DOI: 10.53469/jcmp.2025.07(08).13

The Treatment of Postmenopausal Osteoporosis Targeting Intestinal Flora based on the Theory of "Phlegm" in Traditional Chinese Medicine

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Abstract: ***Postmenopausal osteoporosis (PMOP) is a prevalent metabolic disorder among postmenopausal women, posing significant threats to their health. Recent studies indicate a close association between gut microbiota dysbiosis and the pathogenesis of PMOP. In Traditional Chinese Medicine (TCM), PMOP falls under the categories of "bone impediment" (gubi,) and "bone wilting" (guwei,). As stated in the classical tenet "Phlegm complicates numerous disorders" (Bai bing duo you jian tan zhe,), phlegm-pathogenicity (tan xie) is also recognized as a key pathogenic factor in PMOP. This review explores connections between gut microbiota, phlegm-pathogenicity, and PMOP in terms of etiology and pathogenesis, while identifying common ground between gut microbiota and TCM phlegm-pathogenicity theory. The findings provide a theoretical foundation for treating PMOP through TCM phlegm-resolving approaches.***

Keywords: Postmenopausal osteoporosis, Gut microbiota, Tan xie (phlegm-pathogenicity).

1. Introduction

Postmenopausal osteoporosis (PMOP) is a metabolic disorder characterized by decreased ovarian function and estrogen levels after menopause, leading to increased osteoclastic bone resorption over osteoblastic bone formation [1]. With population aging, its prevalence shows an upward trend: epidemiological data reveal osteoporosis affects 19. 2% of individuals over 50 years (32.1% in women), rising to 32.0% in those over 65 years (51.6% in women) [2]. This high prevalence, disability rate, and mortality pose severe threats to women's health and impose substantial socioeconomic burdens. Recent studies demonstrate that gut microbiota modulates osteoporosis [3-5] through the "gut-bone axis," influencing bone formation and metabolism. According to the TCM theory that "the Kidney governs bones and generates marrow," osteoporosis pathogenesis primarily involves Kidney deficiency, with additional contributions from Spleen deficiency, blood stasis, and Liver dysfunction [6-8]. Notably, phlegm-pathogenicity (tan xie) constitutes another key etiological factor in osteoporosis development [9-10]. This review examines the interconnections among gut microbiota, phlegm-pathogenicity, and PMOP in terms of etiology and pathogenesis. By identifying common ground between gut microbiota dysregulation and TCM phlegm-pathogenicity theory, we aim to strengthen the theoretical foundation for treating PMOP through phlegm-resolving approaches and elucidate the modern scientific implications underlying this TCM therapeutic strategy

2. Gut Microbiota and PMOP

Gut microbiota refers to the microbial community within the human intestine, including bacteria, fungi, etc. It exists from birth and is an indispensable and vital component of the human body [11]. Metabolites produced by the gut microbiota, such as short-chain fatty acids (SCFAs), vitamins, lipopolysaccharides (LPS), and other active substances, can cross the intestinal barrier and enter the systemic circulation, thereby influencing bone metabolism. This ultimately affects changes in bone mineral density (BMD) and bone quality [12]. Furthermore, gut microbiota can influence the immune system, hormone secretion, and bone metabolism regulatory pathways, consequently acting on the processes of bone formation and bone resorption, potentially exacerbating the degree of osteoporosis [13]. Thus, maintaining the balance of gut microbiota has emerged as a novel therapeutic approach for improving osteoporosis. Numerous studies have already demonstrated a close association between gut microbiota and bone metabolism. Sjögren et al. [14] created a germ-free (GF) mouse model by injecting broad-spectrum antibiotics and found that GF mice exhibited increased BMD, along with greater trabecular bone number and wider trabecular spacing compared to mice with normal microbiota. Their further research [15] indicated that this was due to the absence of gut microbiota stimulation for CD4+T cell antigen production, leading to a reduction in CD4+T cells in the blood and lymphoid tissues, which consequently suppressed osteoclast formation and impacted the bone resorption process. Wang Biao et al. [16], through comparisons of gut microbiota between patients with primary osteoporosis and healthy individuals, discovered that specific bacterial species and the abundance of certain microbiota were significantly higher in the osteoporosis group. This provides a theoretical basis for studying the relationship between gut microbiota and bone metabolism. Additionally, gut microbiota can influence intestinal permeability to calcium and phosphorus, thereby affecting their absorption rates and consequently bone metabolism. Gut probiotics such as Bifidobacterium and Clostridium butyricum can produce SCFAs, which effectively promote the dissolution of calcium, phosphorus, and other ions within the intestine, facilitating their absorption by the body and thereby enhancing bone strength [17-19]. Gut microbiota also mediates immune-inflammatory responses. By producing immunomodulatory SCFAs, they can activate regulatory T (Treg) cells, which limit immune-inflammatory reactions and inhibit osteoclast activity, thus exerting regulatory effects on bone metabolism [20]. Conversely, pathogenic gut bacteria can stimulate T helper 17 (Th17) cells,

