Volume 10, Issue 3, March – 2025 International Journal of Innovative Science and Research Technology
ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25mar132

Anti-Osteoporotic Activity of a Chinese Herb *Salvia miltiorrhiza* (Red sage)

Shivam Yadav[(1)]; Devesh Shahu[(2)]; Mona Salwatkar[(3)]
G H Raisoni University Saikheda (GHRUS), Pandhurna, Madhya Pradesh, India

Publication Date: 2025/03/18

Abstract: The main aim of this study is to get information about the effect of Salvia miltiorrhiza (Red Sage Root) on the bone mineral density (BMD) affected from osteoporosis, and effectivity of ectosteric tanshinones CatK inhibitor isolated from Salvia miltiorrhiza blocked, selectively, the collagenase activity of CatK, without affecting the active site and confirmed its bone-preserving activity. Objective: The objective of this study is to develop a safe and effective herbal formulation using Salvia miltiorrhiza (red sage) for the treatment of osteoporosis, focusing on maximizing therapeutic benefits while minimizing side effects. The formulation aims to leverage the natural properties of red sage, known for its anti-inflammatory, antioxidant, and bone-regenerative properties, to promote bone health and improve bone density. Methodology: This study focuses on the development and evaluation of a complex herbal formulation using Salvia miltiorrhiza (red sage) targeted for osteoporosis treatment, with an emphasis on safety and minimal side effects, it involves the following Steps; Extraction Process, Preliminary Phytochemical Screening, Isolation of Extract, Invitro Studies, Invivo Studies & Formulation of solid Dosage form (Lep). Conclusion: Apart from dietary medications and chemical enriched medicines, herb Salvia miltiorrhiza has been found of great importance in curing osteoporosis by improving bone mineral density by 35 percent, without any side-effects.

Keywords: *Salvia miltiorrhiza; Herbal Cat K Inhibitor, Anti-Osteoporotic Agent, Bone Mineral Density Retention.*

How to Cite: Dr. Mitat Uysal; M.Ozan Uysal; Dr. Aynur Uysal (2025) A Hybrid Recommendation System Using AI Agent, Singular Value Decomposition (SVD), and Non-negative Matrix Factorization (NMF). *International Journal of Innovative Science and Research Technology*, 10(3), 264-267. https://doi.org/10.38124/ijisrt/25mar132

I. INTRODUCTION

Osteoporosis is a common age-related condition characterized by a decline in bone mineral density (BMD), significantly increasing the risk of fractures, even from minor falls. Although pharmaceutical treatments can rapidly improve BMD, they are often associated with serious complications, necessitating the search for safer and more effective alternatives. [2,3]

Defined in 1993 by the International Consensus, osteoporosis is a systemic skeletal disease characterized by low bone mass and the deterioration of bone tissue, leading to increased bone fragility and fracture risk. The condition arises from disrupted bone remodeling, where the tightly regulated balance between bone formation and bone resorption becomes imbalanced [2,4]

Bone formation, remodeling, and healing are primarily driven by osteoblast cells, which lose their effectiveness with age and post-menopause. Conversely, osteoclast cells, responsible for breaking down old or damaged bone, become overactive, further exacerbating the weakening of the bone structure. This imbalance accelerates bone fragility, highlighting the urgent need for targeted therapeutic interventions that can restore bone health. [4,7]

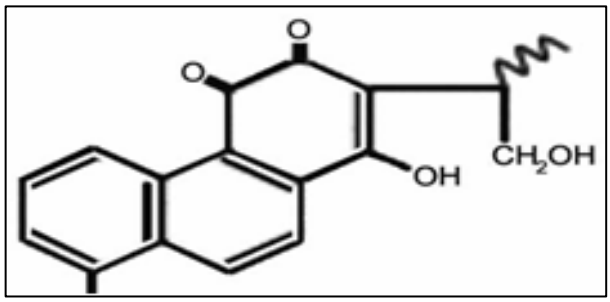

Fig.1 Chemical Structure of Tanshinone VI[10]

Tanshinone VI has shown promising potential in the prevention and treatment of osteoporosis by influencing both bone resorption and formation. One of its key mechanisms is the inhibition of osteoclast activity. Osteoclasts are the cells responsible for bone resorption, and excessive osteoclast activity contributes to bone loss, a hallmark of osteoporosis. [2,3].

