

## A Review on The Evaluation of Synergistic Anti-Osteoporotic Activity of *Cissus Quadrangularis* and *Asparagus Racemosus*

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**ABSTRACT:** Osteoporosis is a metabolic bone disorder characterized by decreased bone mineral density, deterioration of bone microarchitecture, and increased risk of fractures. Conventional therapies are often associated with adverse effects during long-term use, creating a need for safer and more effective alternatives. Herbal medicines have gained attention due to their therapeutic potential and reduced side effects. This review focuses on the synergistic anti-osteoporotic activity of *Cissus quadrangularis* and *Asparagus racemosus* (*Shatavari*), two important medicinal plants widely used in traditional systems of medicine.

*Cissus quadrangularis* possesses osteogenic, anti-inflammatory, and fracture-healing properties by stimulating osteoblast activity, collagen synthesis, and mineralization. *Asparagus racemosus* exhibits phytoestrogenic, antioxidant, and immunomodulatory activities that help reduce bone resorption and maintain hormonal balance, especially in postmenopausal women. When used in combination, these herbs produce a synergistic effect that enhances bone formation, inhibits osteoclast-mediated bone loss, improves calcium absorption, and accelerates fracture healing.

The review also highlights their phytochemical constituents, mechanisms of action, immunomodulatory effects, and therapeutic advantages in osteoporosis management. Evidence from experimental and literature studies suggests that the combined herbal formulation offers improved bone strength, better skeletal protection, and reduced inflammatory damage compared to single-herb therapy. Therefore, the combination of

*Cissus quadrangularis* and *Asparagus racemosus* may serve as a promising natural alternative for the prevention and management of osteoporosis with minimal side effects.

**KEYWORDS:** Synergism, *Asparagus racemosus*, *Cissus quadrangularis*, Osteoblast, Osteoclast, Phytoestrogens, Polyherbal Formulation, Immunomodulatory Activity

### I. INTRODUCTION

Osteoporosis is a chronic metabolic bone disease characterized by decreased bone mineral density (BMD), deterioration of bone tissue, and increased bone fragility, leading to a higher risk of fractures. It is one of the most common skeletal disorders affecting elderly individuals, particularly postmenopausal women due to oestrogen deficiency. The condition develops when bone resorption by osteoclasts exceeds bone formation by osteoblasts, resulting in weak and brittle bones. Common symptoms include bone pain, loss of height, stooped posture, and fractures occurring even with minor trauma.<sup>[1]</sup>

Several factors contribute to osteoporosis, including aging, hormonal imbalance, nutritional deficiency, sedentary lifestyle, smoking, alcohol consumption, and certain chronic diseases. Although conventional anti-osteoporotic drugs such as bisphosphonates, hormone replacement therapy, and calcium supplements are available, long-term use may produce adverse effects. Therefore, there is growing interest in herbal medicines as safer and

more effective alternatives for osteoporosis management.<sup>[2]</sup>

Traditional systems of medicine such as Ayurveda have long utilized medicinal plants for maintaining bone health and promoting fracture healing. Among these, *Cissus quadrangularis* and *Asparagus racemosus* (*Shatavari*) are considered important anti-osteoporotic herbs due to their complementary therapeutic actions. *Cissus quadrangularis* is well known for its bone regenerative, osteogenic, and fracture-healing properties. It stimulates osteoblast proliferation, enhances collagen synthesis, and promotes calcium deposition in bones. On the other hand, *Asparagus racemosus* possesses phytoestrogenic, antioxidant, and immunomodulatory activities that help reduce bone resorption and support hormonal balance, especially in postmenopausal osteoporosis.<sup>[2]</sup>

The concept of synergism refers to the enhanced therapeutic effect produced when two or more agents are used together compared to their individual effects. The combination of *Cissus quadrangularis* and *Asparagus racemosus* provides a dual mechanism of action by stimulating bone formation and simultaneously reducing bone loss. This synergistic interaction improves bone mineralization, accelerates fracture healing, reduces inflammation, and enhances overall skeletal strength.<sup>[3]</sup>

