DOI: 10.53469/jcmp.2025.07(07).14

Research Progress on Traditional Chinese Medicine Treatment for Osteoporosis Based on Gut Microbiota Regulation

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Abstract: ***Osteoporosis is a systemic bone metabolic disorder caused by an imbalance between bone formation and resorption. Research has shown that dysbiosis of the gut microbiota is closely associated with its onset and progression, involving multi-pathway regulation involving the nervous, endocrine, immune, and oxidative stress systems. In calcium metabolism regulation, dysfunction of this axis reduces intestinal calcium absorption and renal calcium reabsorption, while also disrupting the regulatory functions of parathyroid hormone and vitamin D, leading to calcium transport imbalance. In terms of immune regulation, abnormal activation of the brain-gut-bone axis promotes Th17 cell differentiation and inhibits Treg function, leading to excessive secretion of pro-inflammatory factors such as IL-17 and TNF-α, which stimulate osteoclast maturation and enhanced bone resorption activity. The gut microbiota regulates the endocrine system through metabolic products such as short-chain fatty acids, particularly affecting estrogen metabolism. Dysbiosis can reduce β-glucuronidase activity, disrupting the osteoblast-osteoclast balance. At the neurotransmitter level, the gut microbiota regulates serotonin synthesis through tryptophan metabolism, acting on 5-HT receptors in bone tissue to regulate bone metabolism while also influencing the central nervous system. It modulates antioxidant enzymes to mitigate oxidative stress-induced damage to osteoblasts, maintaining redox balance in the bone microenvironment, thereby forming a microbiota-bone metabolism regulatory network. Traditional Chinese medicine has made significant progress in this field. This paper systematically elucidates the mechanisms by which single herbal components such as strychnos glycosides and oleanolic acid, as well as compound formulations like ginseng bone granules and turmeric bone-strengthening pills, improve osteoporosis by regulating the gut microbiota microecology. The aim is to provide theoretical basis for clinical drug development targeting osteoporosis (OP).***

Keywords: Intestinal Flora, Osteoporosis, Traditional Chinese Medicine, Research Progress**.**

1. Introduction

Osteoporosis (OP) is a systemic skeletal disease characterized by reduced bone mass, impaired bone microarchitecture, increased bone fragility, and elevated fracture risk. The primary cause of OP is an imbalance between bone formation and resorption, with excessive resorption leading to bone loss and decreased bone quality. Currently, the incidence of OP is also increasing in tandem with the aging of the population, posing a serious threat to human health [1]. Research indicates that the pathogenesis of osteoporosis (OP) involves multiple pathogenic factors, including low bone mass, abnormal bone loss, and hormonal imbalances [2]. Compared to healthy individuals OP patients and animal models exhibit significant differences in gut microbiota composition, and the extent of bone loss is positively correlated with gut microbiota alterations, suggesting that gut microbiota dysbiosis may play a key role in the development of OP [3]. Existing research confirms that gut microbiota dysbiosis is closely associated with the pathological progression of OP. Gut microbiota and their metabolic products can influence the balance of osteoclast and osteoblast activity by regulating host metabolism, inflammatory responses, and immune homeostasis, thereby participating in bone metabolism regulation and bone mass maintenance [4]. Although the microbiome exhibits co-evolutionary characteristics in disease progression, the specific molecular mechanisms underlying OP caused by gut microbiota dysbiosis remain unclear, and systematic studies evaluating gut microbiota changes associated with OP and their potential triggers are lacking. Therefore, this paper summarizes and reviews the literature on the regulatory mechanisms of the gut microbiota, the mechanisms by which the gut microbiota regulates OP, and the use of traditional Chinese medicine to regulate the gut microbiota for the treatment of OP, with the aim of providing new therapeutic targets and strategies for the prevention and treatment of OP using traditional Chinese medicine.