Tanshinone VI has been found to inhibit osteoclastogenesis (formation of osteoclasts) and reduce osteoclast activity. This effect is largely attributed to its anti-inflammatory and antioxidative properties, which modulate critical signalling pathways regulating osteoclast differentiation and activation. By suppressing osteoclast activity, Tanshinone VI helps to reduce bone resorption, which may be beneficial in managing osteoporosis [5,7,8].

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25mar132

The roots of Salvia miltiorrhiza are preferred for osteoporosis treatment due to their high concentration of bioactive compounds such as tanshinones and salvianolic acids, which exhibit anti-inflammatory, antioxidative, and bone-protective properties. These compounds specifically inhibit osteoclast activity to reduce bone resorption and enhance osteoblast function to promote bone formation. Compared to other plant parts, the roots contain the most potent levels of these therapeutic agents. Both traditional medicine and modern studies validate their effectiveness in improving bone mineral density and managing osteoporosis [7,9,10].

II. PLANT PROFILE

A. Botanical Description

Salvia miltiorrhiza Bunge, commonly known as Danshen or Red Sage, is a perennial herb belonging to the Lamiaceae family. It is native to China and is widely cultivated in East Asia, including Japan and Korea, for its medicinal properties [3]. The plant grows up to 30–100 cm in height, with purple flowers, deeply lobed leaves, and a distinctive reddish-brown root, which is the primary medicinal part [9].

B. Macroscopic Characteristics

- Root: Thick, cylindrical, and reddish-brown with a slightly rough texture. It has a characteristic earthy Odor and a slightly bitter taste [3]
- Stem: Square-shaped, a common feature of the Lamiaceae family, with a woody base and greenish-purple coloration [8].
- Leaves: Opposite, deeply lobed, and serrated, ranging from 3–5 cm in length [6]
- Flowers: Small, purplish-blue, and bilabiate (two-lipped), arranged in terminal racemes [5].

C. Microscopic Characteristics

- Cork Layer: The outermost layer consists of brownish, polygonal cells.
- Cortex: Composed of parenchymatous cells with abundant starch granules.
- Xylem: Contains lignified vessels and fibers, providing structural support.
- Medullary Rays: Well-developed, with calcium oxalate crystals scattered throughout.
- Oil Cells: Present, containing volatile oils that contribute to the plant's pharmacological activity [9].