triggering an immune response to eliminate the pathogens. This enhances the expression of RANKL (Receptor Activator of Nuclear Factor Kappa-B Ligand), thereby activating osteoclast function and increasing bone resorption [21]. Moreover, gut microbiota can influence key signaling pathways regulating bone metabolism, which are critical for the occurrence and progression of osteoporosis. The Wnt signaling pathway is closely associated with skeletal development. It plays a vital role by regulating the differentiation and functional expression of osteoblasts and osteoclasts and is a key pathway in maintaining bone homeostasis [22]. Recent research indicates that butyrate, a gut metabolite induced by Lactobacillus rhamnosus GG, can increase the production of the osteogenic Wnt ligand Wnt10b by CD8+ T cells, stimulating bone formation [23]. The Wnt signaling pathway induces osteoblast differentiation and suppresses osteoclast differentiation through both the canonical (β-catenin dependent) and non-canonical (cAMP/PKA) pathways [24-25]. Therefore, gut microbiota directly and indirectly influences the development of postmenopausal osteoporosis by modulating the immune system, affecting calcium absorption, and regulating key bone metabolism signaling pathways.

3. The TCM Understanding of Phlegm Pathogen

The character for "phlegm" was anciently written as "dan", sharing the water radical, indicating the ancient belief in its association with water. As stated in the General Treatise on the Causes and Manifestations of Diseases (Zhu Bing Yuan Hou Lun): "Drinking water accumulates and fails to disperse, thus forming phlegm" [26]. When the metabolism of body fluids becomes abnormal, ingested water and other fluids cannot be properly transported, distributed, or excreted. They accumulate within the body and fail to disperse. These stagnated fluids gradually become thick and viscous, forming what Traditional Chinese Medicine (TCM) terms "phlegm". Wu Cheng of the Qing Dynasty, in The Unsettled Compendium (Bu Ju Ji), stated: "The Lung governs Qi; when Lung Metal is injured, Qi stagnates and transforms into phlegm. The Spleen governs dampness; when Spleen Earth fails to transport, dampness stirs and transforms into phlegm. The Kidney governs water; when Kidney Fire is deficient, water floods and transforms into phlegm. Therefore, the binding of phlegm invariably lies in the Lung; the transformation of phlegm invariably lies in the Spleen; but the root of phlegm invariably lies in the Kidney. Hence, these three methods govern the essentials of phlegm" [27]. This illustrates the close relationship between the phlegm pathogen and the three Zang organs: Lung, Spleen, and Kidney. The Lung governs regulation and dredges the waterways. If Lung Qi is deficient or it is invaded by external wind-cold pathogens, the Lung's functions of diffusion and depuration become impaired. Body fluids then accumulate to form phlegm and thin mucus. If this condition further leads to Lung Yin deficiency or constrained Lung heat transforming into fire, it can "condense and scorch" the body fluids, refining them into phlegm. The Spleen resides in the Middle Jiao and is the root of the acquired constitution. If Spleen transportation fails, dampness and body fluids cannot be distributed throughout the body. Dampness then accumulates internally, congealing into phlegm. The Jingyue's Complete Compendium (Jing Yue Quan Shu) states: "Phlegm is essentially water; its root lies in the Kidney, while its manifestation lies in the Spleen. In the Kidney, it is because water fails to return to its source, flooding to become phlegm" [28]. The Kidney governs water and is the lower source of fluids. If Kidney essence is deficient, Yin deficiency leads to exuberant fire, which scorches fluids into phlegm. If Kidney Yang is insufficient, fluids cannot be vaporized and transformed, instead congealing into phlegm. The Liver governs free coursing and regulates the flow of Qi throughout the body. If the movement of Qi becomes obstructed, the flow of body fluids is impeded, leading to their accumulation as phlegm-dampness. As stated in the Danxi's Experiential Therapy (Dan Xi Xin Fa): "Those skilled in treating phlegm do not treat phlegm itself but treat Qi. When Qi flows smoothly, the body fluids throughout the body will also follow Qi and flow smoothly" [29]. The saying "A hundred diseases are often complicated by phlegm" [30] precisely reflects the versatile nature of the phlegm pathogen. It moves throughout the body following the ascent and descent of Qi, obstructing the meridians and collaterals, as well as the Zang-fu organs, thereby causing a multitude of disorders.

4. Phlegm Pathogen as a Pathogenic Factor in PMOP

The Spiritual Pivot (Ling Shu) · On Depletion of Body Fluids (Jue Qi) states: "Depletion of fluids leads to inflexibility in the bending and stretching of the bones" [31], emphasizing that deficiency or stagnation of body fluids (Jin Ye) can deprive the bones of nourishment. The Basic Questions (Su Wen) · Treatise on Abnormal Regulations (Ni Tiao Lun) further links the Kidney's governance over fluid metabolism to bone disease, stating "The Kidney is the water organ, governing the body fluids" [32]. This provides a basis for the theory of "Kidney deficiency generating phlegm leading to bone disease." While discussing "bone wilting" (Gu Wei) in The Basic Questions (Su Wen) · Treatise on Wilting (Wei Lun), it emphasizes "Kidney Qi is hot, the bones become withered and the marrow decreases" [33]. Although not explicitly mentioning the phlegm pathogen, this implies that abnormal Kidney water metabolism can lead to phlegm-turbidity obstructing the meridians and collaterals, exacerbating the bone withering. Zhu Danxi, in Danxi's Experiential Therapy (Dan Xi Xin Fa), was the first to directly link the phlegm pathogen with bone disease: "Difficulty in movement and pain throughout the body indicate phlegm has entered the bones" [34]. These passages collectively describe how Kidney deficiency generates phlegm that enters the bones, causing symptoms like generalized pain and skeletal malnourishment. The decline of Kidney Qi after menopause in women forms a crucial foundation for the internal generation of phlegm-turbidity. The Kidney stores Essence. If Kidney Essence is deficient, Yin deficiency leads to hyperactive Yang and the generation of deficient fire internally. As stated in Jingyue's Complete Compendium (Jing Yue Quan Shu) · Treatise on Miscellaneous Diseases: "Yin deficiency can generate heat; this is due to true Yin depletion where water fails to control fire" [35]. This deficient fire scorches the body fluids, refining them into phlegm. If Kidney Qi is deficient, its functions of vaporization and transformation become impaired. Deficient Kidney Qi disrupts fluid metabolism, preventing normal vaporization,