2. The Correlation between Gut Microbiota and OP

2.1 Overview of the Intestinal Microbiota

The gut microbiota is an extremely complex microecological system primarily composed of intestinal epithelial cells, a large number of indigenous microbiota, and the local mucosal system of the intestine. Its diversity and complexity continue to evolve and change throughout life, participating in various physiological functions such as nutrient metabolism, immune regulation, and endocrine processes. It is an “organ” that exists in a state of dynamic equilibrium [5]. cohort studies indicate that the most common gut microbiota is primarily composed of the phyla Actinobacteria, Bacteroidetes, Firmicutes, and Proteobacteria. Under physiologically healthy conditions, the gut microbiota maintains a dynamic equilibrium, with these bacteria forming a symbiotic and mutually beneficial relationship with our bodies [6]. The primary functions of the gut microbiota include food digestion, vitamin synthesis, immune regulation, inhibition of pathogen growth, and toxin clearance. However, an imbalance in the gut’s internal environment may lead to a range of diseases, including colitis, diabetes, asthma, obesity, rheumatoid

arthritis, osteoporosis, depression, and systemic lupus erythematosus [7].

2.2 Mechanism of OP Regulation by Intestinal Microbiota

2.2.1 Neural regulation mechanism

In the neuro-regulatory mechanism, the central nervous system and the gut microbiota mediate bidirectional brain-gut communication through chemical signals [8]. Recent studies have confirmed that the brain-gut-bone axis plays a crucial regulatory role in the pathophysiological mechanisms of osteoporosis (OP) [9]. This axis constitutes a finely tuned regulatory network comprising the brain, gut, gut microbiota, and skeleton, and disruption in any of these components can lead to overall functional dysfunction [10]. Specifically, brain-derived and gut-derived signals can directly or indirectly influence bone homeostasis through independent or synergistic mechanisms, participating in bone metabolism regulation by modulating the balance of osteoblast and osteoclast activity [11]. Clinical observations show that the incidence of OP is significantly higher in patients with stroke and cerebral ischemia, with mechanisms involving disuse osteoporosis, central nervous system dysfunction, and deficiencies in neurotrophic factors along the brain-gut-bone axis [12]. Studies have confirmed that the gut microbiota can influence bone homeostasis by regulating the secretion of estrogen-like substances and calcium-phosphorus metabolism [13]. Further studies have found that microbiota dysbiosis can lead to calcium transport disorders, Th cell activation, and the release of pro-inflammatory factors, thereby triggering systemic inflammatory responses and promoting osteoclast activation and enhanced bone resorption [14]. These findings suggest that the gut microbiota participates in the development of OP through the brain-gut-bone axis regulatory network.

2.2.2 Endocrine Regulatory Mechanisms

The gut microbiota, as a virtual endocrine organ, can directly synthesize or regulate various hormone-like chemicals and modulate the physiological functions of multiple systems through the systemic circulation [15]. Estrogen plays a key role in maintaining bone homeostasis; its deficiency can activate the RANKL/RANK/OPG signaling pathway, significantly enhancing osteoclast activity and accelerating bone loss. Additionally, estrogen deficiency disrupts the integrity of the intestinal mucosal barrier, increases intestinal permeability, and promotes the release of pro-inflammatory factors such as tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β), thereby upregulating osteoclast numbers and activity and exacerbating the progression of osteoporosis (OP). Ma et al. [16] found that rats with ovarian ablation-induced OP exhibited significant intestinal microbiota dysbiosis, characterized by a significantly increased Firmicutes/Bacteroidetes ratio, with Ruminococcus, Clostridium, and Prevotella genera positively correlated with bone loss, while Bacteroidetes showed a negative correlation. In addition to the estrogen pathway, Yadav et al. [17] confirmed that the gut microbiota can influence bone metabolism by regulating serotonin synthesis, with the mechanism involving Htr1b/PKA/CREB/cyclin signaling pathway-mediated regulation of osteoblast proliferation. Yu et al. [18] further elucidated that parathyroid hormone promotes the proliferation of bone marrow regulatory T cells (Tregs) through butyrate, which in turn promotes the expression of the osteogenic-related Wnt ligand Wnt10b through BM CD8+ T cells, ultimately activating the Wnt signaling pathway and promoting osteoblast proliferation and differentiation.