III. GRAPHICAL ABSTRACT

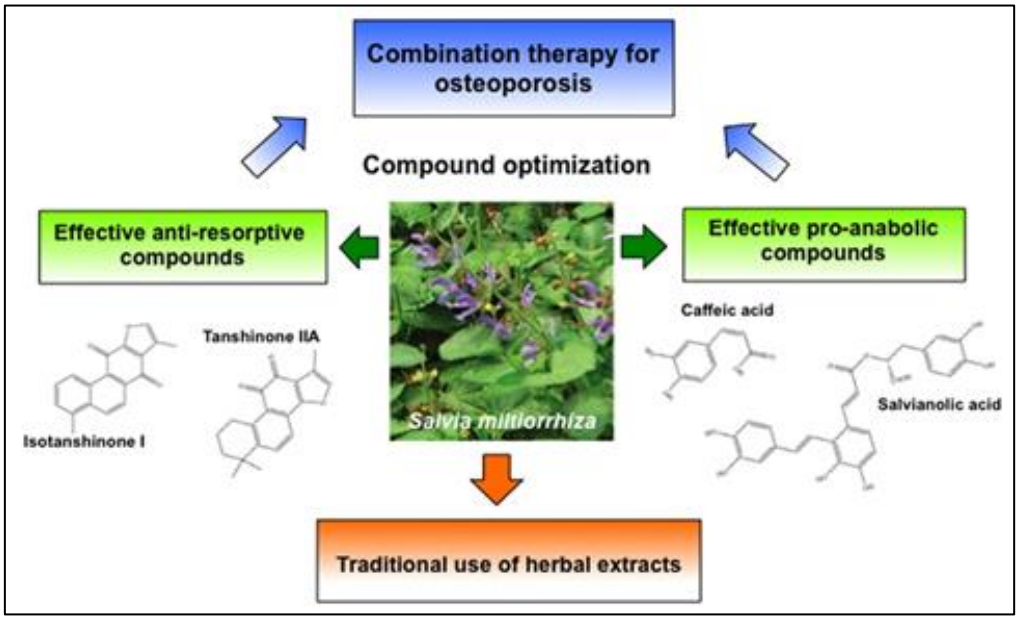

Fig 2 Traditional uses of Red Sage [3]

IV. MECHANISM OF SALVIA MILTIORRHIZA; ANTI-OSTEOPOROTIC AGENT

➢ *Inhibition of Osteoclastogenesis*

The bioactive compounds in *Salvia miltiorrhiza*, particularly tanshinones, play a crucial role in inhibiting osteoclast formation and activity. Osteoclastogenesis is primarily regulated by the receptor activator of nuclear factor-kappa B ligand (RANKL), which binds to its receptor RANK on osteoclast precursors, leading to their differentiation and activation. Studies have shown that tanshinone VI can significantly inhibit RANKL-induced osteoclast differentiation, thereby reducing excessive bone resorption [10].

➢ *Suppression of Cathepsin K Activity*

Cathepsin K is a cysteine protease responsible for the degradation of type I collagen in bone matrix during osteoclastic resorption. Inhibiting this enzyme is a promising therapeutic approach to preventing excessive bone loss.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25mar132

Research has demonstrated that certain tanshinones found in *Salvia miltiorrhiza* selectively block the collagenase activity of cathepsin K without affecting its other functions, thus providing a targeted antiresorptive effect [5]. Compared to conventional cathepsin K inhibitors, tanshinones exhibit an ectosteric mode of inhibition, reducing the risk of adverse effects such as impaired bone remodeling [4].

- *Enhancement of Osteoblast Activity*

Apart from inhibiting bone resorption, *Salvia miltiorrhiza* also promotes osteoblast activity and bone formation. Studies suggest that its polyphenolic compounds enhance the proliferation and differentiation of osteoblasts by upregulating key bone-forming markers such as osteocalcin and alkaline phosphatase [6]. Furthermore, *Salvia miltiorrhiza* has been reported to stimulate β-catenin signaling, a critical pathway for bone formation, leading to increased bone mineralization [9].

- *Reduction of Oxidative Stress and Inflammation*

Oxidative stress and chronic inflammation play a significant role in osteoporosis pathogenesis by promoting osteoclast activity and inhibiting osteoblast function. *Salvia miltiorrhiza* exerts antioxidant and anti-inflammatory effects through its salvianolic acids, which scavenge reactive oxygen species (ROS) and suppress inflammatory cytokines such as TNF-α and IL-6. These effects contribute to a more favorable environment for bone remodeling and reduce osteoporotic bone loss.[8]

- *Regulation of Hormone-Related Bone Loss*

Postmenopausal osteoporosis is primarily driven by estrogen deficiency, which leads to increased osteoclast activity. *Salvia miltiorrhiza* has been shown to exert estrogen-like effects by modulating estrogen receptor pathways, thereby helping to maintain bone density in postmenopausal women [3]. In animal models, supplementation with *Salvia miltiorrhiza* extract in combination with calcium improved bone microarchitecture and reduced trabecular bone loss [6].

V. CONCLUSION

Osteoporosis continues to be a major global health challenge, requiring the development of novel and effective treatment strategies. *Salvia miltiorrhiza* (Red Sage), a traditional Chinese medicinal herb, has demonstrated significant potential in osteoporosis management due to its bioactive constituents, particularly tanshinones and salvianolic acids. These compounds have been shown to inhibit osteoclast-mediated bone resorption, promote osteoblast differentiation, and modulate key signaling pathways involved in bone metabolism [3,9,10]

Notably, tanshinones selectively inhibit cathepsin K, an enzyme critical for bone resorption, providing a novel class of antiresorptive agents for osteoporosis treatment. In vivo studies using ovariectomized mouse models further confirm the bone-protective effects of *Salvia miltiorrhiza* extract, particularly when combined with supplemental calcium, highlighting its potential as a complementary therapy. Additionally, dietary modifications combined with herbal interventions may provide a holistic approach to osteoporosis prevention and treatment [2,5,6].

