WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 6, 64-76. Review Article ISSN 2277–7105

COMPARATIVE STUDIES OF *CISSUS QUADRANGULARIS* AND *PISONIA GRANDIS* ON ANTI OSTEOPOROTIC ACTIVITY – REVIEW

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Article Received on 15 Feb. 2026,
Article Revised on 05 March 2026,
Article Published on 16 March 2026,

https://doi.org/10.5281/zenodo.19043005

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How to cite this Article: Anbarasu D.* M.Pharm., Preetha Ranjani T., Sangeetha S., Thariga V., Sujitha R., Nepolean R. (2026). Comparative Studies Of Cissus Quadrangularis And Pisonia Grandis On Anti Osteoporotic Activity – Review. World Journal of Pharmaceutical Research, 15(6), 64–76.

ABSTRACT

Osteoporosis is a metabolic bone disorder characterized by reduced bone density and increased fracture risk due to an imbalance between bone resorption and formation. Osteoclast activity is accelerated and bone structure is weakened by factors like age, estrogen insufficiency, and nutritional imbalance. Interest in using natural therapeutic substances for safer management is growing. Rich in bioactive phytochemicals, Cissus quadrangularis and Pisonia grandis have anti-inflammatory, anti-osteoclastic, antioxidant, and bone-supporting qualities. Their potential as natural anti-osteoporotic medicines is highlighted by their pharmacological properties and traditional use. The phytochemistry, pharmacology, and molecular processes of CQ and PG are thoroughly examined in this study, which also indicates research needs for further investigation and reveals variations in their osteoprotective capabilities. The results unequivocally show that whereas PG needs more mechanistic and clinical testing, CQ is a validated natural option for osteoporosis therapy.

KEYWORDS: Osteoporosis; bone remodeling; osteoclast inhibition; *Cissus quadrangularis*; *Pisonia grandis*; phytochemicals; anti-osteoporotic activity.

CQ-*Cissus quadrangularis*, PG-*Pisonia grandis*, RANK-, RANKL-, OPG-, SERM-, ALP-, DKK.

1. INTRODUCTION

The skeletal disorder known as osteoporosis is defined by a reduction in the density (mass/unit volume) of typically calcified bone. The bone's mechanical strength is weakened by the decreased density, increasing its susceptibility to fracture. It often affects the wrist, hip, and spine and is considered a "silent disease" with no symptoms prior to fracture.[1] The most common fractures associated with osteoporosis are those of the wrist, hip, and vertebra. More than 90% of the costs are related to hip fractures.[2]

The illness is known as a "silent epidemic" because it frequently advances silently until a fracture happens. A one-year mortality rate of up to 20–24% is linked to hip fractures alone, which account for almost 90% of all osteoporosis-related medical expenses.

Osteocytes, the main mechanosensing cells, coordinate osteoclast-mediated bone resorption and osteoblast-mediated bone creation in the strictly controlled process of bone remodeling. Oxidative stress, hormonal imbalance, nutritional inadequacies, and disruptions in the RANK/RANKL/OPG axis all lead to increased resorption and decreased creation, which eventually weakens bone structure.

although traditional treatments which include bisphosphonates, calcitonin, denosumab, teriparatide, and SERMs are clinically powerful, their long-term use is restrained by means of damaging results inclusive of gastrointestinal irritation, hypocalcemia, bizarre femoral fractures, venous thromboembolism, and osteonecrosis of the jaw. This has inspired growing hobby in herbal-based healing procedures that could offer advanced protection profiles with multifunctional healing effects.

conventional scientific structures like Ayurveda and Siddha understand several flora with bone-strengthening and fracture-restoration properties. Cissus quadrangularis is some of the maximum revered, frequently called “Hadjod,” meaning “bone setter.” Pisonia grandis, although now not immediately used for bone recuperation, is thought for 07b031025f5f96dfa8443f843db463b6 and antioxidant activity that could in a roundabout way benefit bone metabolism.

This assessment provides a comprehensive clinical evaluation and comparison of CQ and PG for his or her relevance in osteoporosis management, that specialize in molecular mechanisms, phytochemistry, and proof from preclinical and medical research.