transformation, and distribution, leading to congealed fluids forming phlegm-turbidity. Furthermore, prolonged Kidney deficiency and Essence depletion inevitably affect Spleen Earth. As stated in Essential Meaning of the Golden Cabinet (Jin Gui Yao Lue Xin Dian): "The dynamic Qi between the Kidneys is the root of the five Zang and six Fu organs... When this Qi floats upwards, it causes panting and gasping; when stagnant in the middle, it causes distention and fullness; when rebellious downwards, it causes swelling and fullness" [36]. When the Kidney fails to warm the Spleen, it leads to Spleen deficiency and impaired transportation-transformation. Required Readings for Medical Professionals (Yi Zong Bi Du) records: "When Spleen Earth is weak, the clear is difficult to ascend, the turbid is difficult to descend; they linger in the center and obstruct the diaphragm, congealing and transforming into phlegm" [37]. Spleen deficiency results in the failure of clear Yang to ascend and the pervasion of turbid Yin; the essence of food and water cannot be properly distributed and accumulates to form phlegm. Additionally, as "women take the Liver as their congenital foundation," most women manifest Liver Qi stagnation after menopause. This leads to dysfunction of the Liver's free coursing function, causing Qi stagnation. Consequently, body fluids stagnate and accumulate as phlegm. Danxi's Experiential Therapy (Dan Xi Xin Fa) · Phlegm states: "Phlegm, as a substance, follows the ascent and descent of Qi and can reach everywhere" [30]. When this formless phlegm flows into the meridians, collaterals, and joints, the bones are deprived of nourishment by Qi, blood, and essence, leading to osteoporosis. Modern medicine recognizes that hyperlipidemia in Western medicine can be categorized under the TCM concept of "phlegm-turbidity". Hyperlipidemia affects the differentiation and function of both osteoclasts and osteoblasts, thereby inducing osteoporosis [38]. Studies show that the sharp decline in estrogen after menopause in women leads to lipid metabolism disorders, contributing to osteoporosis. Hyperlipidemia is closely related to osteoporosis: high levels of HDL-C (high-density lipoprotein cholesterol) can promote inflammatory responses and oxidative stress, while low levels can weaken anti-inflammatory and antioxidant capacity, leading to an imbalance in bone metabolism [39]. Clinical evidence indicates that lipid-lowering drugs can simultaneously treat osteoporosis. For example, statins enhance bone mineral density by upregulating osteoblasts and reducing osteoclast differentiation and activity. Similarly, drugs used to treat osteoporosis also affect lipid metabolism; for instance, zoledronic acid administered to osteoporosis patients lowers blood lipid levels [40-41]. Concurrently, gut microbiota can regulate the body's lipid metabolism, while lipid metabolism disorders can affect the composition of gut microbiota. This mutual influence exacerbates lipid metabolism disorders and contributes to gut dysbiosis [42-43]. Therefore, the phlegm pathogen is a pathological product of gut dysbiosis and is closely related to the pathogenesis of postmenopausal osteoporosis.

