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The mechanism and effects of traditional Chinese medicine in treating diseases through the regulation of intestinal microbiota

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Abstract. Traditional Chinese Medicine (TCM) is a traditional medical system based on natural plants, animals and minerals, emphasizing holistic regulation and treating both symptoms and root causes. In recent years, the role of TCM in regulating the intestinal microbiota has become a research hotspot. By analyzing 80 articles, this paper summarizes the regulatory effects of 48 TCM single herbs or compound preparations on the intestinal microbiota, involving 67 target sites. Among them, core microbiota such as Lactobacillus, Bifidobacterium and Akkermansia are frequently regulated. Studies have shown that TCM improves host metabolism (such as diabetes and obesity) and repairs intestinal barrier function through short-chain fatty acids (SCFAs) and bile acid metabolism axis (FXR/TGR5). In addition, TCM has shown significant regulatory effects on the microbiota in digestive system diseases, neurological diseases and immune inflammatory diseases. However, current research has limitations such as the gap between animal models and clinical translation, insufficient research on the mechanism of compound preparations, and individual differences. Future research can further promote the development and modernization of TCM.

Keywords: Traditional Chinese medicine; Gut microbiota; Short-chain fatty acids; Bile acid metabolism; Multi-target regulation.

1. Introduction

Traditional Chinese medicine (TCM) is a traditional medicinal system that uses natural plants, animals, and minerals as raw materials and follows traditional Chinese medical theories for disease prevention and treatment. It is the crystallization of the wisdom of ancient Chinese people. Its significance lies in inheriting the essence of traditional Chinese medicine, emphasizing holistic conditioning, and treating both the symptoms and the root causes of diseases. The value of TCM is manifested in disease prevention and treatment, health preservation, and cultural inheritance. With the development of modern medicine, the unique value of TCM has been further confirmed, making it an important resource in the global health field. Inheriting and promoting TCM culture is not only a respect for life but also a profound contribution to the cause of human health. According to PubMed data from the past three years (2021 - 2024), the annual growth rate of TCM research exceeds 15%, with 60% of the research focusing on metabolic diseases (such as type 2 diabetes and obesity) and digestive system diseases (such as ulcerative colitis and liver fibrosis). Its core value lies in regulating the host's micro - ecological balance through the synergistic effect of "multiple targets - multiple pathways", especially in reshaping the gut microbiota. During the COVID - 19 pandemic, TCM played a crucial role in the final victory against the epidemic [1]. Studying the effect of TCM on gut microbiota is necessary because microbiota are considered as targets of drug action, which can clarify the mechanism of TCM and confirm its importance.

In recent years, Many researchers study traditional Chinese medicine through the way of gut microbiota. For example, in the bile acid metabolism axis, Radix scutellariae activates the FXR signaling pathway by increasing the abundance of Akkermansia muciniphila, thereby improving glucose and lipid metabolism in T2DM mice [2]; in the SCFA - immune regulation axis, wheat bran polysaccharides promote butyric acid production by Lachnospiraceae and inhibit the MAPK/NF - κB pathway to relieve colitis [3]; in the gut - brain axis, polygala oligosaccharide esters upregulate the

abundance of Lachnospiraceae and Ruminococcaceae, reducing depressive - like behaviors in CUMS rats[4]. These findings confirm that the microbiota is a key mediator of the efficacy of TCM. However, current research has significant limitations: Most studies focus on single - herb analysis, and the mechanism research of compound prescriptions (such as Jiangtang Sanhuang Pills and Xianglian Pills) is insufficient; There is a lack of systematic summaries of common targets across different diseases; The evidence for clinical translation is weak, especially lack of comprehensive analysis of traditional Chinese medicine.

Through the analysis of 80 research papers, a total of 48 kinds of TCM herbs or compound prescriptions have been found to act on more than 60 targets in the gut microbiota. Currently, the study of the effect of TCM on gut microbiota is a popular research area. We hope that this review on the effect of TCM on gut microbiota can further promote TCM research, enhance the global recognition of TCM, and inherit our important traditional culture.

2. Result

Treatment of diseases with traditional Chinese medicine can be classified according to disease types,include metabolic disorders such as type 2 diabetes, hyperlipidemia, and obesity; digestive system diseases like diarrhea, ulcerative colitis, constipation, and liver cirrhosis; liver diseases including liver damage, liver fibrosis, non-alcoholic fatty liver disease, and cholestatic liver injury; neurological disorders such as Parkinsons disease, Alzheimers disease, and depression; cardiovascular diseases such as hypertension and atherosclerosis;immune and inflammatory diseases like rheumatoid arthritis, allergic purpura, and mild inflammation; cancerous diseases like colon cancer and prostate cancer; as well as renal fibrosis and radiation-induced pulmonary fibrosis.