2.2.3 Immunoregulatory mechanisms

The gut microbiota regulates the development and maturation of the host immune system through continuous interaction with dendritic cells and immune cells at the endodermal boundary, thereby stimulating the release of inflammatory factors and altering the immune cell population in bone tissue, participating in bone metabolism regulation [19]. Sjögren et al. [20] reported that germ-free (GF) mice exhibited significantly reduced osteoclast numbers, along with decreased levels of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and receptor activator of nuclear factor κB ligand (RANKL) in bone tissue, confirming the pro-inflammatory and osteoclastogenic effects of these cytokines. Intestinal microbiota transplantation from conventionally housed mice can restore immune system function in GF mice. Additionally, the intestinal microbiota promotes B cell differentiation by regulating gene expression, enhancing the production of antibodies such as immunoglobulin A (IgA) and immunoglobulin G (IgG), thereby maintaining intestinal mucosal barrier function [21]. Studies have also found that the gut microbiota influences the local and systemic immune microenvironment by regulating the differentiation and development of helper T cells (Th cells) and regulatory T cells (Tregs), thereby modulating osteoclast and osteoblast function and altering the dynamic balance between bone resorption and bone formation [22]. Notably, lipopolysaccharides (LPS) derived from the gut microbiota exert a dual regulatory effect on osteoclast differentiation: In the absence of RANKL stimulation, LPS promotes the differentiation of osteoclast precursors into phagocytes, inhibiting osteoclast generation and bone resorption; however, in the presence of RANKL, LPS promotes the conversion of osteoclast precursors through the toll-like receptor (TLR) signaling pathway, accelerating osteoclast differentiation and maturation, and enhancing bone resorption activity [23].

2.2.4 Oxidative stress regulatory mechanism

Oxidative stress refers to a pathophysiological process characterized by an imbalance between the body's oxidative and antioxidant systems, leading to excessive accumulation of reactive oxygen species (ROS). As byproducts of free radical metabolism, ROS have been shown to be closely associated with abnormal bone metabolism [24]. Rozenberg et al. [25] demonstrated that estrogen promotes osteogenesis over osteoclastogenesis through its antioxidant properties, thereby maintaining bone homeostasis. Further studies have revealed that the clearance of reactive oxygen species requires the synergistic action of antioxidant enzymes such as superoxide dismutase and catalase, suggesting that the gut microbiota may influence bone metabolism by regulating the expression levels and activity of these enzymes, thereby improving osteoporosis symptoms. However, the underlying molecular mechanisms remain to be elucidated [26].

3. Traditional Chinese Medicine Regulation of Gut Microbiota for the Treatment of OP

3.1 Regulatory Effects of Single Chinese Herbal Medicines and Active Ingredients

Strychnine is the primary bioactive component of the cycloartenolide class in the traditional Chinese medicine Cornus officinalis. Modern pharmacological studies have demonstrated that strychnine possesses multiple pharmacological effects, including anti-inflammatory, immunomodulatory, and bone metabolism-regulating activities. XIE Youhong et al. [27] found that strychnine can increase femoral bone mineral density (BMD), bone volume fraction (BV/TV), bone trabecular number, and serum level of N-terminal propeptide of type 1 procollagen (P1NP), while reducing serum levels of C-terminal cross-linked peptide (CTX) of type I collagen and tartrate-resistant acid phosphatase. Additionally, the abundance of Lactobacillus increased, and a decrease in Lactobacillus abundance, indicating that strychnine glycosides can inhibit harmful bacteria and promote the growth of beneficial bacteria, thereby improving intestinal microbiota dysbiosis in ovariectomized mice, inhibiting osteoclast formation, and exerting therapeutic effects on OP. Its mechanism of action may be related to regulating intestinal microbiota abundance, reducing inflammatory responses, and increasing neuropeptide levels.

Oleanolic acid is one of the main active components of traditional Chinese medicines such as Ligustrum lucidum and Eclipta prostrata, and it has potential anti-inflammatory and antioxidant effects. Studies have shown that it has good natural advantages in the prevention and treatment of OP [28]. MA Chenghong et al. [29] found that oleanolic acid increases BMD, BV/TV, and IL-10 levels, reduces P1NP, β-collagen degradation products, TRACP5b, TNF-α, and IL-6 levels, and increases the abundance of Actinobacteria, Staphylococcus, Enterobacteriaceae UCG-002, and Enterobacteriaceae, while reducing the abundance of Clostridium, indicating that oleanolic acid can slow bone loss, increase bone mass, and thus exert therapeutic effects on OP. The mechanism may involve reducing inflammatory responses, improving intestinal permeability, and regulating intestinal microbiota structure.