5. Similarities Between Gut Microbiota and the Pathogenic Theory of Phlegm Pathogen

The Spleen and Stomach are considered the "Root of the Acquired Constitution and Source of Qi and Blood Generation." They govern the reception and decomposition of food and drink, as well as the transformation and transportation of water-dampness. The living environment and functional activities of gut microbiota are closely linked to the Spleen-Stomach's transportation and transformation functions. Therefore, modern research often categorizes gut microbiota under the TCM concept of the "Spleen-Stomach" [44]. After food and drink are decomposed by the Spleen-Stomach, they are transmitted to the Small Intestine. The "clear" (refined essence) is absorbed by the Small Intestine and transported by Spleen Qi to the Five Zang and Six Fu organs. The "turbid" (waste) is transmitted to the Large Intestine. During this process, Spleen Qi is responsible for absorbing water from the waste material, thereby completing the conduction and transformation of the dregs. If Spleen-Stomach function is impaired and its transportation-transformation fails, food and fluids cannot be properly digested and transported, leading to internal accumulation of water-dampness. This readily generates phlegm-turbidity, illustrating the principle that "The Spleen is the source of phlegm generation." The fundamental basis for phlegm pathogen generation lies in Spleen-Stomach deficiency or dysfunction. Conversely, the balance of gut microbiota directly depends on the Spleen-Stomach's transportation-transformation function: When the Spleen-Stomach is strong and functions properly, with moderate diet and effective transformation of water-dampness, gut microbiota can maintain diversity and stability. When the Spleen-Stomach is deficient or its transportation - transformation is abnormal — such as from excessive consumption of raw/cold foods damaging Spleen Yang, or overeating/stuffing leading to stagnation of Stomach Qi—it results in dysbiosis of the gut microbiota structure. This manifests as an increase in opportunistic pathogens like Clostridium and a decrease in beneficial bacteria like Bifidobacterium. This imbalance subsequently affects intestinal absorption of nutrients and water-fluid metabolism, promoting the internal generation of phlegm-dampness [45]. When gut dysbiosis occurs, such as the overgrowth of gas-producing bacteria, it readily leads to stagnation of intestinal Qi movement, causing symptoms like abdominal distension and loose stools. Simultaneously, it impairs the transformation and transportation of water-dampness, causing internal retention of damp-turbidity that congeals into phlegm. This aligns with the pathogenic characteristic of the phlegm pathogen to "obstruct Qi movement", demonstrating that gut dysbiosis causes the internal generation of phlegm pathogen by interfering with the Spleen-Stomach's ascending/ descending functions. The Spleen-Stomach, as the "Source of Qi and Blood Generation," requires sufficient Qi and Blood for its normal function. Gut microbiota participates in Qi and Blood generation and nutrient supply by metabolically producing substances like short-chain fatty acids (SCFAs) and vitamins. This echoes the Spleen - Stomach's function of transforming food and drink into nourishing essence to sustain the whole body. If gut dysbiosis occurs, abnormal metabolites—such as reduced SCFAs and increased endotoxins—will affect the Spleen-Stomach's ability to generate and distribute Qi and Blood, leading to Qi-Blood deficiency and internal retention of damp-turbidity. This corresponds to the statement in Jingyue's Complete Compendium: "Phlegm fundamentally stems from Qi and Blood; disorder in the movement of Qi and Blood transforms it into phlegm". This further illustrates that gut microbiota, as an extension of Spleen-Stomach function, shares the same

pathological basis with phlegm pathogen generation: dysfunction in the Spleen-Stomach's movement and transformation of Qi, Blood, and fluids. The similarities between gut microbiota and the pathogenesis of the phlegm pathogen are evident not only in the shared pathological root of "The Spleen being the source of phlegm generation" but also permeate the entire process of dysfunction in the Spleen-Stomach's functions: transportation-transformation, ascending/descending movement, and Qi-Blood generation.

6. Treating PMOP from the Perspective of "Phlegm"

Regulating gut microbiota is one of the effective targets for treating PMOP. Current approaches include increasing probiotic or dietary fiber intake, fecal microbiota transplantation (FMT), consuming targeted bacteriophages, or utilizing light therapy. Studies indicate that light exposure can stimulate the "gut-skin" axis, activating the immune system and releasing inflammatory cytokines to modulate gut microbiota [46]. Based on the etiology and pathogenesis in postmenopausal women, the Kidney, Spleen, and Liver Zang organs are closely related to both phlegm generation and the development of postmenopausal osteoporosis. Therefore, the treatment of PMOP should adhere to the principles of fortifying the Spleen, tonifying the Kidney, soothing the Liver, and resolving phlegm.

Fortifying the Spleen: The Spleen is the root of the acquired constitution, governs the flesh, and controls the limbs. Su Wen · Wei Lun states: "The Spleen governs the muscles of the body." Ling Shu · Jue Qi says: "When Qi fills the bones, they become well-nourished and moistened" [11]. Su Wen · Tai Yin Yang Ming Lun explains: "The limbs all receive Qi from the Stomach, but this Qi cannot reach the channels directly; it must rely on the Spleen to be received. If the Spleen is diseased and cannot transport the Stomach's fluids, the limbs will not receive the Qi of food and water. Qi will daily decline, the vessels will become obstructed, and the sinews, bones, and muscles will lack Qi for generation, hence becoming useless" [47]. This demonstrates that the Spleen, through its functions of transporting and transforming food essence and governing the ascent of the clear, determines muscle strength and limb function. Normal Spleen function results in strong muscles and powerful limb movement; Spleen deficiency leads to muscle wasting, limb weakness, disuse, and secondary osteoporosis. Furthermore, as "The Spleen is the source of phlegm generation", Spleen deficiency obstructs the vessels, impedes fluid movement, and prevents the distribution of food essence, leading to phlegm-turbidity obstruction, which also causes osteoporosis. Clinical research [48] shows that Buzhong Yiqi Tang (Center-Supplementing Qi-Boosting Decoction), which fortifies the Spleen, boosts Qi, and dries dampness to resolve turbidity, has good clinical efficacy for elderly osteoporosis patients with Spleen deficiency complicated by phlegm-dampness. Studies on Kidney-warming and Spleen-fortifying formulas [49-50] found they not only have good clinical effects on osteoporosis but also increase the abundance of Firmicutes in the gut microbiota. Therefore, fortifying the Spleen and resolving phlegm is essential for treating PMOP.