Traditional Chinese medicines for treating metabolic diseases mainly include Coptis, Astragalus, Corydalis, Eucommia Leaf, wheat bran, and Curcuma. Prepared Chinese medicines include Shengmai Drink, Si Miao Pills, and Gouty Diabetes Pills. Among these, drugs for treating type 2 diabetes include Coptis, Astragalus, Gouty Diabetes Pills with Astragalus and Dioscorea Kidney Granules, Astragalus Linghua Powder, and Qingqianliu-Gegen-Sangye. Traditional Chinese medicines using animals as medicinal targets include Coptis, Gouty Diabetes Pills, Qingxin Jieyu Granules, and the formula of Qingqianliu-Gegen-Sangye. These all aim to enhance beneficial bacteria such as bifidobacteria, lactobacilli, and acinetobacter, thereby increasing their levels and strengthening the intestinal barrier function. The production of short-chain fatty acid-producing bacteria (such as Peptoclostridium and Ruminococcus) increases, promoting the generation of anti-inflammatory metabolites (such as butyric acid). Harmful bacteria, such as Enterobacter, Desulfovibrio , and Shigella , which promotes inflammation, are significantly reduced, lowering endotoxin and oxidative stress. Traditional Chinese medicines for treating hyperlipidemia include wheat bran, Eucommia Leaf, Si Miao Pills, and Yinchen Qin Gui Shu Gan Decoction. These aim to promote the proliferation of beneficial bacteria, such as those producing short-chain fatty acids, enhancing intestinal barrier function and inhibiting fat absorption. They also inhibit harmful bacteria like Desulfovibrio and Enterobacteriaceae, reducing endotoxin release and inflammatory responses. By regulating bile acid metabolism through the microbiota-bile acid axis, they improve abnormal cholesterol metabolism. They activate signaling pathways such as FXR, TGR5, and SIRT 1/Nrf2The pathway enhances lipid oxidation and energy consumption.

The primary herbal medicines for treating digestive system and liver disorders include wheat bran, moutan bark, aconite, senna leaves, licorice, artemisia capillaris, vine tea, and forsythia. Among the traditional Chinese patent medicines, notable formulations include Ginseng Four Gentlemen Decoction, Seven Ingredients Atractylodes Powder, Intestinal Cleansing and Liver Benefiting Formula, Atractylodes Two Aged Ingredients Decoction, and Artemisia Capillaris, Poria, Cinnamon Twig, Atractylodes, and Licorice Decoction.In digestive system diseases, ulcerative colitis, using animal models, where beneficial bacteria like lactic acid bacteria, bifidobacteria, Akkermansia, and short-chain fatty acid-producing bacteria are increased, while harmful bacteria such as Proteus,

Escherichia coil, Shigella, and Enterobacteriaceae that promotes inflammation are reduced (such as Desulfovibrio). Diarrhea is often treated with traditional Chinese medicines like aconite root and senna leaves, which increase beneficial bacteria: lactic acid bacteria, bifidobacteria, and short-chain fatty acid-producing bacteria, while inhibiting harmful bacteria: Proteus, Enterobacteriaceae, and Clostridium.Hepatic injury in liver diseases, the herbs used are licorice, fine-haired wormwood, and vine tea. The therapeutic effects of these traditional Chinese medicines include increasing beneficial bacteria like lactic acid bacteria, bifidobacteria, Akkermansia, and short-chain fatty acid-producing bacteria, while inhibiting harmful bacteria such as Enterobacteriaceae, Desulfovibrio, and pro-inflammatory bacteria.

Medicine for the treatment of cardiovascular diseases include Tianxiong granules, Qingxin Jieyu granules, Huangqi Chifeng soup, etc. The bacteria that play a role in the treatment of such diseases are all anti-inflammatory and metabolic regulation, promoting the production of SCFAs-producing bacteria such as Lactobacillus Bifidobacterium Roseburia to enhance the production of anti-inflammatory metabolites and reduce systemic inflammation.Inhibit pro-inflammatory bacteria (such as Enterobacteriaceae, Desulfovibrio) and reduce LPS and endotoxin levels.Vascular function protection, SCFAs activates the intestinal brain axis signal (such as GPR43), and regulates vascular tension and blood pressure (such as Du Zhong-Cistanche). Akkermansia enhances the intestinal barrier and reduces oxidative stress damage (such as Huangqi Chifeng Decoction).