Hence, this review aims to evaluate the synergistic anti-osteoporotic activity of *Cissus quadrangularis* in combination with *Asparagus racemosus* and to highlight their mechanisms, phytochemical constituents, therapeutic benefits, and potential role in the management of osteoporosis.<sup>[3]</sup>

#### Objectives

- The main objective of studying the anti-osteoporotic activity of *Cissus quadrangularis* and *Asparagus racemosus* is to evaluate their potential in preventing and treating osteoporosis by improving bone health naturally.<sup>[4]</sup>
- The study aims to investigate their ability to enhance bone mineral density, stimulate osteoblast (bone-forming cell) activity, and reduce osteoclast (bone-resorbing cell) activity.<sup>[4]</sup>
- It also focuses on assessing their calcium-rich and phytoestrogenic properties, antioxidant effects, and immunomodulatory actions that help maintain bone strength and reduce fracture risk.<sup>[4]</sup>

- To determine the synergistic effect of combining both herbs for better therapeutic efficacy and safer long-term management of osteoporosis compared to synthetic drugs.<sup>[4]</sup>

#### Synergistic Anti-Osteoporotic Mechanism

The synergistic anti-osteoporotic mechanism of action of *Cissus quadrangularis* and *Asparagus racemosus* involves multiple pathways that work together to improve bone health and prevent osteoporosis. *Cissus quadrangularis* promotes rapid bone formation by stimulating osteoblast activity, increasing collagen synthesis, and enhancing calcium absorption and mineralization of bones. It also helps in faster bone regeneration and fracture healing. *Asparagus racemosus* (*Shatavari*) contains phytoestrogens that mimic estrogen-like activity, which helps reduce bone loss commonly seen in postmenopausal osteoporosis. It also exhibits antioxidant and immunomodulatory properties that protect bone cells from oxidative stress and inflammation. When used together, these herbs produce a synergistic effect by simultaneously increasing bone formation, decreasing bone resorption through inhibition of osteoclast activity, improving calcium utilization, and maintaining hormonal balance. This combined action enhances bone mineral density, strengthens bone structure, and reduces the risk of fractures naturally and effectively.<sup>[6]</sup>

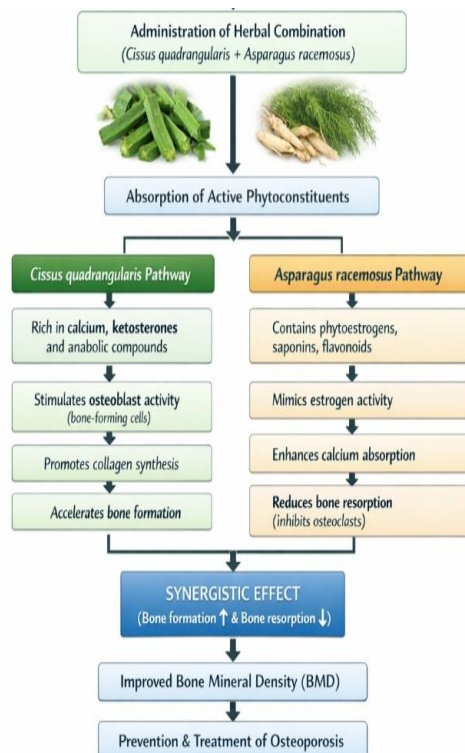
*Cissus quadrangularis*, commonly known as Hadjod or Veldt grape, belongs to the Vitaceae family and is well known for its fracture-healing and osteogenic properties. It contains flavonoids, triterpenoids, phytosterols, stilbenes, and vitamins that stimulate osteoblast activity, enhance collagen synthesis, and promote mineral deposition in bone tissue. The plant accelerates callus formation and improves bone strength by increasing calcium uptake and bone matrix formation. Its anti-inflammatory and antioxidant activities also contribute to reduced bone pain and faster recovery from fractures.<sup>[5]</sup>

