

Mechanism Application and Safety of Regulating the Human Intestinal Microbiome Regulation

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Abstract. Dysbiosis of human intestinal microbiota induced by modern unhealthy diets and living habits acts as a core pathogenic factor for multiple chronic metabolic and inflammatory disorders. This review systematically compares five mainstream intestinal microbiota intervention strategies and constructs a three-tier risk classification framework for standardized safety management. This paper first elaborates the spatial distribution characteristics of intestinal flora and three core host-microbe signal axes dominated by short-chain fatty acids. It further expounds the regulatory mechanisms, applicable crowds and clinical limitations of dietary intervention, probiotics, fecal microbiota transplantation, traditional Chinese medicine and phage therapy, and sorts their multi-scenario application values in clinical treatment, health food industry and adolescent daily conditioning. This study divides intervention risks into short-term gastrointestinal reactions and long-term metabolic hidden dangers, and puts forward step-by-step standardized operation specifications suitable for teenagers and immunocompromised populations. The graded safety assessment system established in this paper fills the blank of unified industrial evaluation criteria and provides operable theoretical reference for individualized, low-risk intestinal microecological intervention and public daily health maintenance.

Keywords: Gut microbiome, flora regulation, functional mechanism, probiotics, safety evaluation

1. Introduction

Modern unhealthy lifestyles dominated by highly processed food intake, insufficient sleep, sustained psychological stress, sedentary behavior and antibiotic overexposure constantly disrupt the dynamic balance of intestinal microbial communities. A lot of studies have verified that structural disturbance of gut microbiota is closely associated with obesity, type 2 diabetes, enteritis, fatty liver, emotional anxiety and various other diseases [1, 2]. Gut microbiota ferments food to produce metabolites like short-chain fatty acids (SCFAs), which modulate human metabolism and immune responses. Regulating gut microbiota has become a vital strategy to prevent chronic diseases and improve physical health [3]. Microbiota regulatory approaches, including prebiotics, probiotics, FMT, dietary adjustment and TCM conditioning, have gained more and more popularity. A wide range of probiotic health supplements are available on the market, and multiple domestic hospitals have gradually carried out FMT for refractory intestinal diseases [4]. However, most people only focus on

conditioning efficacy without understanding the mechanisms of different intervention methods, and they ignore potential adverse consequences caused by blind regulation, such as abdominal distension, metabolic disorders, drastic fluctuations of intestinal microecology and immune dysfunction. Given the rapid expansion of the gut health intervention market, it is urgent to establish scientific and accessible standards for microbiota regulation and safety assessment.

Overseas research teams mainly concentrate on the gut microbiota-immune axis and complex interorgan crosstalk that connects the intestinal tract with nearly all systemic organs across the human body. Plenty of laboratory and clinical trials have clearly clarified the unique physiological functions of core beneficial gut bacteria, including common genera such as *Bifidobacterium* and *Akkermansia*. Up to now, a relatively complete and standardized clinical trial evaluation system has been formally built for three mainstream intervention methods: long-term dietary adjustment, oral probiotic supplementation and fecal microbiota transplantation (FMT) [5, 6]. Different from foreign research directions, domestic academic work has gradually formed its own distinctive research advantages over the past decade. A large number of research projects carry out extensive exploration to figure out how traditional Chinese medicine (TCM) and various medicinal-edible homologous ingredients regulate the overall structure of gut microbiota. Meanwhile, the whole industrial chain of functional health foods gains rapid growth in both basic research and real market application [7].

Nonetheless, many prominent deficiencies and obvious research bottlenecks still exist within this research field. Most existing published studies only observe and record the intervention effects brought by a single regulatory method, while they rarely carry out systematic horizontal comparative analysis to compare the differences among multiple intervention strategies side by side. Besides, the practical application scenarios of all kinds of intervention programs remain scattered and disconnected. There are no mature individualized microbiota conditioning regimens that can be precisely tailored for different age groups, physical conditions and disease populations. In terms of safety assessment, most current evaluation standards are merely limited to simple observation of short-term gastrointestinal discomfort after intervention. Researchers still collect insufficient long-term follow-up data to answer two key questions: whether disturbed gut microbiota can restore its original homeostasis independently after months or years of prolonged intervention, and whether long-term microbiota regulation will trigger hidden potential risks such as persistent metabolic abnormalities and mild chronic inflammation [4].

