health and preventing and treating related diseases.

3. Regulation of microbial community composition and diversity

Medicine-food homologous substances play an important role in regulating intestinal microecology through their abundant active components. These compounds are capable of boosting the growth of beneficial bacteria and suppressing the growth of harmful bacteria, which helps maintain the balance of intestinal microbiota. Substrates including dietary fiber and polysaccharides can be fermented by intestinal microbiota to generate SCFAs including acetic acid, propionic acid and butyric acid. These metabolites are able to lower intestinal pH, strengthen intestinal barrier function, and modulate immune responses as well as metabolic homeostasis. Through these mechanisms, medicine-food homologous substances exert a positive impact on the balance of intestinal microecology and overall health.

The intestinal microbiota is a complex ecosystem in the human body with a high degree of diversity, mainly composed of probiotics and harmful bacteria [6]. Probiotics such as Lactobacillus and Bifidobacterium have anti-inflammatory, immunomodulatory and antimicrobial effects, contributing to the maintenance of intestinal health; while harmful bacteria such as Escherichia coli and Proteus may be associated with intestinal diseases. Intestinal health and microbial community composition can be improved by regulating intestinal microecological diversity, which is achieved specifically through enhancing beneficial bacteria abundance and reducing the propagation of harmful bacteria. Such diversity regulation can be achieved through approaches such as increasing probiotic substrates, alternate feeding of different probiotics and modification of intestinal microecology by probiotics. For example, oligosaccharides (such as β-glucan and fructose) can serve as substrates for probiotics, promoting their growth and inhibiting the reproduction of harmful bacteria, thus optimizing the structure of intestinal microbiota.

SCFAs are important metabolites of intestinal microbiota fermentation, with the functions of regulating intestinal immunity and metabolic processes [7]. SCFAs can exert immunomodulatory effects in intestinal epithelial cells, immune cells and adipose tissue through receptors such as GPR41 and GPR43, and can also activate G protein-coupled receptors and inhibit histone deacetylases, thereby providing energy for intestinal epithelial cells and maintaining a stable intestinal environment [8]. Studies have shown that SCFAs are involved in the maintenance of intestinal health through multiple mechanisms such as enhancing intestinal barrier function, reducing the release of inflammatory factors, regulating immune responses and improving metabolic disorders. In addition, butyric acid and other SCFAs produced by the fermentation of dietary fiber can promote the differentiation of Treg cells, support intestinal homeostasis, slow down inflammatory responses, and thus effectively prevent the occurrence of intestinal diseases.

In summary, the active components of medicine-food homologous substances can be selectively utilized at the microbial community level, increasing the abundance of probiotics and inhibiting the reproduction of harmful bacteria. SCFAs generated through the fermentation and metabolism of intestinal microbiota can enhance immune tolerance, improve metabolic behaviors and reduce inflammatory responses.

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4. Medicine-food homologous substances-related physiological axes and a multi-omics perspective

With the in-depth research on the gut-brain axis, people have gradually recognized the profound impact of intestinal microecology and dietary intervention on mental health. The gut-brain axis (GBA) is a bidirectional communication network between the intestinal microbiota and the central nervous system (CNS), involving multiple pathways such as neural, immune and humoral pathways. Intestinal microbiota and its metabolites such as SCFAs play an important role in maintaining the normal operation of gut-brain signal transduction pathways, and can regulate psychological disorders such as anxiety and depression by affecting the activity of neurotransmitters. The function of the central nervous system can be modulated by Short-chain fatty acids including propionic acid and butyric acid, via the regulation of neuroinflammation, synaptic plasticity and neuronal survival. In addition, neurotransmitters such as serotonin (5-HT) and γ-aminobutyric acid (GABA) are also regulated by the metabolism of intestinal microbiota, further affecting mood, cognition and memory [9]. By regulating the structure of intestinal microbiota, medicine-food homologous substances indirectly affect the synthesis and metabolism of these neurotransmitters, thus showing potential anxiolytic and antidepressant effects.

In addition to the gut-brain axis, the gut-liver axis is also a key physiological pathway that regulates the intestinal microbiota and liver health. Intestinal microbiota plays an important role in the gut-liver axis through the metabolism of bile acids (BAs). Bile acids are secreted by the liver into the intestine, participating in fat digestion and regulating the intestinal microbiota, and then are absorbed by the intestine and recycled back to the liver [10]. Intestinal microbiota affects the metabolic balance of bile acids by modifying them, especially by converting primary bile acids into deoxycholic acid (DCA). Probiotics such as Lactobacillus and Bifidobacterium play a crucial role in this process; they deconjugate bile acids by secreting bile salt hydrolases (BSHs), avoiding damage to the intestine. In addition to participating in the digestion and absorption of fat, bile acids also function as signaling molecules. They can regulate host immune and metabolic reactions via binding to farnesoid X receptor (FXR) or TGR5 receptor. Metabolites of intestinal microbiota such as SCFAs also further safeguard liver health by regulating inflammatory responses, maintaining the integrity of the intestinal barrier and promoting liver repair.

With the changes in modern lifestyles, metabolic dysfunction has become a major global health issue, especially metabolic dysfunction-associated steatotic liver disease (MASLD). Accumulating evidence has demonstrated that the disturbance of intestinal microecology is closely associated with the development of MASLD [11]. The imbalance of intestinal microbiota can result in the damage of intestinal barrier function, which enables harmful substances to enter the bloodstream, aggravating the inflammatory response of the liver and promoting fat deposition. Medicine-food homologous substances such as Tartary buckwheat tea and inulin can help reduce hepatic fat deposition and lower the risk of fatty liver by regulating intestinal microbiota and improving bile acid metabolism. However, these substances cannot completely replace drug therapy, but should be used as adjuvant measures to optimize liver health and metabolic functions.

5. Conclusions and prospects

Medicine-food homologous substances show significant potential in the prevention and alleviation of chronic diseases by regulating intestinal microbiota, promoting the production of beneficial metabolites and repairing the intestinal barrier. However, current research still faces problems such as non-unified quality control standards, large individual differences and unclear mechanisms of

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action, which limit their clinical application and industrial development. Future research should focus on establishing a standardized quality control system, promoting the innovation of functional foods, analyzing individual differences combined with multi-omics technologies, and conducting large-sample clinical trials to solve the problems of individual differences and insufficient clinical data, thus fully unleashing the potential of medicine-food homologous substances in health management.

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