*Asparagus racemosus* (*Shatavari*), a medicinal plant belonging to the Asparagaceae family, is traditionally regarded as a rejuvenating herb with phytoestrogenic activity. The roots contain steroidal saponins known as shatavarins along with flavonoids and phenolic compounds that support hormonal balance and protect against postmenopausal bone loss. *Shatavari* acts mainly by reducing osteoclast-mediated bone resorption and improving calcium metabolism. In addition, its

antioxidant and immunomodulatory properties help reduce oxidative stress and inflammatory cytokines involved in osteoporosis progression. [5]

The synergistic combination of *Cissus quadrangularis* and *Asparagus racemosus* provides a dual mechanism for osteoporosis management. *Cissus quadrangularis* primarily stimulates bone formation by enhancing osteoblast proliferation and collagen synthesis, whereas Shatavari supports hormonal regulation and suppresses excessive bone resorption through phytoestrogenic activity. Together, these herbs improve bone mineral density, accelerate fracture healing, and maintain balanced bone remodelling. The combination also exhibits anti-inflammatory and antioxidant effects that protect bone cells from oxidative damage and chronic inflammation. [5]

Several studies have reported the beneficial effects of this herbal combination in osteoporosis. Experimental investigations demonstrated enhanced osteoblast differentiation, inhibition of osteoclast genesis, increased alkaline phosphatase activity, and improved bone mineral content in animal models. Polyherbal formulations containing these two herbs were found to produce better therapeutic outcomes compared to single-drug therapy because of their complementary mechanisms of action.



❖ **Effect on osteoblast activity(bone formation):cissus quadrangularis**

• **Osteogenesis(Bone Formation):** It stimulates the proliferation and differentiation of osteoblasts (bone-forming cells). It increases the activity of alkaline phosphatase (ALP), a marker for bone formation.[7]

• **Mineralization:** It speeds up the deposition of essential minerals like calcium and phosphorus into the bone matrix, which accelerates the healing of fractures.[7]

• **Collagen Synthesis:** It promotes the early development of collagen fibres and mucopolysaccharides, which are critical for forming the "callus" that joins broken bones.[7]

• **Anti-inflammatory & Analgesic:** It acts as a dual inhibitor of the COX (Cyclooxygenase) and LOX (Lipoxygenase) pathways, effectively reducing swelling and pain in joints and muscles.[8]

• **Anabolic Effects:** Some studies suggest it contains unique phytosterols that may act like natural anabolic steroids to strengthen tissues without the typical side effects.[9]

❖ **Effect on osteoclast activity (bone resorption): Shatavari (Asparagus Racemosus)**

• **Hormonal Regulation (Phytoestrogenic):** It contains steroidal saponins (Shatavarins) which act as phytoestrogens. These bind to estrogen receptors, helping to balance hormones naturally, especially when levels are low during menopause or irregular during PCOS.[10]

• **Galactagogue Effect:** It stimulates the production of prolactin, the hormone responsible for milk secretion, thereby increasing milk supply in lactating mothers.[10]

• **Adaptogenic & Anti-stress:** It modulates the HPA (Hypothalamic-Pituitary-Adrenal) axis, reducing cortisol levels and helping

the body cope with physical and emotional stress.<sup>[11]</sup>

- **Antioxidant & Rejuvenate:** It scavenges free radicals and increases levels of antioxidants like Superoxide Dismutase (SOD), which protects the ovaries and improves oocyte (egg) quality.<sup>[12]</sup>
- **Gastroprotective:** It increases the production of protective gastric mucus and reduces acid secretion, making it effective for treating stomach ulcers and acidity.<sup>[13]</sup>

#### Key Therapeutic Benefits of the Combination

- **Increased Bone Mineral Density (BMD):** The combination helps reverse bone density loss and improves overall bone strength.<sup>[14]</sup>
- **Faster Fracture Healing:** Enhances the regeneration of connective tissues and speeds up callus formation.<sup>[14]</sup>
- **Reduced Biochemical Markers of Resorption:** Studies indicate a decrease in serum levels of C-terminal telopeptide of type I collagen (CTX), a key marker of bone resorption.<sup>[15]</sup>

This combination is frequently used in Ayurveda as a holistic approach to prevent bone resorption, particularly in postmenopausal women.<sup>[15]</sup>

#### Immunomodulatory Effects in Bone Health

The combination of *Cissus quadrangularis* and *Shatavari* (*Asparagus racemosus*) shows important **immunomodulatory effects** that help maintain bone health by regulating immune responses involved in bone remodelling.