2. Bone Biology evaluation

Osteoclast

The osteoclast is outline because the breakdown of bone. The bone lining mobile that causes bone resorption is the osteoclast, a huge multinucleated cellular that may attain a diameter of 100 mm. it's far derived from hematopoietic cells of the mononuclear lineage. They secrete hydrochloric acid and cathepsin k to degrade the mineral and organic matrix. immoderate osteoclast interest is the hallmark of osteoporosis.

Osteoblast

The osteoblast is define because the mobile formation. The additives of the bone matrix are produced by means of the osteoblast. in preference to working on my own, osteoblasts are placed in organizations alongside the floor of the bone, lining the layer of bone matrix. They secrete kind I collagen, osteocalcin, osteopontin, and alkaline phosphatase (ALP). decreased osteoblast interest results in impaired bone mineralization.

Osteocytes

Osteocytes adjust bone turnover via mechanotransduction and release of sclerostin and DKK-1, inhibitors of the Wnt/β-catenin signaling pathway.

3. Cause

Anti-osteoporotic activity aims to prevent bone loss caused by various risk factors such as aging, hypogonadism, and hypercortisolism, which accelerate bone resorption and reduce bone formation. Conditions like menopause further promote osteoporosis due to estrogen deficiency, while hereditary osteoporosis increases susceptibility through genetic defects in bone metabolism. In some cases, bone weakness may appear idiopathic, especially during growth spurts or pregnancy, when increased calcium demand affects bone density. Nutritional factors like vitamin D deficiency impair calcium absorption and contribute to bone demineralization, and hormonal disorders such as primary hyperparathyroidism enhance osteoclastic activity, worsening bone loss. Anti-osteoporotic agents work by improving calcium utilization, regulating hormones, and inhibiting excessive bone resorption to maintain skeletal strength and stability.

4. Signs and symptoms

- Acute back pain
- Groin or thigh pain

In severe cases

- Deformity of the spine
- Chronic pain
- Gastrointestinal or respiratory issues

5. Risk factors

- Age
- Low body weight (less than 58 kg or 127 lb)
- Prior adult fractures, particularly those to the hip, spine, or wrist
- Hip fracture history in the parents
- Treatment with glucocorticoids, either current or previous (>5 mg prednisolone daily for ≥3 months)
- Present-day smoking
- Overconsumption of alcohol
- Early menopause (less than 40 years of age)
- Hypogonadism
- Rheumatoid arthritis.

6. Pathophysiology[25,26,27]

Bone Cell Imbalance

↑ Osteoclasts, ↓ Osteoblasts

RANK/RANKL/OPG Dysregulation

↑ Osteoclastogenesis

↓

Osteocyte Dysfunction

↑ Sclerostin / DKK-1

↓ Wnt/β-catenin → ↓ Osteoblasts

↓

↑ Oxidative Stress / Cytokines

↑ Osteoclast, ↓ Osteoblast

↓

Nutritional/Metabolic Factors

↓ Ca^{2+} / ↓ Vitamin D → ↑ PTH

↑ Bone Resorption

↓

Structural Bone Changes

Thinner trabeculae, ↑ porosity

↓ Bone strength

↓

Fractures

7. Diagnosis[4]

- X-rays
- Bone densitometry
- Dual-energy X-ray absorptiometry [DXA]
- Bone mineral density [BMD] with T-score 2.5 indicating osteoporosis

The diagnosis is based on the existence of fragility fractures and/or the evaluation of bone mineral density (BMD) using dual X-ray absorptiometry (DXA), which is reported as the T-score. “A fracture caused by injury that would be insufficient to fracture a normal bone: the result of reduced compressive and/ortorsional strength of the bone” is how the World Health Organization (WHO) describes a fragility fracture. Accordingly, a fragility fracture may be clinically described as one that results from no discernible trauma or from minor trauma, such as a fall from a standing height or less. At almost every skeletal location, low bone mass increases the risk of fractures.

