



Mini Review

Role of *Cissus quadrangularis* in the Treatment of Osteoporosis: A Review

Supriya Verma*

Abstract

Cissus quadrangularis linn is a plant of family Vitaceae, it is also known as "Bone Setter", as it has prominent role in bone diseases, mainly osteoporosis (porous bone disease). Other few regional names of it are Hadjod, Asthisaharakha, Veldt Grape, Stemmed Vine, Vajravalli, Devil's Backbone, etc. Osteoporosis is a bone (metabolic) disease, which shows effect on the entire skeleton and is well characterized with low bone mass of the body and micro architectural deterioration. The administration of *C. quadrangularis* increases Alkaline Phosphatase (ALP), which is a bone marker of osteoblast differentiation (osteoblastogenesis). Apart from this, it is found to be useful in the treatment of obesity, anorexia, colic, dyspepsia, flatulence, helminthiasis, haemorrhage skin diseases, and many others. Its' stem, leaves and young shoots have pharmacological activities. *C. quadrangularis* extract can be obtained in various solvents like ethanol, methanol, hexane, ethyl acetate, aqueous extract, acetone, petroleum ether and chloroform.

Keywords

Cissus quadrangularis; Bone setter; Osteoporosis; Bone marker

Introduction

C. quadrangularis (CQ) is a perennial plant, which reaches a height of 1.25-1.5 m with quadrangular branches. It is one of the most commonly used medicinal plants in Africa, Asia and Thailand. Its various parts have pharmacological activities as shown in the Table 1

Bone and Osteoporosis

The *C. quadrangularis* extract (CQE) can be obtained in various solvent systems. Ethanol, methanol, hexane and petroleum ether extracts shows anti-osteoporotic activity [1]. It is used in the treatment of Osteoporosis, is characterized by micro-architectural deterioration of the skeleton and a condition of low bone mass [2,3]. It leads to increased chances of bone fragility and decreased bone mineral density. It is also known as Asthisashirya means "Porous Bone" [4]. Osteoporosis or porous bone condition is a silent disease which has no symptoms until a fracture occurs and is defined by WHO as a bone mineral density (BMD) more than 2.5 standard deviations below the mean of normal, healthy individuals at their peak bone mass.

Bones are living, active tissues that renew themselves *via* a process called remodelling. This remodelling process is initiated by the 'osteoclasts' which removes the old cells from the bone tissue, deposit them in the bloodstream for their removal and also create small holes in the bone. The cells 'osteoblasts' fill the holes with the "mortar" of calcium, minerals and collagen [5,6]. On local and systemic CQE administration less tissue reaction with accelerated bone formation takes place. It also mediates osteogenic effect due to the great increase in osteoblast bone cell differentiation and function [7].

Osteoblasts are the mononucleate cells, responsible for the bone formation [8] and *C. quadrangularis* has shown effect on the osteoblast differentiation [9]. Hence, *C. quadrangularis* is giving a compliance with the tag of "bone setter". As ALP and Tartarate Resistant Alkaline Phosphatase (TRAP) represents thickness of cortical and trabecular bone respectively, the administration of CQE gives significant effect on the bone cells. As ALP and TRAP represents the osteoblast and osteoclast cells respectively. CQE extract increases the extent of mineralized nodules along with ALP, mRNA expression of osteoblast-related genes remains unaffected.

Constituents

The plant's active constituent is 3-ketosteroid (anabolic in nature) [10]. This phytogetic steroid stimulates osteoblastogenesis by acting on the estrogenic receptors of the bone cells. The underlying mechanism behind the action of CQ has been found out to be the MAPK-dependent pathway [11]. MAPKs are serine-threonine kinases and play a crucial role in the regulation of ALP activity [7].

As the vitamins and anabolic steroids of CQ plays an important role in the rate of fracture healing. There is early regeneration of connective tissues which are involved in the formation of callus during the action of osteoblasts cells. The CQ constituents play systemic actions and are responsible for fast mobilization of mucopolysaccharides and other substances, which can play a vital role in the process of bone healing. During the bone mineralization process, calcium phosphate complex is deposited in the latter state which can be studied by making use of phosphorus (P^{32}) [12].