##### 1. Regulation of Inflammatory Cytokines

- Chronic inflammation increases bone loss by stimulating osteoclast activity.<sup>[17]</sup>
- The herbal combination helps **reduce pro-inflammatory cytokines** such as TNF- $\alpha$ , IL-1, and IL-6.
- This leads to **decreased bone resorption** and protection against osteoporosis.

##### 2. Suppression of Osteoclast Activation<sup>[17]</sup>

- Inflammatory mediators promote osteoclast differentiation.
- The herbs help **inhibit excessive osteoclast formation** by modulating immune signals.
- This maintains a healthy balance between bone formation and resorption.

##### 3. Enhancement of Anti-inflammatory Response<sup>[17]</sup>

- *Cissus quadrangularis* exhibits **anti-inflammatory activity**, reducing tissue damage.
- *Shatavari* supports immune balance and reduces chronic inflammatory conditions.
- Together, they promote a **protective anti-inflammatory environment** for bone tissue.

##### 4. Modulation of Immune Cells<sup>[17]</sup>

- Regulates activity of immune cells like **T-cells and macrophages**, which influence bone metabolism.
- Helps prevent immune-mediated bone degradation seen in conditions like arthritis.

##### 5. Antioxidant Support to Immune Function

- Both herbs possess **antioxidant properties**, reducing oxidative stress.
- Protects bone cells from damage caused by free radicals and inflammation.

##### 6. Overall Impact on Bone Health<sup>[16]</sup>

- Reduces inflammation-induced bone loss.
- Supports bone regeneration.
- Enhances skeletal strength and stability.

#### Advantages of *Cissus quadrangularis* in Combination with *Shatavari* (*Asparagus racemosus*)

##### 1. **Enhanced Osteoprotective Effect<sup>[16]</sup>**

The combination improves bone mineral density and provides better protection against osteoporosis compared to individual use.

##### 2. **Dual Mechanism of Action**

*Cissus quadrangularis* stimulates osteoblast activity (bone formation),

while *Shatavari* inhibits osteoclast activity (bone resorption), ensuring balanced bone remodelling.

3. **Acceleration of Fracture Healing**<sup>[16]</sup>  
Promotes faster bone regeneration and callus formation, aiding in fracture repair and recovery.

4. **Hormonal Regulation**<sup>[15]</sup>  
*Shatavari* exhibits phytoestrogenic activity, helping in maintaining hormonal balance and preventing postmenopausal bone loss.

5. **Anti-inflammatory and Antioxidant Effects**<sup>[15]</sup>  
Reduces inflammation and oxidative stress, thereby protecting bone cells and supporting overall skeletal health.

6. **Improved Joint Health**  
Helps in reducing joint pain, stiffness, and improves mobility, making it useful in arthritis.

7. **Safety and Natural Origin**  
Being herbal in nature, the combination is relatively safe with fewer side effects and is suitable for long-term use.

8. **Postmenopausal Support**<sup>[18]</sup>  
For women, *Shatavari* helps balance hormones (acting as a phytoestrogen) to

counteract the bone density loss typically caused by decreased estrogen levels.

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Hence, this review aims to evaluate the synergistic anti-osteoporotic activity of *Cissus quadrangularis* in combination with *Asparagus racemosus* and to highlight their mechanisms, phytochemical constituents, therapeutic benefits, and potential role in the management of osteoporosis.<sup>[19]</sup>