Eucommia leaf is the dried leaf of Eucommia ulmoides, a plant belonging to the Eucommiaceae family, and has the effects of tonifying the liver and kidneys and strengthening the tendons and bones. Research shows that the total flavonoid content in Eucommia leaf can reach up to 10. 05%, and it possesses various physiological activities and pharmacological effects [30]. ZHANG Yun et al. [31] reported that after intervention with Eucommia leaf total flavonoids, the abundance of Bacteroidetes decreased in rats, while the abundance of Firmicutes increased. Additionally, it increased bone mass in ovariectomized rats, reduced body weight, and increased bone density. Although there were no significant changes in gut microbiota diversity, the abundance of the Firmicutes phylum increased, while that of the Bacteroidetes phylum decreased. This suggests that total flavonoids from Eucommia ulmoides leaves can improve bone metabolism in OP by regulating the gut microbiota.

Astragalus polysaccharides are bioactive water-soluble heteropolysaccharides extracted from the stems or roots of Astragalus membranaceus, representing the most important natural active component in Astragalus. Studies have shown that they possess anti-OP effects [32]. LIU Jun et al. [33] found that Astragalus polysaccharides significantly improved bone microstructure, reduced the levels of acid phosphatase ACP5, TNF-α, and IL-2, altered the gut microbiota structure of OP rats, increase the methylation level of colonic epithelial cells in OP rats, and alter the gene expression level of colonic epithelial cells, thereby enhancing the expression of certain proteins in the osteoclast differentiation pathway and calcium pathway in the colonic epithelial tissue of OP rats, promoting intestinal calcium release, and inhibiting osteoclast differentiation. The mechanism may be related to anti-inflammatory effects and reduced osteoclast differentiation, among other pathways, contributing to its anti-OP activity.

Puerarin is an isoflavone compound extracted from the traditional Chinese medicine Pueraria root. Research has shown that puerarin, as a plant-based estrogen, can improve postmenopausal osteoporosis (PMOP). Li Bo et al. [34] found that after administering puerarin to ovariectomized (OVX) osteoporosis model rats, it significantly increased the levels of short-chain fatty acids (SCFAs) in the rats, repaired intestinal mucosal integrity, improved the bone microenvironment, reduced serum TRAcP-5b and CTX-1 levels, and exerted an anti-osteoporosis effect.

Epimedium is derived from the dried leaves of the Epimedium plant, which belongs to the Berberidaceae family. It has the effects of tonifying kidney yang, strengthening tendons and bones, and dispelling wind-dampness, and is a commonly used traditional Chinese medicine for the prevention and treatment of OP. Research has shown that Epimedium water extract can promote bone formation through pathways such as neuropeptide Y and vasoactive intestinal peptide, thereby achieving an anti-OP effect [35]. LIN Qing et al. [36] found that Epimedium water extract can improve the microstructure and collagen fiber count of the femur in ovariectomized rats, increase the content of Runt-related transcription factor 2 (RUNX2), reduce the abundance of the Firmicutes phylum in the gut microbiota, and increase the abundance of the Bacteroidetes and Proteobacteria phyla. The abundance of the Bacteroidetes phylum, Ruminococcus family, Candidatus Saccharimonas genus, and Ruminococcus family, Candidatus Saccharimonas genus. Therefore, the mechanism by which Epimedium water extract treats OP and improves bone microstructure may be closely related to the regulation of changes in gut microbiota abundance.

Dipsacus asper, a classic herb in traditional orthopedics, has the effects of tonifying the kidneys and strengthening bones, as well as promoting blood circulation and healing injuries. Modern pharmacological studies indicate that the primary active components responsible for its clinical efficacy include flavonoids, steroids, and phenylpropanoids [37]. WANG Jie et al. [38] found that bone-setting herb can improve bone quality in OP model rats, alleviate bone microstructural damage, and increase the expression of Wnt3a, β-catenin, and RUNX2 protein expression to reduce bone loss. Additionally, it increases the abundance and diversity of the intestinal

microbiota in OP model rats, regulating the proportion and quantity of beneficial bacteria, thereby improving bone health. Therefore, it is speculated that bone-mending herb may reduce bone loss in OP model rats by improving the composition of the intestinal microbiota and mediating the Wnt/β-catenin signaling pathway.