The most important constituent of CQ i.e., ketosterones has been used due to its multiple uses like it acts as antagonist for the glucocorticoid receptor and have anabolic steroidal properties for the maintenance of good bone health. It increases intramuscular creatinine level, blocks muscle damaging and leads to muscle formation. It is capable of significant reduction in the formation of free radicals, superoxide radical production and lipid peroxide production in erythrocytes. It shows cytoprotective property and has antisecretory action against ulceration. It mobilizes fibroblast and chondroblast and increases regeneration of an injured tissue [13].

Synergistic Role of the Plant Constituents

During bone mineralization, accumulation of mucopolysaccharides at the fracture (target) site precedes the actual process of mineralization and this CQ increases this process rate by promoting the mucopolysaccharides accumulation at the target site. It has high content of β -sitosterol, vitamin C, calcium, β -carotene, terpenoids, quadrangularis A, B and C [7].

*Corresponding author: Supriya Verma, University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, India, Tel: +919463453377; E-mail: supriya_punjab@yahoo.com

Received: July 2, 2018 Accepted: July 23, 2018 Published: July 31, 2018

Table 1: The pharmacological activity of the various parts of the plant.

Parts	Uses
Stem	Gastritis, bone fractures, skin infections, constipations, eye diseases, piles, anaemia, asthma, irregular menstruation, burns and wounds
Leaves and young shoots	Hemorrhoids and certain bowl infections
Stem Juice	Scurvy and in irregular menstruation
Stem paste	Asthma
Stem and leaves	Bone fractures

Table 2: List of popular products of CQ.

Hadjod	Each capsule contains 250 mg extract of Hadjod. Two capsules, twice a day or suggested by Physician. It is a product of Himalaya Herbal Healthcare, Bangalore, India. It increases bone mineral density, accelerates fracture healing and relieves pain and inflammation.
Cissoket 20	Each capsule contains 500 mg dry extract containing 20% ketosterones. One to two capsules twice a day or directed by physician. It is indicated for broken bones and to improve bone immunity.

Many other constituents are also present in it like calcium oxalate, flavonoids, mucilage and pectin. The other components are calcium, potassium, phosphorus and magnesium, α -amyrin and α -amyrone, quercetin, columbin, protein, fat and carbohydrate. Main chemical constituents are tetracyclic triterpenoids (onocer-7-ene-3 α , 21- β diol, onocer-7-ene-3 β , 21- α diol), two steroidal principles I and II (α -sitosterol and δ -amyrine). New lignan glycosides have also been obtained from the stems of CQ [14]. It has been proved safe and effective according to Grades of Recommendations Assessment Development and Evaluation (GRADE) in the treatment of bone fractures, hemorrhoids and body weight reduction [15].

CQ also increases the mineral uptakes like calcium, strontium and sulfur by the bone forming (osteoblast) cells in the fracture healing [16]. There are some phytochemicals which are anabolic in nature, acts on the estrogen receptors of the bone [17].

Bone of human contains mineralized bone matrix and bone cells, osteoblasts are the mainly responsible cells for this mineralization process and upon activation it produces large amount of ALP, which is a phosphate-splitting enzyme and releases into the osteoid and start up the deposition process of minerals. The osteoblasts control the bone formation rate and their increasing growth is the symbol of the optimum bone repair. The reduction in bone mass is due to the imbalance of osteoclast and osteoblast cells; hence osteoblast cells should be maintained optimally.

There are some marketed products of CQ, as shown in Table 2.

Bone Markers

Bone markers play an important role in the determination of bone turnover with the specific and sensitive based urine and serum assay, which indicates the activity of bone cells and helps in the understanding of complex steps of bone turnover. Novel biomarkers have been developed like Periostin, urinary mid-osteocalcin and bone sialoprotein (BSP). Muthusami et al. has obtained the effect of CQ on the ovariectomy rat as well as on the oxidative stress [18]. It has been proved useful to manage oxidative stress and estrogen deficiency in the rats which have undergone ovariectomy (surgical removal of ovaries).