Tonifying the Kidney: The Kidney is the root of the congenital constitution, stores essence, governs the bones, and generates marrow. TCM holds that osteoporosis is primarily caused by Kidney deficiency. Su Wen · Liu Jie Zang Xiang Lun states: "The Kidney governs storage; it is the root of sealing and storing, the residence of essence" [51]. Su Wen · Wei Lun states: "The Kidney is the water Zang. If water fails to overcome fire, the bones become withered and the marrow becomes deficient. Hence, the feet cannot support the body, and bone wilting (Gu Wei) develops." As the water Zang, if Kidney essence is insufficient, the bones lose nourishment, leading to osteoporosis [52]. Wang Jiezhai of the Ming Dynasty stated: "The root of phlegm lies in the Kidney." Jingyue's Complete Compendium states: "Although diseases of all five Zang can generate phlegm, none do so apart from the Spleen and Kidney. For the Spleen governs dampness, and when dampness stirs, phlegm is generated; the Kidney governs water, and when water floods, phlegm is also generated. Thus, the transformation of phlegm invariably lies with the Spleen, but its root invariably lies with the Kidney." This shows the Kidney is the root of phlegm, and the Spleen is the source. If Kidney Yang is deficient, it cannot warm Spleen Yang; Spleen Earth fails to generate, and Kidney Water counter-restricts Spleen Earth, leading to impaired Spleen transportation-transformation and internal generation of phlegm-dampness [53]. Clinical studies have shown that Kidney-tonifying and phlegm-resolving formulas can effectively treat PMOP [54]. Furthermore, it was found that such formulas regulate the gut microbiota in mice, increasing the abundance of Firmicutes, including Clostridium, thereby proving they can modulate intestinal immunity and inhibit osteoporosis development [55].

Soothing the Liver: The Liver governs free coursing, stores blood, and is associated with the sinews. Normal Liver coursing ensures smooth Qi and blood flow, nourishing the Zang-fu organs and bone marrow. Smooth Qi-blood flow prevents phlegm-turbidity generation. Su Wen · Wu Zang Sheng Cheng states: "Hence, when a person lies down, the blood returns to the Liver... The feet receiving blood can walk; the palms receiving blood can grasp; the fingers receiving blood can hold." This shows that all movement in the body depends on the Liver's blood-storing function. If the Liver's coursing and blood-storing functions are normal, the sinews and bones are nourished, and movement is flexible [28]. Ye Tianshi, in Case Records as a Guide to Clinical Practice (Lin Zheng Zhi Nan Yi An), stated: "Women take the Liver as their congenital foundation." Therefore, the aging of postmenopausal women is closely related to the Liver. After menopause, Liver depression becomes pronounced. Depressed Liver Qi transforming into fire can easily scorch Liver Yin. Moreover, due to the childbearing stage, women often experience Liver blood deficiency. Deficient Liver and withered blood lead to an inability to nourish the bone marrow, causing osteoporosis. Although there are no direct clinical reports on using Liver-soothing and phlegm-resolving methods for PMOP, the theory that "Those skilled in treating phlegm do not treat phlegm itself but treat Qi" suggests that Liver-Qi regulating herbs curb phlegm generation at its source. Clinical studies have found that Liver-soothing and Spleen-fortifying formulas have good clinical efficacy for osteoporosis and can restore the osteoblast-osteoclast balance. Herbs like Chai Hu (Bupleurum) and Xiang Fu (Cyperus) in the formula are Liver-Qi regulating agents. In

postmenopausal osteoporosis patients, they also soothe the emotions, benefiting physical and mental health [56]. Mouse studies found that Saikosaponins can inhibit oxidative stress and exert anti-osteoporotic effects by activating the Keap1/Nrf2/ARE signaling pathway [57]. Studies show that patients with liver cirrhosis have reduced gut microbiota diversity compared to healthy individuals, and this reduction correlates negatively with disease progression [58]. This indicates a connection between the Liver and gut microbiota. Thus, we can use Liver-Qi regulation to suppress phlegm generation and treat osteoporosis. As Jingyue's Complete Compendium states: "Those skilled in treating phlegm are only those who can prevent it from being generated; this is the hand that mends heaven" [59]. Therefore, the key to treating phlegm lies in fundamentally preventing its generation at the source, which is more root-oriented and long-term significant than simply expelling phlegm.

In summary, when treating postmenopausal osteoporosis complicated by phlegm-turbidity, we should simultaneously Fortify the Spleen, Soothe the Liver, Tonify the Kidney, and Resolve Phlegm.

7. Conclusion

Western medicine primarily treats osteoporosis with anti-osteoporotic drugs, some of which have severe adverse effects. Traditional Chinese Medicine, centered on the holistic concept and emphasizing the combination of disease differentiation and pattern identification, highlights unique advantages in treatment. The close relationship between gut microbiota, the TCM phlegm pathogen, and osteoporosis progression provides richer theoretical support for TCM's approach to treating osteoporosis from the perspective of phlegm. By reviewing the correlations between gut microbiota, the phlegm pathogen, and osteoporosis in terms of etiology and pathogenesis, and analyzing the similarities between gut microbiota and the pathogenic theory of phlegm, this paper reveals the modern scientific significance embedded in the "treating osteoporosis from phlegm" approach. It is hoped that by integrating modern medicine with traditional TCM theory, novel therapeutic avenues for osteoporosis diagnosis and treatment can be explored, ultimately promoting the advancement of clinical management.

References

[1] Yan Yiyun, Yao Zengyi, Cheng Meng. Research Progress of GREB1 Gene in Postmenopausal Osteoporosis [J]. Chinese Journal of Osteoporosis, 2025, 31(04):592-596+603.