Theoretical Significance: Summarize the interaction rules between gut microbiota and human hosts; sort out the similarities and differences of various strategies for reshaping gut microbiota; improve fundamental cognition of host-microbiota interactions. **Practical Significance:** Distinguish applicable populations and risk levels of diverse microbiota regulatory approaches, construct a graded safety evaluation system to help the general public and adolescents select rational conditioning methods, and provide scientific evidence for health food development and daily health management. The gut microbiota structure of adolescent populations presents remarkable uniqueness, and scientific intervention is particularly critical for adolescent growth and development [8].

2. Compositional features and host-microbe interaction mechanisms of intestinal microbiota

2.1. Spatial distribution characteristics of intestinal flora

The dominant bacterial phyla in the healthy human intestine are Firmicutes and Bacteroidetes, while Actinobacteria and Proteobacteria exist as auxiliary flora; *Lactobacillus* and *Bifidobacterium* are the core beneficial genera maintaining microecological balance [9]. Microbial abundance varies greatly

in different intestinal segments: the small intestine presents low microbial density dominated by aerobic bacteria, while the colon has an anaerobic environment with ultra-high microbial load, which is the main site of microbial fermentation and metabolite production. Multiple factors, including age, dietary structure, geographical environment and circadian rhythm, will reshape flora composition. Long-term intake of whole grains and vegetables can enrich butyrate-producing strains; long-term high-sugar, high-fat refined diet will reduce microbial diversity and enrich conditional pathogenic bacteria. Each individual has a unique microbial fingerprint, which explains the obvious individual difference in the efficacy of the same probiotic product [10].

2.2. Three core host-microbe regulatory axes

The symbiotic relationship between intestinal flora and the human body relies on three mutually linked regulatory pathways. First, metabolic axis: flora decomposes indigestible dietary fiber to produce acetate, propionate and butyrate; SCFAs act as energy substrates of colonocytes and participate in systemic glucose and lipid metabolism regulation to relieve chronic inflammation [3]. Second, intestinal barrier axis: stable flora tightens epithelial intercellular connections and blocks endotoxin leakage into blood circulation to avoid metabolic endotoxemia [7]. Third, immune and neuroendocrine dual axis: commensal flora induces normal differentiation of immune cells and modulates systemic anti-inflammatory ability; meanwhile, it transmits signal molecules through gut-brain and gut-liver axes to regulate emotion, sleep and hepatic lipid metabolism [5]. Once flora homeostasis is destroyed, multi-system metabolic and immune dysfunction will occur synchronously.

3. Action mechanisms of diverse intestinal microecology modulation strategies

3.1. Dietary fiber and prebiotic intervention

Dietary intervention represents the most potent and safest strategy to modulate gut microbiota, and serves as the foundation for all microbiota conditioning approaches [9]. Prebiotics are indigestible carbohydrates mainly including fructooligosaccharides, inulin and resistant starch. These substances cannot be directly absorbed by the human body, but provide carbon sources for beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, selectively enriching beneficial flora, elevating SCFA production and alleviating chronic intestinal inflammation.

Soluble dietary fiber is fermented by gut microbiota to produce abundant butyrate for intestinal mucosal repair; insoluble dietary fiber accelerates intestinal peristalsis and shortens the colonization time of pathogenic bacteria in the gut. The Mediterranean diet (rich in fruits, vegetables, whole grains and olive oil) significantly improves the alpha diversity of gut microbiota and reduces the risk of cardiovascular diseases. In contrast, ketogenic and low-carb diets may ameliorate obesity in the short term yet reduce gut microbial diversity with long-term intervention, implying potential hidden health hazards [9].

3.2. Probiotics and synthetic microbiota regulation

Commercial probiotics are mainly derived from *Lactobacillus* and *Bifidobacterium*. Their core functions include competing for mucosal adhesion sites with pathogenic bacteria, secreting bacteriostatic metabolites and strengthening intestinal barrier function [2]. Postbiotics refer to inactivated probiotics and purified metabolites, which have higher safety and are suitable for

immunocompromised people, making up for the infection risk of live bacterial preparations [11]. At present, genetically engineered probiotics that can directionally secrete active regulatory factors are under preclinical research, which can break the limitation of weak colonization ability of natural strains.