**Synergistic Anti-osteoporotic Action** <sup>[17]</sup>

Mechanism	<i>Cissus quadrangularis</i> (Anabolic Lead)	<i>Shatavari</i> (Hormonal Support)	Synergistic Result
<b>Bone Formation</b>	Stimulates <b>osteoblast proliferation</b> and differentiation via the $\beta$ -catenin pathway.	Increases bone formation and encourages <b>mesenchymal stem cell</b> health.	Rapid increase in <b>Bone Mineral Density (BMD)</b> and structural integrity.
<b>Bone Resorption</b>	Inhibits <b>RANKL-induced osteoclast genesis</b> , slowing down bone breakdown.	Contains <b>phytoestrogens</b> that mimic estrogen to reduce postmenopausal bone loss.	Balanced bone remodelling cycle where formation exceeds resorption.
<b>Matrix Synthesis</b>	Enhances <b>collagen type I</b> and mucopolysaccharide production.	Protects bone cells from oxidative stress-induced cell death.	Faster mineralization and a stronger organic bone matrix.
<b>Mineralization</b>	Speeds up the uptake and deposition of <b>calcium and phosphorus</b> .	Provides a nourishing, adaptogenic environment for mineral deposition.	Quick callus formation and significantly reduced fracture healing time.
<b>Inflammation</b>	Lowers pro-inflammatory cytokines (IL-1 $\beta$ , TNF- $\alpha$ ) that	Reduces systemic stress and inflammation through high	Marked reduction in bone pain and joint swelling.

	trigger bone loss.	saponin content.	
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Table 1: Synergistic Anti-Osteoporotic Action

**Other Actions of Cissus quadrangularis in Combination with Shatavari<sup>[19]</sup>**

- **Analgesic Action**  
Helps reduce bone and joint pain associated with osteoporosis and fractures.
- **Adaptogenic Effect**  
Improves the body's resistance to stress and supports overall wellbeing.
- **Gastroprotective Activity**  
Protects the gastric mucosa and helps reduce gastric irritation.
- **Anabolic Effect**  
Promotes tissue growth and regeneration, especially in bone and muscle tissues.
- **Collagen Synthesis Enhancement**  
Supports collagen production, improving bone matrix formation and connective tissue strength.
- **Joint Protective Action**  
Helps maintain healthy joints and reduces stiffness and degeneration.
- **Anti-arthritis Activity**  
Reduces symptoms of arthritis such as inflammation, swelling, and pain.
- **Mineralization Support**  
Enhances deposition of minerals like calcium and phosphorus in bones.
- **General Tonic Effect**  
Improves physical strength, energy, and recovery.
- **Neuroprotective Action**  
Antioxidant constituents may help protect nerve cells and reduce stress-related damage.
- **Anti-fatigue Effect**  
Helps reduce weakness and fatigue commonly seen in chronic bone disorders.
- **Endocrine Supportive Activity**  
Supports hormonal and metabolic functions involved in bone remodelling.
- **Wound Healing Property**  
Accelerates healing of damaged tissues and fractures.
- **Anti-aging Effect**  
Antioxidant and rejuvenating properties help delay age-related degeneration.
- **Improves Musculoskeletal Health**  
Supports healthy bones, muscles, tendons, and ligaments together.

**II. CONCLUSION**

The combination of *Cissus quadrangularis* and *Asparagus racemosus* represents a promising natural approach for the prevention and management of osteoporosis. Their synergistic action enhances bone formation, reduces bone resorption, improves fracture healing, and supports overall skeletal health with minimal side effects. This herbal combination may serve as a valuable alternative or complementary therapy for osteoporosis, especially in postmenopausal women and elderly patients. Further clinical studies are necessary to establish standardized formulations, dosage regimens, and long-term safety for therapeutic applications.

The dual action improves skeletal strength and accelerates fracture repair. Hormonal balance and antioxidant effects further contribute to bone protection. This natural combination shows therapeutic potential with minimal side effects.

Hence, it can be considered a valuable alternative in bone health care. Therefore, this combination holds strong potential in future clinical applications.

**SOME OF THE ADVANAGES FROM THE ABOVE RESULTS**

- Stimulates osteoblast activity (bone forming cells)
- Reduces osteoclast – mediated bone resorption and prevents bone loss.
- Improves calcium absorption and bone mineralization for stronger bones.
- Provides antioxidant and anti-inflammatory effects that protect bone cells.
- Shows synergistic anti-osteoporotic activity with better bone strength and fracture healing.

- Useful in the postmenopausal osteoporosis.

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