[2] Yang Cheng, Wu Dou, Liu Qiang. Research Progress on Epidemiology, Influencing Factors and Related Mechanisms of Osteoporosis [J]. Chinese Journal of Bone and Joint, 2023, 12(04):306-310.

[3] Wei Wei, Wang Shixuan, Zhan Libin. Research on the Correlation between Sarcopenia-Osteoporosis and Intestinal Flora [J]. World Science and Technology - Modernization of Traditional Chinese Medicine, 2024, 26(09):2434-2443.

[4] Fang Zhijie, Ma Qiangping, Dong Wantao, et al. Genetic Association between Gut Microbiota and Osteoporosis: Analysis of 211 Gut Microbiota from the UK Database [J]. Chinese Journal of Tissue Engineering Research, 2025, 29(18):3941-3947.

[5] Wang Zihao, Wang Yu, Yang Xin, et al. Research Progress on Molecular Mechanisms Related to Gut Microbiota and Osteoporosis [J]. Chinese Journal of Microecology, 2024, 36(04):487-492+497.

[6] Hua Zhen, Peng Hongcheng, Yin Yubao, et al. Treatment of Osteoporosis with Traditional Chinese Medicine from the Perspective of Spleen - Theory [J]. Chinese Journal of Osteoporosis, 2022, 28(08): 1223-1227+1243.

[7] Zhang Pengwei, Zhou Mingwang, Wang Yulei, et al. Research Progress on the Treatment of "Blood - deficiency and Blood - stasis" in Osteoporosis by the Method of Nourishing and Activating Blood [J]. Chinese Journal of Osteoporosis, 2023, 29(01):99-103.

[8] Zhang Zechen, Huang Hai, Jiang Xin, et al. Investigation into the Correlation between Emotional Disorders and Osteoporosis Based on the Theory of "Liver Governs the Free Flow of Qi and Regulates Emotions"[J]. Chinese Journal of Osteoporosis, 2024, 30(06):858-862.

[9] Xiong Mengxin, Xiang Nan, Xue Yaojun, et al. Role of Dysregulation of Bone-Lipid Metabolism Based on the Theory of "Kidney Phlegm" in the Pathogenesis of Postmenopausal Osteoporosis[J]. Chinese Journal of Osteoporosis, 2022, 28(03):455-459.

[10] Shi Hengwei, Li Hongzhuan, Zhang Min, et al. Investigation into the Correlation between "Stagnation," "Phlegm," and "Blood Stasis" and Postmenopausal Osteoporosis Based on the Theory of "Latent Pathogen" [J]. Liaoning Journal of Traditional Chinese Medicine, 2023, 50(05): 61-64.

[11] Feng Jie, Huang Hai, Chen Qi, et al. Investigation into the Effects and Mechanisms of Gut Microbiota Dysbiosis on Osteoporosis Based on the Theory of "Spleen Failing to Ascend Clear Qi and Obstruction of Meridian Channels"[J]. Lishizhen Medicine and Materia Medica Research, 2023, 34(12):2974-2976.

[12] Li Mengying, Zhou Xuan, Zhang Minjie, et al. Research Progress on the Mechanisms of Gut Microbiota Metabolites in Metabolic Bone Diseases[J]. Chinese Journal of Bone and Joint Surgery, 2025, 18(03): 268-274.

[13] Gao Zhijie, Wang Yuedong, Zhang Zhihai. Causal Relationship between Specific Gut Microbiota and Osteoporosis[J]. Journal of Medical Research & Combat Trauma Care, 2024, 37(05):449-455.

[14] Sjögren K, Engdahl C, Henning P, Lerner UH, Tremaroli V, Lagerquist MK, Bäckhed F, Ohlsson C. The gut microbiota regulates bone mass in mice. J Bone Miner Res. 2012 Jun; 27(6): 1357-67.

[15] Ohlsson, Claes, and Klara Sjögren. "Effects of the gut microbiota on bone mass." Trends in endocrinology and metabolism: TEM vol. 26, 2 (2015): 69-74.

[16] Wang Biao, Zhao Heping, Gao Wenjie, et al. Diversity Analysis of Gut Microbiota in Osteoporosis Patients[J]. Chinese Journal of Osteoporosis, 2017, 23(06):715-718.

[17] Scholz-Ahrens, Katharina E et al. "Prebiotics, probiotics, and synbiotics affect mineral absorption, bone mineral content, and bone structure." The Journal of nutrition vol. 137, 3 Suppl 2 (2007): 838S-46S.