3.3. Fecal microbiota transplantation (FMT)

FMT transfers complete gut microbiota from healthy donors to recipients' intestinal tracts, acting as the most effective intervention to correct severe microbiota dysbiosis. This technique comprehensively restores gut microbial diversity, reconstructs butyrate-producing flora and repairs damaged intestinal barriers. It achieves relatively high cure rates for recurrent refractory ulcerative colitis and also yields favorable outcomes in treating obesity and inflammatory bowel disease. Nevertheless, FMT involves complicated operational procedures and carries latent risks of cross-transmission of pathogens [10, 12].

3.4. Pharmaceutical and traditional Chinese medicine regulation

Broad-spectrum antibiotics indiscriminately eliminate both beneficial and pathogenic intestinal bacteria, drastically reducing gut microbial diversity and easily inducing persistent microbiota dysbiosis accompanied by diarrhea and impaired digestion and absorption. Therefore, antibiotics must be administered under standardized specifications and blind overuse should be avoided [13].

TCM compound prescriptions and medicinal-edible homologous materials such as wolfberry and astragalus are rich in polysaccharide active ingredients with natural prebiotic activity, which selectively enrich beneficial intestinal bacteria. Adhering to a holistic regulatory philosophy, TCM simultaneously optimizes microbiota structure, repairs intestinal barriers and inhibits systemic chronic inflammation, exerting definite therapeutic effects on chronic gastrointestinal disorders [7]. However, TCM contains complex components; long-term high-dose administration may increase host metabolic burden and entail certain safety risks.

3.5. Innovative phage therapy

Phage therapy is an emerging precision gut microbiota regulatory technique that targets and eliminates specific pathogenic bacteria without disrupting the overall structure of indigenous gut flora, effectively compensating for the limitations of broad-spectrum antibiotics. This technology remains in clinical trial stages and has not been widely applied in clinical practice at scale [6, 13].

4. Multi-scenario practical applications of intestinal microecology modulation technology

4.1. Clinical medical applications

In gastroenterology, microbiota regulation is applied to intervene in inflammatory bowel disease, irritable bowel syndrome and chronic recurrent diarrhea. Endocrinology adopts microbiota intervention to comprehensively regulate obesity, type 2 diabetes and non-alcoholic fatty liver disease. Neurology leverages the gut-brain axis to alleviate anxiety, sleep disorders and other psychosomatic symptoms. During tumor treatment, modulating gut microbiota mitigates intestinal injury induced by radiotherapy and chemotherapy and improves overall clinical efficacy [14].

4.2. Functional food and nutritional health industry

Prebiotics, compound probiotics and fermented foods have formed a large-scale industrial market. Enterprises develop various microecological health products targeting diverse health demands including bowel regulation, weight management, immune enhancement and sleep improvement, which serve as the primary approach for the general public to conduct daily intestinal health intervention, especially suitable for adolescents suffering from heavy academic pressure and irregular dietary and rest schedules [8].

4.3. Animal husbandry and public health control

In livestock breeding, microecological preparations can partially replace antibiotics to lower livestock morbidity, reduce antibiotic residues in animal-derived foods and ensure food safety. From a public health perspective, popularizing scientific dietary knowledge to improve adolescents' intestinal microecology can decrease the incidence of intestinal infectious diseases [13].

5. Safety risk research of various gut microbiome regulatory strategies

5.1. Short-term adverse reactions

Individuals with severe gut microbiota dysbiosis often experience abdominal distension, excessive flatulence and mild diarrhea in the initial stage of probiotic or prebiotic supplementation, which represent normal adaptive responses during microbiota reconstruction. FMT may trigger transient gastrointestinal discomfort. Long-term administration of bitter-cold TCM directly irritates intestinal mucosa and aggravates intestinal dysfunction. Intervention with broad-spectrum antibiotics readily induces acute gut microbiota dysbiosis [4].

5.2. Long-term potential risks

First, microbial dependence risk: Long-term single-strain supplementation inhibits the autonomous proliferation of indigenous gut flora. Once intervention is discontinued, the original gut microbiota structure fails to restore homeostasis spontaneously. Long-term ketogenic diets continuously reduce gut microbial diversity, elevating the incidence risk of inflammatory diseases [9]. Second, metabolic disorder risk: Significant individual physiological differences exist; blind microbiota intervention without preliminary assessment may cause abnormal fluctuations in blood glucose and lipid levels. Third, infection risk for special populations: Random administration of probiotic preparations carries an extremely low risk of bacteremia in immunocompromised individuals. FMT may transmit pathogens if donor screening procedures are inadequate. TCM possesses complex ingredients and imposes extra hepatic and renal metabolic burden with long-term intake, while long-term follow-up data in this field remain insufficient [4].