8. PLANT PROFILE

8.1 Cissus quadrangularis

The Vitaceae family includes the succulent plant *Cissus quadrangularis L*., which is used in traditional Indian medicine as well as as a food item.[5] Among the many phytochemicals found in the plant are alkaloids, triterpenoids, and flavonoids. Among the many phytochemicals found in the plant are alkaloids, triterpenoids, and flavonoids.[6]

It has long been utilised in Ayurvedic and Unani medicine to treat a variety of conditions, including as skin disorders, bone fractures, and digestive problems.[7] Commonly referred to as "Hadjod," Cissus quadrangularis is a perennial plant in the Vitaceae family. Adamant

creeper, square-stemmed vine, veldt grape, devil's backbone, asthisamharaka, hadjod and pirandai, Sannalam, Nalleru, Vajravelli, and Mangara valli are some of its other.[8]

Figure 1: *Cissus quadrangularis*

8.1.1 Botanical description[9]

- Kingdom : Plantae
- Subkingdom : Tracheobionta
- Super division : spermatophyte
- Division : Magnoliophyta
- Class : Magnoliopsida
- Subclass : Rosidae
- Order : Vitales
- Family : Vitaceae
- Genus : Cissus
- Species : quadrangularis
- Phylum : angiosperms

8.1.2 Vernacular names[10]

- English : Adamant creeper, edible stemmed vine.
- Tamil : Vajjravalli, Pirandai.
- Hindi : Hadjod, Hadjora, and Hadsarihari
- Malyalam : Peranta, Cannalamparanta.

8.1.3 Chemical constituents[11]

The plant contain various chemical constituent including

- α- and β- amyrins,
- βsitosterol,
- ketosteroids,
- phenols,
- tannins,
- carotene,
- vitamin C
- Alpha _ amyrine,
- beta _ amyrine,
- beta_sitosterol,
- stigmasterol,
- resveratrol,
- quadrangularis A.

Seven alicyclic lipids constituents have also been reported from Cissus quadrangularis. unsymmetric tetracyclic triterpenoids such as d-amyrin, onocer-7-ene-3a, 21b-diol, damyrone and 3,3',4,4'-tetra hydroxy biphenyl, 3,3',4,4'-tetrahydroxybiphenyl have been isolated from plant and were quantitatively determined by HPTLC and HPLC methods in samples collected from five different geographic zones of India.

Several other constituents such as flavonoids quercetin and kaempferol, and stilbene derivatives, quadrangularins A,B,C and many others e.g. resveratrol, piceatanon, pallidol, perthenocissi and phyto-sterols have been isolated from plant. Stem extract contains a high percentage of calcium ions and phosphorus, both essential for bone growth.

8.1.4 Therapeutic uses[12 –16]

Cissus quadrangularis exhibits a wide range of therapeutic activities that contribute to its value in traditional and modern medicine. It is well known for its bone healing activity, supporting rapid fracture recovery through stimulatory activity on osteoblasts and mineralization. The plant also shows strong anti-inflammatory activity, reducing swelling and tissue damage, along with analgesic activity, which helps relieve pain during injury or inflammation. Its antioxidant and free radical scavenging properties protect tissues from oxidative stress, while its anti-microbial and anti-bacterial activity prevents infections. Additionally, *Cissus quadrangularis* demonstrates anti-ulcer activity, protecting the gastrointestinal tract, and central nervous system activity, which may help in controlling

stress and nervous conditions. It also has significant anti-hemorrhoidal activity, reducing bleeding and inflammation in hemorrhoids, and remarkable wound healing activity, promoting faster tissue repair. Together, these pharmacological properties highlight its broad medicinal potential.

9.1 Pisonia grandis R. Br

Pisonia grandis R.Br, commonly known as Leechaikottaikeerai is a widespread evergreen tree with significant medicinal properties.[17] The plant leaves, stems, and roots are extensively used in traditional medicine for various ailments.[18]

The herb has antifungal, anti-inflammatory, anti-diabetic, antioxidant, and wound-healing qualities. According to phytochemical investigations, P. grandis extracts contain flavonoids, phenolic compounds, and alkaloids.[19]

Figure 2: Pisonia grandis.

9.1.1 Biological description

- Kingdom : plantae
- Subkingdom : Tracheobionta
- Superdivision : Spermatophyto
- Division : Magnoliophyto
- Class : Magnoliopsida
- Subclass : Caryophyllidae
- Order : Caryophyllales
- Family : Nyctaginaceae
- Genus : Pisonia
- Species : Pisonia grandis R.Br

9.1.2 Vernacular names

- English : Lettuce tree
- Tamil : Leechaikottaikeerai [sandimurungai]
- Telugu : Lanchamundaku
- Gujarat : Velati salet.