[18] Behera, Jyotirmaya et al. “The role of gut microbiota in bone homeostasis.” Bone vol. 135 (2020): 115317.
[19] Locantore, Pietro et al. “The Interplay between Immune System and Microbiota in Osteoporosis.” Mediators of inflammation vol. 2020 3686749. 26 Feb. 2020,
[20] Wiechers, Carolin et al. “The microbiota is dispensable for the early stages of peripheral regulatory T cell induction within mesenteric lymph nodes.” Cellular & molecular immunology vol. 18, 5 (2021): 1211-1221.
[21] Li, Jau-Yi et al. “IL-17 Receptor Signaling in Osteoblasts/Osteocytes Mediates PTH-Induced Bone Loss and Enhances Osteocytic RANKL Production.” Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research vol. 34, 2 (2019): 349-360.
[22] Yang Zhou, Gao Jingyuan, Tian Faming. Role of Wnt Signaling Pathway in Bone Homeostasis[J]. Chinese Journal of Osteoporosis, 2022, 28(01):109-113.
[23] McHugh, Jessica. “WNT signalling in the gut microbiota-bone axis.” Nature reviews. Rheumatology vol. 15, 1 (2019): 4.
[24] Lee, Wen-Chih et al. “Energy Metabolism of the Osteoblast: Implications for Osteoporosis.” Endocrine reviews vol. 38, 3 (2017): 255-266.
[25] Weivoda, Megan M et al. “WNT Signaling Inhibits Osteoclast Differentiation by Activating Canonical and Noncanonical cAMP/PKA Pathways.” Journal of bone and mineral research: the official journal of the American Society for Bone and Mineral Research vol. 31, 1 (2016): 65-75.
[26] Wang Tao, Zhang Zhenqiang, Xie Zhishen, et al. Interpretation of the Correlation between “Phlegm” in Traditional Chinese Medicine and Stress Granules[J]. Journal of Traditional Chinese Medicine, 2025, 66(04): 329-334.
[27] Zou Jiajia, Sun Zikai. Treatment of Pulmonary Nodules Based on the Theory of Latent Pathogens[J]. Western Journal of Traditional Chinese Medicine, 2022, 35(08): 48-51.
[28] Yang Rui, Song Shangyi, Wang Xingxin, et al. Discussion on the Treatment Idea of Du - moxibustion for Infertility of Phlegm - Dampness Constitution Based on the Theory of “Kidney as the Root of Phlegm and Spleen as the Source of Phlegm”[J/OL]. Liaoning Journal of Traditional Chinese Medicine, 1-10[2025-06-30].
[29] Gong Xue, Liu Zhihui, Liu Fang, et al. Exploration on the Pathogenesis and Treatment of Children’s Cough - Variant Asthma Based on the Theory of “General Qi Stagnation”[J/OL]. Journal of Beijing University of Traditional Chinese Medicine, 1-13[2025-06-29].
[30] Shi Zhouying, Chen Jihong, Li Huixin, et al. Analysis of Zhu Danxi’s Academic Thoughts on Differentiation and Treatment of Obesity [J]. Journal of Traditional Chinese Medicine, 2024, 39(08):4406-4409.
[31] Jiang Yang, Li Yiwen, Chen Lihua. Exploration on Acupuncture Therapy for Osteoporosis Based on the Theory of “Xigu” [J]. Chinese Journal of Osteoporosis, 2024, 30(11):1649-1652.
[32] Huang Xiaohua, Zheng Chenghong, Ding Nian, et al. Exploration on the Pathogenesis Basis of Different Diseases with the Same Treatment for Hepatic Encephalopathy and Renal Encephalopathy Based on the Theory of Turbid - Toxin Pathogenesis[J]. Journal of Traditional Chinese Medicine, 2025, 40(04):1647-1651.
[33] Xu Tingting, Ding Ying, Zhang Xia, et al. Theoretical Discussion and Research Progress on the Treatment of Glucocorticoid - Induced Osteoporosis with Traditional Chinese Medicine [J/OL]. China Journal of Chinese Materia Medica, 1-12[2025-07-03].
[34] Zhu Wei, Zhou Guangwen, Wu Yonggui. Preliminary Exploration on the Connotation of “Kidney Phlegm” in the Pathogenesis of Post - menopausal Osteoporosis [J]. Lishizhen Medicine and Materia Medica Research, 2021, 32(10): 2468-2471.
[35] Sun Qice, Du Yu, Xie Guanqun, et al. Analysis of the Etiology and Pathogenesis of “Shanghuo” from the Perspective of Sanjiao Qi - Transformation Disorder[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2020, 35(02):972-974.
[36] Lin Mingxin. Review of research on the life - gate theory in traditional Chinese medicine [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2025, 40(01): 13-19.
[37] Tan Yupei, Li Mingxuan, Liu Hongxu, et al. Analysis of the Treatment of Paroxysmal Atrial Fibrillation from the Perspective of “Lung Fire and Phlegm - Excess”[J]. China Journal of Traditional Chinese Medicine and Pharmacy. 2024, 39(12):6508-6511.
[38] Wang Longmei, Liu Kangjia, Liu Zixin, et al. Research Progress on the Relationship between Lipid Metabolism and Related Diseases and Osteoporosis [J]. Chinese Journal of Osteoporosis, 2021, 27(05):767-770+775.
[39] Xie Rong, Zhu Liguo, Jin Zikai, et al. Analysis of Clinical Characteristics and Influencing Factors of Post - menopausal Osteoporosis Patients with Dyslipidemia [J]. China Journal of Orthopaedics and Traumatology, 2025, 38(05):487-493.
[40] Ren, Huiping et al. “AN698/40746067 suppresses bone marrow adiposity to ameliorate hyperlipidemia-induced osteoporosis through targeted inhibition of ENTR1.” Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie vol. 176 (2024): 116843.
[41] Luo, Wei et al. “Use of zoledronic acid in antiosteoporosis treatment is associated with a decreased blood lipid level in postmenopausal women with osteoporosis: a cohort study in China.” Postgraduate medicine vol. 134, 4 (2022): 406-412.
[42] Jia, Xiaokang et al. “Impact of Gut Microbiota and Microbiota-Related Metabolites on Hyperlipidemia.” Frontiers in cellular and infection microbiology vol. 11 634780. 19 Aug. 2021,
[43] Xia, Meng et al. “Structural and functional alteration of the gut microbiota in elderly patients with hyperlipidemia.” Frontiers in cellular and infection microbiology vol. 14 1333145. 15 May. 2024,
[44] Li Tongtong, Ma Weiwei, Xiong Yong, et al. Exploration on the Relationship between Gut Microbiota and Post - menopausal Osteoporosis Based on the Theory of “Earth Restraining Water” [J]. Journal of Beijing University of Traditional Chinese Medicine, 2023, 46(10): 1367-1373.
[45] Li Xiaoya. Research on the Intestinal Micro - ecological Mechanism of Sishen Pill Decoction in the Treatment of Diarrhea Mice with Kidney - Yang Deficiency