3.2 Multi-target Synergistic Effects of Traditional Chinese Medicine Formulas

ShenGu Granules were developed by Professor Lü Zhaohui based on the long-term humid and hot climate characteristics of Lingnan, combining the core principles of the two classic formulas Shen Ling Bai Zhu San and Si Miao Wan. They have the effects of removing dampness, strengthening the spleen, and reinforcing the tendons and bones, showing significant efficacy for OP patients with spleen deficiency and dampness obstruction [39]. LI Weiju et al. [40] found that after treatment with Shen Gu Granules, intestinal mucosal inflammatory infiltration and ulcers in ovariectomized rats were significantly improved, and the secretion of short-chain fatty acids in the intestine was significantly increased. Additionally, serum levels of bone alkaline phosphatase and osteocalcin were elevated, and decreased serum levels of type I collagen cross-linked N-terminal peptide, suggesting that the Ginseng Bone Granules can increase bone density, improve bone microstructure, restore intestinal microbiota diversity, and repair intestinal mucosal inflammation and ulcers. It is speculated that the mechanism may involve restoring intestinal microbiota imbalance, using short-chain fatty acids as intermediaries to activate the Wnt/β-catenin osteogenic pathway proteins, thereby improving OP.

Tenghuang JianGu Wan is a traditional Chinese medicine compound formulation developed by Professor Liu Bailing, a master of traditional Chinese medicine, based on his years of clinical experience. It has the effects of tonifying the kidneys, promoting blood circulation, and alleviating pain, showing significant improvements in local pain and functional disorders, and is widely used in the treatment of various orthopedic diseases [41]. ZHANG Wenjing et al. [42] found that Tenghuang Jiangu Wan can enhance the richness and diversity of the intestinal microbiota in ovariectomized rats, positively influencing the intestinal microenvironment. It increases the abundance of Bacteroidetes, Lactobacillus, Akkermansia, and Bacteroides, while reducing the abundance of Ruminococcus, Firmicutes, Curcuma longa, and improve intestinal homeostasis after OP. It exerts its pharmacological effects on OP through lipid metabolism, and its mechanism of action may involve promoting the differentiation of bone marrow mesenchymal stem cells into osteoblasts, inhibiting their differentiation into adipocytes, and reducing the production of fatty acid compounds, thereby further influencing the intestinal microenvironment and exerting its pharmacological effects.

Bushen Huoxue Decoction originates from the "Comprehensive Treatise on Orthopedics" and has the effects of tonifying the kidneys, activating blood circulation, and strengthening bones. It is a classic formula for treating orthopedic diseases. Modern pharmacological studies have shown that the Bushen Huoxue Decoction can exert anti-inflammatory, antioxidant, and cartilage repair effects through multiple pathways [43]. HAN Jingchen et al. [44] found that the Bushen Huoxue Decoction can restore intestinal microbiota diversity, reduce colonic inflammatory infiltration, and lower serum levels of IL-1β, IL-6, and TNF-α. Additionally, the expression of TLR4, myeloid differentiation factor 88, nuclear factor-κB (NF-κB) p65 protein in the colon and femur tissues was significantly reduced, indicating that the Bushen Huoxue Decoction can mitigate systemic inflammatory responses by improving intestinal microbiota structure and inhibiting TLR4/MyD88/NF-κB pathways. NF-κB) p65 protein expression in the colon and femur tissue, indicating that the Bushen Huoxue Decoction can alleviate systemic inflammatory responses by improving the gut microbiota structure, inhibit the TLR4/MyD88/NF-κB signaling pathway, thereby modulating bone microenvironment inflammation levels and influencing bone metabolism, thereby achieving the prevention and treatment of OP.

Zhuanggu Zhitong Capsules have the effects of tonifying the liver and kidneys, strengthening tendons and bones, and promoting blood circulation to relieve pain, and can increase bone density, thereby delaying the onset and progression of OP [45]. ZHANG Tianhui et al. [46] found that Bone Strengthening and Pain-Relieving Capsules can reduce IL-17 levels, increase TGF-β levels, significantly improve intestinal inflammation, and also reduce the abundance of Firmicutes while increasing the abundance of Bacteroidetes, which plays a crucial role in helping the host maintain intestinal microecological balance. Additionally, it can effectively regulate bone metabolism through interactions with estrogen. Therefore, it is speculated that the Bone-Strengthening and Pain-Relieving Capsules can restore rat bone microstructure by regulating intestinal microbiota structure, reducing inflammatory factor production, and improving intestinal inflammation, thereby exerting a preventive and therapeutic effect on OP.