6. Construction of safety evaluation system for gut microbiota regulation and risk prevention & control strategies

6.1. Establishment of graded safety evaluation system

6.1.1. Low-risk intervention modes

This category covers regular intake of dietary fiber and certified postbiotic preparations. Such approaches deliver mild modulatory impacts and will not impair the self-renewal ability of native intestinal flora. Healthy residents, teenagers and people with weakened immune systems can adopt these solutions for long-term daily conditioning as the primary choice.

6.1.2. Medium-risk intervention modes

Representative items contain compound probiotic products and common medicinal and edible raw materials such as astragalus and wolfberry. Continuous intake without intervals may trigger microbial dependence. Healthy adults and teenagers can take these products intermittently, while vulnerable populations need to shorten the whole course of use.

6.1.3. High-risk intervention modes

This range consists of fecal microbiota transplantation, broad-spectrum antibiotic therapy and compound herbal formulas with complicated ingredients. These means bring drastic reconstruction to intestinal microbial communities and may lead to pathogen transmission as well as extra metabolic pressure on visceral organs. Relevant operations can only be carried out after comprehensive professional medical evaluation together with real-time monitoring of physical indicators throughout the process.

6.2. Systematic risk prevention and control strategies

The first rule follows a progressive intervention logic. Practitioners should take dietary regulation from the low-risk category as the primary measure. Compound probiotics under medium risk can be adopted only if dietary adjustment cannot reach expected outcomes. High-risk therapies should be avoided without clear medical suggestions, and this rule carries extra importance for teenagers in the growth period. The second requirement focuses on standardized usage cycles. Users should avoid uninterrupted intake of single-strain probiotics over three consecutive months, and intermittent application helps prevent microbial dependence. All high-risk treatments need to be confined within standardized limited courses. Long-term high-fiber diets are essential to stabilize microbial balance after high-risk intervention. The third measure establishes pre-intervention physical screening mechanisms. People with demands for long-term microecological conditioning need to complete basic gastrointestinal examinations to receive customized conditioning plans. Complete donor screening and liver and kidney function tests are mandatory before any high-risk medical operation.

7. Conclusion

This paper systematically analyzes modulation approaches and supporting safety evaluation frameworks of human intestinal microecology. It first sorts the phylum composition and segmental distribution characteristics of normal intestinal flora, and three core symbiotic regulatory pathways

covering energy metabolism, intestinal mucosal barrier maintenance and systemic immune modulation mediated by short-chain fatty acids. Then it elaborates the respective advantages, internal regulatory pathways and applicable crowds of five mainstream modulation technologies, including dietary intervention, probiotic/postbiotic supplementation, fecal microbiota transplantation, herbal regulation and phage therapy, and divides their multi-industry application scenarios in clinical gastroenterology, adolescent daily health care and standardized livestock breeding. The research further distinguishes transient short-term adverse reactions and chronic long-term latent risks of all conditioning methods, and establishes a three-tier graded safety evaluation system classified by risk intensity, matching stepwise intervention principles and targeted monitoring schemes for special groups such as teenagers. This study clarifies the overall research context of intestinal microecology modulation and standardizes risk judgment criteria lacking unified industrial specifications. Its theoretical value lies in supplementing the comparative analysis framework of diverse flora intervention pathways, while the practical value is to offer simple, operable conditioning standards for the public and medical practitioners to avoid blind microecological regulation and reduce potential health risks.

This paper only carries out qualitative sorting of existing literature, without quantitative meta-analysis of clinical cohort data; the proposed three-tier safety grading system lacks long-term population follow-up data verification, and differential risk thresholds for children, pregnant women and other special groups are not refined enough. Subsequent research can adopt multi-omics combined technology to reveal complete molecular regulatory networks of various modulation modes, accumulate large-sample long-term safety cohorts to optimize the grading evaluation system, develop personalized flora intervention plans based on individual microbial fingerprints, and further excavate characteristic herbal microecological products with clear functional targets to promote the standardized development of the intestinal health industry.

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