Syndrome [D]. Hunan University of Chinese Medicine, 2023.
[46] Luo Jianzhou, Wu Tailin, Duan Chunguang, et al. A New Target for Immunoprevention and Treatment of Post - menopausal Osteoporosis: Gut Microbiota [J]. Chinese Journal of Bone and Joint Surgery. 2021, 14(08): 727-732.
[47] Gao Mei, Tang Aihua, Chen Wenhui, et al. Discussion on the Etiology, Pathogenesis and Treatment of Primary Osteoporosis Based on the “Chongyang Thought” [J]. Chinese Journal of Osteoporosis, 2021, 27(07): 1081-1083+1087.
[48] Wu Yadong, Guo Zhenguang, Deng Wenjie, et al. Exploration on the Clinical Efficacy and Influence on Bone Turnover Markers of Buzhong Yiqi Decoction for Osteoporotic Vertebral Compression Fracture after Surgery Based on the Theory of “Spleen Governing Muscles”[J]. Chinese Journal of Experimental Traditional Medical Formulae, 2022, 28(17):91-97.
[49] Fang Jiaqi, Zhong Yanyuan, Sun Xin, et al. Mechanism of Wenshen Jianpi Decoction in Preventing and Treating Osteoporosis via HIF - 1α Signaling Pathway [J]. Chinese Journal of Osteoporosis, 2025, 31(04):469-475.
[50] Shi Yuying, Fu Jingran, Chen Jingwen, et al. Effect of Wenshen Jianpi Decoction on Intestinal Flora in Rats with Diarrhea-Predominant Irritable Bowel Syndrome [J]. Traditional Chinese Drug Research and Clinical Pharmacology, 2024, 35(11):1713-1721.
[51] Li Yan, Dou Qunli, Yang Feng. Study on the Theory of “Kidney Being the Root of Storage” and the Pathogenesis of Primary Osteoporosis[J]. Chinese Journal of Osteoporosis, 2021, 27(09):1369-1372.
[52] Lin Yanping, Huang Jiachun, Guo Haiwei, et al. Study on the Distribution Law of TCM Syndrome Types and the Relationship between Muscle - Bone - Fat in Patients with Primary Osteoporosis [J/OL]. Chinese General Practice, 1-6[2025-07-06].
[53] Li Liquan. Clinical Efficacy Observation of Bushen Huatan Decoction in the Treatment of Post - menopausal Osteoporosis of Kidney - deficiency and Phlegm - turbidity Type [D]. Hubei University of Chinese Medicine, 2021.
[54] Zhou Guangwen, Xiang Nan, Zhang Yan, et al. Study on the Effect of Bushen Huatan Decoction on the Structure and Diversity of Intestinal Flora in Ovariectomized Osteoporotic Rats by High - throughput Sequencing [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2019, 34(07):3305-3310.
[55] Yang Rui, Song Shangyi, Wang Xingxin, et al. Discussion on the Treatment Idea of Du - moxibustion for Infertility with Phlegm - damp Constitution Based on the Theory of “Kidney as the Root of Phlegm and Spleen as the Source of Phlegm” [J/OL]. Liaoning Journal of Traditional Chinese Medicine, 1-10[2025-07-06].
[56] Hu Miaofeng, Hu Jintao, Liu Qiming, et al. Efficacy of Shugan Jianpi Decoction in the Treatment of Postmenopausal Osteoporosis with Depression of Liver Stagnation and Spleen Deficiency Type [J]. Zhejiang Clinical Medical Journal, 2024, 26(12):1820-1822.
[57] Guo Zhonghua, Shi Dongliang, Cao Yuju, et al. Saikosaponin A Exerts a Protective Effect on Osteoporosis Rats by Activating the Keap1/Nrf2/ARE Signaling Pathway[J]. Chinese Journal of Hospital Pharmacy, 2023, 43(22):2500-2506.
[58] Guo Xiaoxia, Hu Na, Lian Xiaoxiao, et al. Analysis of Characteristics and Driving Factors of Intestinal Flora Dysbiosis in Cirrhosis Patients [J]. Journal of Clinical Hepatobiliary Diseases, 2020, 36(07):1527-1533.
[59] Li Xiao, Lü Ling, Jin Xinyao, et al. Highlights of the Characteristics of Phlegm - Syndrome Differentiation and Treatment by Medical Practitioners in Ming and Qing Dynasties[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2021, 36(03):1345-1347.