9.1.3 Chemical composition

Alkaloids, phenolic compounds, flavonoids, carbohydrates, proteins, amino acids, saponins, sterols, and tannins are among the several phytochemical elements found in this plant. P. grandis leaves (PGL) were investigated for chemical profile and biological potentiality using a range of solvents with varying polarity. α-amylase, α-glucosidase, and tyrosinase inhibitory assays were used to assess the enzyme's inhibitory property.[20]

In rat models, plant leaf extracts—especially ethanolic and aqueous extracts—have demonstrated strong antioxidant capacity and hepatoprotective benefits.[21] Phytol (27.5 and 12.3%) and squalene (14.6 and 4.9%) are identified as major compounds in petroleum ether (PEE) and ethyl acetate extracts (EAE).

The EAE demonstrated substantial α-amylase inhibitory action with an IC 50 of 29.04 ± 0.16 µg/mL. The PGL extract's potential biological qualities may be due to the phytochemicals it contains. The findings demonstrated this neglected vegetable's effectiveness in the food and pharmaceutical industries as a dietary supplement and in other uses.[22]

9.1.4 Therapeutic uses

It is widely distributed in India and traditionally used for various therapeutic purposes. The plant has demonstrated.

- anti-inflammatory
- anti osteoclast activity
- anti-fungal
- antioxidant
- anti-microbial
- anti-diabetic
- diuretic
- analgesic
- wound healing properties.[23]

The methanolic leaf extract demonstrated notable wound-healing capacity in a study conducted on Wistar rats, as evidenced by enhanced wound contraction, tensile strength, and histological characteristics. Additionally, the extract demonstrated antibacterial activity on par with that of common antibiotics.[24]

10. Mechanisms of Anti-Osteoporotic Action

10.1 Cissus quadrangularis

- **Evidence-supported mechanisms**

Inhibits osteoclastogenesis

Downregulation of RANKL

Upregulation of OPG

- **Promotes osteoblast differentiation**

↑ RUNX2, ALP, osteocalcin

Activation of Wnt/β-catenin

- **Reduces inflammatory cytokines**

↓ TNF-α, IL-6

- **Antioxidant activity protects osteoblasts**
- **Enhances bone mineralization**

Due to calcium and phosphorus content

Preclinical evidence: Improvement in BMD, trabecular thickness, and bone strength in ovariectomized rats.

Clinical evidence: Supports fracture healing; reduces bone turnover markers.

10.2 Pisonia grandis

- No direct studies on osteoporosis
- Theoretical mechanisms only:

1. Antioxidant effects may reduce oxidative bone loss
2. Anti-inflammatory activity may indirectly reduce osteoclast activation

However, no animal or human evidence supports anti-osteoporotic action.

11. Analytical Profile of Ethnomedicinal Plants Employed in Bone and Musculoskeletal Disorders

Parameters	Cissus quadrangularis	Pisonia grandis
Botanical family and part used	Vitaceae Mostly stem are used	Nyctaginaceae Mostly leaves are used
Traditional / ethnomedicinal role in bone disorder	Used traditionally for bone fractures, bone healing and bone weakness	Used traditionally for joint /musculoskeletal complaints, wound healing, edema, swelling
Anti resorptive mechanism	Inhibits osteoclast differentiation via RANKL/OPG modulation	Anti oxidant and anti inflammatory effects may indirectly reduce bone resorption
Animal evidence	Improves BMD, trabecular thickness and biomechanical strength in osteoporotic rodents	No reported osteoporosis animal studies and it has only inflammation studies
Clinical evidence	Supports fracture healing and bone regeneration	No clinical evidence available
Potential as anti osteoporotic candidate	High potential; validate mechanism and clinical evidence	Unproven ; potential only theoretical based on phytochemistry

12. CONCLUSION

Cissus quadrangularis and Pisonia grandis both possess significant medicinal value, but their roles in bone health differ greatly. C. quadrangularis shows strong anti-osteoporotic potential, supported by its rich phytochemistry, osteoblast-stimulating properties, and proven animal and clinical evidence for fracture healing. In contrast, P. grandis demonstrates mainly anti-inflammatory, antioxidant, and wound-healing benefits, with only theoretical potential for bone protection and no direct studies on osteoporosis. While both plants offer valuable therapeutic effects, current evidence clearly favours C. quadrangularis as a validated natural candidate for managing bone loss and promoting bone regeneration.

Thus, CQ emerges as a validated natural therapy for osteoporosis, while PG serves as a theoretical candidate worthy of future investigation.

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