In other diseases, such as mental disorders, immune and inflammatory diseases, and tumor - related diseases, the main traditional Chinese herbs include Piper nigrum, Schisandra chinensis, Polygala tenuifolia, Tripterygium wilfordii, Iris japonica, and Astragalus membranaceus. The patent Chinese medicines are Shenqi Yizhi Granules, Chaihu Shugan San, Aconite Decoction, Rhubarb and Moutan Cortex Decoction, and Pinellia Decoction for Purging Stomach - Fire. The compound prescriptions involve Astragalus membranaceus - Curcuma zedoaria. Among them, Alzheimer's disease, a type of mental illness, the traditional Chinese medicine is schisandra, and the patent medicine is Shenqi Yizhi Granules. The mechanisms of action all involve promoting the proliferation of beneficial bacteria, increasing the abundance of short-chain fatty acid-producing or anti-inflammatory bacteria, improving intestinal barrier function and metabolic balance. They also inhibit harmful bacteria, reduce the overgrowth of pro-inflammatory or pathogenic bacteria, and alleviate neuroinflammation and oxidative stress.Immunological and inflammatory diseases,the common mechanism for treating such diseases is to promote beneficial bacteria, such as SCFAs-producing bacteria and anti-inflammatory bacteria, and inhibit harmful bacteria, such as pro-inflammatory bacteria and LPS-producing bacteria.Oncological diseases,these treatments all aim to suppress pro-inflammatory bacteria and reduce the abundance of carcinogenic bacteria such as Enterobacteriaceae and Fusobacteriaceae. They also promote the growth of protective bacterial communities: increasing the proliferation of short-chain fatty acid-producing bacteria (such as Bacteroides) and anti-inflammatory bacteria (such as Akkermansia).

3. Discussion

TCM has a long history. As early as the Xia, Shang and Western Zhou periods, Chinese people began to use traditional Chinese medicine to treat diseases. With the development of the times, traditional Chinese medicine has gradually become known to more people around the world. However, compared with Western medicine, traditional Chinese medicine does not have a clear target, which has led many Western scholars to question its efficacy. Traditional Chinese medicine often treats diseases by activating the body's immune system. The intestinal microbiota is regarded as a new type of immune organ, and the intestinal microbiota-host symbiotic system is an ideal target for the multi-component action of traditional Chinese medicine. This bidirectional regulatory effect reflects the therapeutic concept of "tonifying the right and eliminating the evil" in traditional Chinese medicine. By altering the microbial community in the intestine and interacting with the body, the microbial metabolic network is the material basis for the synergistic action of multiple components of traditional Chinese medicine. This "emperor-minister-assistant-ambassador" microecological regulation model.

The individual differences in the microbiome provide a basis for personalized treatment with traditional Chinese medicine. This "same disease, different treatment" characteristic of microecological regulation is highly consistent with the principle of syndrome differentiation and treatment in traditional Chinese medicine. It provides a new idea for the research of traditional Chinese medicine formulas. This is similar to the mechanism of action of traditional Chinese medicine, so some people speculate that there may be potential targets of traditional Chinese medicine in the intestinal microbiota. Therefore, a large number of current studies on the mechanism of traditional Chinese medicine focus on the changes in the intestinal microbiota community.

A comprehensive analysis of the gut microbiota in 48 TCMs and Chinese patent medicine compound prescriptions has identified a total of 67 action targets. Among them, Lactobacillus was detected 48 times, Bifidobacterium 39 times, Akkermansia 28 times, and Escherichia coli 24 times. After the action of most TCMs, the quantities of Lactobacillus, Bifidobacterium, and Akkermansia increased. Their common characteristics include providing prebiotic substrates, inhibiting competitive harmful bacteria, repairing the intestinal barrier, and regulating bile acid metabolism. Lactobacillus is a group of Gram - positive, facultative anaerobic lactic acid bacteria that can ferment carbohydrates to produce lactic acid, lower the intestinal pH value, and inhibit the growth of pathogenic bacteria. An increase in Lactobacillus can improve blood glucose and inflammation in type 2 diabetes mellitus (T2DM) mice [5]. Bifidobacterium is an important group of probiotics that can maintain the integrity of the intestinal barrier and regulate immune balance. In obesity and autoimmune disease models, TCMs such as ginseng and poria cocos can significantly increase the abundance of Bifidobacterium [6]. Bifidobacterium promotes the polarization of M2 macrophages, thereby improving obesity, accompanied by a decrease in the levels of inflammatory factors and an improvement in metabolic indicators. Multiple studies have shown that TCMs such as Astragalus membranaceus and Coptis chinensis can promote the proliferation of Akkermansia, enhance the intestinal mucosal barrier, and reduce the entry of endotoxins into the blood, thus improving metabolic endotoxemia and low - grade chronic inflammation. Escherichia coli is the most frequently decreased microbiota. Fifteen TCMs or Chinese patent medicine preparations can inhibit it, mostly by enhancing the barrier and improving the intestinal microenvironment. By reducing the abundance of Proteobacteria, they can improve the metabolism of aromatic amino acids in T2DM[7].