The Kidney-Tonifying and Spleen-Strengthening prescription is derived from modified Deer Antler Gelatin Pills, possessing the functions of tonifying the kidneys and replenishing essence, as well as strengthening the spleen and invigorating qi. Its efficacy in preventing and treating OP has been clinically validated over many years, and it also possesses unique advantages in maintaining intestinal microbiota balance [47]. SONG Caiqiu et al. [48] found that the Kidney-Tonifying and Spleen-Strengthening prescription can increase Lactobacillus abundance, inhibit Clostridium growth, upregulate growth hormone and insulin-like growth factor-1 levels, activate the PI3K/AKT signaling pathway, and upregulate Osterix protein expression, thereby promoting osteoblast proliferation and differentiation, increasing bone formation, and achieving the prevention and treatment of OP.

Bushen Huatan Decoction is composed of Epimedium, Dipsacus, Cuscuta, Trichosanthes, Hawthorn, and Red Yeast Rice, this formula has the effects of tonifying the kidneys and strengthening bones, as well as invigorating the spleen and resolving phlegm. Research by Xue Yaojun et al [49]. showed that intervention with the kidney-tonifying and phlegm-resolving formula could increase the abundance and composition ratio of Firmicutes/ Bacteroides in ovariectomized rat models, reduce TNF-α/RANKL levels,

and increase ALP and RUNX2 expression, thereby improving trabecular bone loss. Additionally, it was found that secondary bile acid production mediated by gut microbiota influences bone metabolism. It regulates bile acid-PTHrP/β-arrestin2, significantly downregulating the levels of sodium taurocholate (THDCA) and ursodeoxycholic acid (UDCA), thereby improving bone remodeling in PMOP rats. This suggests that the bile acid metabolic pathway may be a potential target for PMOP treatment.

ZuoGuiWan is composed of Rehmannia glutinosa, Dioscorea opposita, Lycium barbarum, Cornus officinalis, Achyranthes bidentata, Cuscuta chinensis, Carapax testudinis, and Cervus nippon, and has the efficacy of nourishing yin, replenishing marrow, and tonifying the kidneys. It demonstrates significant therapeutic effects for osteoporosis caused by kidney yin deficiency. Li Junjie et al. [50] found that ZuoGuiWan intervention in ovariectomized osteoporosis model mice reduced the relative abundance of the Firmicutes phylum, increased the relative abundance of the Bacteroidetes phylum, and significantly increased the abundance of the Lachnospiraceae NK4A136 group genus. Compared to single drugs, compound formulas represented by Zuo Gui Wan demonstrate potential advantages in multiple signaling pathways and biological functions.

4. Conclusion and Outlook

Gut microbiota metabolites are intricately linked to bone metabolism, influencing bone metabolic balance through multiple pathways, including regulation of host metabolism, calcium homeostasis, endocrine function, immune responses, and neural signaling. Microbiota metabolites can reflect their impact on bone metabolism, emerging as new therapeutic targets for the prevention and treatment of osteoporosis (OP). Studies have shown that single herbs and herbal formulas in traditional Chinese medicine can treat OP by regulating the microbiota. Single herbs primarily focus on tonifying the liver and kidneys, while herbal formulas often address kidney tonification, liver tonification, blood stasis resolution, and pain relief, reflecting the principle of addressing both symptoms and root causes. Currently, the mechanisms by which TCM regulates intestinal microbiota pathways to treat OP are becoming increasingly clear, but there are still some limitations: current studies primarily use animal experimental models to simulate the pathological characteristics of osteoporosis (OP), but these models differ significantly from human OP and are limited in type (mostly established via bilateral ovariectomy). TCM intervention studies have primarily focused on single pathway regulation, with insufficient exploration of the potential for compensatory damage caused by multi-pathway synergistic effects and bidirectional regulation. Clinical translation evidence in this field is insufficient, lacking high-quality evidence-based medical support, and mechanism studies have not yet addressed key issues such as multi-pathway cross-regulation and multi-system synergistic integration. Existing gut microbiota spectrum studies primarily analyze common microbiota, with insufficient exploration of the mechanisms underlying complex microbiota interactions. Future research should expand the scope of TCM single-component and compound studies, combine multi-omics technologies to elucidate the gut microbiota-bone axis interaction mechanisms, and strengthen clinical research to provide new theories and insights.

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