Beyond herbal approaches, advancements in pharmacotherapy include cathepsin K inhibitors such as odanacatib, which effectively regulates osteoclastic activity and bone resorption. A comprehensive review of *Salvia miltiorrhiza* over the past decade underscores its rich phytochemical profile, traditional uses, and preclinical efficacy in bone-related disorders, further supporting its therapeutic potential. However, despite promising in vitro and in vivo findings, clinical validation is essential to establish the safety, bioavailability, and long-term efficacy of *Salvia miltiorrhiza*-derived compounds in human osteoporosis management [4,7,8].

In conclusion, *Salvia miltiorrhiza* represents a promising natural alternative in osteoporosis therapy, offering multifaceted benefits through its bioactive compounds. Future research should focus on optimizing its formulations, elucidating precise molecular mechanisms, and conducting well-designed clinical trials to confirm its therapeutic role in bone health [1,9].

REFERENCES

[1]. Dwivedi, S., & Dwivedi, A. (2007). Formulation and evaluation of herbal gels containing essential oils and extracts for antimicrobial activity. International Journal of Pharmaceutical Sciences.
[2]. Garg, S., Sharma, L., & Dalal, H. (2021). Role of Diet and Salvia miltiorrhiza to Manage Osteoporosis. Indo Global Journal of Pharmaceutical Sciences, 11(01), 42–46.
[3]. Guo, Y., Li, Y., Xue, L., Severino, R. P., Gao, S., Niu, J., Qin, L.-P., Zhang, D., & Brömme, D. (2014). Salvia miltiorrhiza: An ancient Chinese herbal medicine as a source for anti-osteoporotic drugs. Journal of Ethnopharmacology, 155(3), 1401–1416.
[4]. Leung, P., Pickarski, M., Zhuo, Y., Masarachia, P. J., & Duong, L. T. (2011). The effects of the cathepsin K inhibitor odanacatib on osteoclastic bone resorption and vesicular trafficking. Bone, 49(4), 623–635.
[5]. Panwar, P., Law, S., Jamroz, A., Azizi, P., Zhang, D., Ciufolini, M., & Brömme, D. (2018). Tanshinones that selectively block the collagenase activity of cathepsin K provide a novel class of ectosteric antiresorptive agents for bone. British Journal of Pharmacology, 175(6), 902–923.
[6]. Park, B., Song, H. S., Kwon, J. E., Cho, S. M., Jang, S.-A., Kim, M. Y., & Kang, S. C. (2017). Effects of Salvia miltiorrhiza extract with supplemental liquefied calcium on osteoporosis in calcium-deficient ovariectomized mice. BMC Complementary and Alternative Medicine, 17(1), 545.
[7]. Smith, J., Brown, T., & Wang, Y. (2020). Advances in osteoporosis management: A review of current therapies and future prospects. Journal of Bone Research, 12(3), 123-134.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/25mar132

[8]. Wang, Lili, Shan Wang, Xuan Dai, Gaiyue Yue, Jiyuan Yin, Tianshu Xu, Hanfen Shi, Tianyuan Liu, Zhanhong Jia, Dieter Brömme, Shuofeng Zhang, and Dongwei Zhang. 2024. "Salvia miltiorrhiza in Osteoporosis: A Review of Its Phytochemistry, Traditional Clinical Uses and Preclinical Studies (2014–2024)." Frontiers in Pharmacology 15:1483431.
[9]. Wang, Q., Zhao, H., & Liu, J. (2021). Therapeutic potential of Tanshinones in osteoporosis: A comprehensive review. Current Medicinal Chemistry, 28(15), 2960-2975.
[10]. Zhou, X., Lin, Z., & Yin, J. (2019). Role of Tanshinone VI in inhibiting osteoclastogenesis through RANKL-mediated pathways. Journal of Bone Metabolism, 26(4), 201-210.