In the research on traditional Chinese medicine and intestinal microbiota, approximately 80 types of bacteria and 14 pathways have been identified. The most frequently mentioned are short-chain fatty acids and bile acids. The key receptors of bile acids are FXR (farnesoid X receptor) and TGR5, which increase secondary bile acids (such as DCA, LCA, UDCA, etc.) or conjugated bile acids (such as TCA, TCDCA) by inhibiting CYP7A1 (reducing bile acid synthesis) or activating CYP7A1 (promoting bile acid synthesis), mainly through the FXR-FGF15/SHP or FXR-BDNF-TrkB signaling axes [8]. Chaihu Shugan San increases the generation of secondary bile acids (such as DCA, LCA) by bacteria (such as Bacteroides), activates the FXR-BDNF-TrkB signaling axis, and improves neurological function. It also promotes the proliferation of SCFAs-producing bacteria (such as Bifidobacterium, Akkermansia), enhances intestinal barrier function, and inhibits pro-inflammatory bacteria (such as Desulfovibrionaceae). The metabolism of short-chain fatty acids (SCFAs) is mainly carried out by bacteria such as Lactobacillus, Bacteroides, and Muribaculaceae, which produce SCFAs to exert anti-inflammatory effects, repair the intestinal barrier, and activate the SIRT1/Nrf2 antioxidant pathway or GPR43/41 receptors [9]. Glycyrrhiza regulates the FXR/Nrf2 signaling pathway, affecting bile acid metabolism-related proteins (such as CYP7A1), reducing the accumulation of harmful bile acids. This leads to an increase in beneficial bacteria (such as Lactobacillus, Bifidobacterium, Akkermansia), promotes the production of SCFAs, repairs the intestinal barrier, and activates the antioxidant pathway (SIRT1/Nrf2).

Despite the remarkable progress made in the research on the regulation of gut microbiota by traditional Chinese medicine (TCM), there are still the following significant limitations: Firstly, there are issues regarding the translatability of model systems. Currently, the vast majority of studies utilize mouse models. However, there are notable differences between mice and humans in terms of gut

microbial composition, immune systems, and metabolic characteristics. These differences may render the results of animal experiments inapplicable for direct extrapolation to clinical applications. In the future, more human clinical trials are required to validate the findings from animal studies. Secondly, TCM has complex components, and the active ingredients may exhibit synergistic or antagonistic effects. This complexity is both an advantage of TCM and a challenge in mechanism research. Finally, there are problems related to individual differences and standardization. The gut microbiome is highly individualized, being influenced by multiple factors such as genetics, diet, and the environment. The same TCM may elicit different microbiota responses in different individuals, which poses challenges for efficacy evaluation and standardization. Future research needs to take personalized factors into account and develop efficacy prediction models based on microbiota characteristics.

4. Conclusions

Traditional Chinese Medicine (TCM), as a cultural heritage preserved throughout Chinese history, plays a pivotal role in disease treatment. Through an analysis of 80 literature sources, 67 therapeutic targets have been identified; core microbial communities including Akkermansia and Lactobacillus, among 11 categories, serve as common regulatory targets for over 50 TCM herbs such as Coptis chinensis and Astragalus membranaceus. 89% of the studies demonstrate that TCM improves host metabolism (diabetes, obesity) through the short-chain fatty acids (SCFAs) and bile acid metabolism axis (FXR/TGR5). This paper presents a comprehensive microbial regulation database encompassing 48 TCM herbs including Coptis chinensis and Astragalus membranaceus, providing a foundation for compound optimization and microbial target discovery.

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