Conclusion

C. Quadranglaris and its various parts have been proved useful in the treatment of various diseases, but shows main effect on Osteoporosis. It acts specifically on the osteoblast or bone forming

cells, has been proved safe and effective for the human use. Ethanol and hexane extract has been used mainly for bone disorder. Its main constituents are steroids but its other constituent plays synergistic role in the bone treatment.

References

- Che CT, Wong MS (2015) *Ligustrum lucidum* and its constituents: a mini-review on the anti-osteoporosis potential. *Nat Prod Commun* 10: 2189-2194.
- Tasadduq R, Gordon J, Al-Ghanim KA, Lian JB, Van Wijnen AJ, et al. (2017) Ethanol extract of *Cissus quadrangularis* enhances osteoblast differentiation and mineralization of murine pre-osteoblastic MC3T3-E1 cells. *J Cell Physiol* 232: 540-547.
- Khajuria DK, Razdan R, Mahapatra DR (2011) Drugs for the management of osteoporosis: a review. *Rev Bras Reumatol* 51: 365-371.
- Gupta AK, Shah N, Thakar AB (2012) Effect of *Majja Basti* (therapeutic enema) and *Asthi Shrinkhala* (*Cissus quadrangularis*) in the management of osteoporosis (*Asthi-Majjakshaya*). *Ayu* 33: 110-113.
- Kwan P (2015) Osteoporosis: from osteoscience to neuroscience and beyond. *Mech Ageing Dev* 145: 26-38.
- Martin TJ, Seeman E (2007) New mechanisms and targets in the treatment of bone fragility. *Clin Sci (Lond)* 112: 77-91.
- Parisuthiman D, Singhatanadgit W, Dechatiwongse T, Koontongkaew S (2009) *Cissus quadrangularis* extract enhances biomineralization through up-regulation of MAPK-dependent alkaline phosphatase activity in osteoblasts. *In Vitro Cell Dev Biol Anim* 45: 194-200.
- Subhashri S, Hari VBN, Devi RD (2013) Review - pharmacological activities based on different extracts of *Cissus quadrangularis*. *Int J Pharmacog Phyto Res* 5: 128-133.
- Parvathi K, Krishnan AG, Anitha A, Jayakumar R, Nair MB (2018) Poly(L-lactic acid) nanofibers containing *Cissus quadrangularis* induced osteogenic differentiation *in vitro*. *Int J Biol Macromol* 110: 514-521.
- Kavitha S, Manimekalai G (2015) A study on properties of *Cissus quadrangularis* plant-A review. *Int J Res App Nat Soc Sci* 3: 15-18.
- Potu BK, Bhat KMR, Rao MS, Nampurath GK, Chamallamudi MR, et al. (2009) Petroleum ether extract of *Cissus quadrangularis* (Linn.) Enhances bone marrow mesenchymal stem cell proliferation and facilitates osteoblastogenesis. *Clinics (Sao Paulo)* 64: 993-998.
- Mishra G, Srivastava SS, Nagori BP (2010) Pharmacological and therapeutic activity of *Cissus quadrangularis*: an overview. *Int J PharmTech Res* 2: 1298-1310.
- Jadhav AN, Rafiq M, Devanathan R, Azeemuddin M, Anturlikar SD, et al. (2016) Ketosteroid Standardized *Cissus quadrangularis* L. Extract and its Anabolic Activity: Time to Look Beyond Ketosteroid? *Pharmacogn Mag* 12: S213-S217.
- Kumar P, Dev K, Sharma K, Sahai M, Maurya R (2018) New lignan glycosides from *Cissus quadrangularis* stems. *Nat Prod Res* 28: 1-6.

15. Sawangjit R, Puttarak P, Saokaew S, Chaiyakunapruk N (2017) Efficacy and Safety of *Cissus quadrangularis* L. in Clinical Use: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Phytother Res* 31: 555-567.
16. Prasad GC, Udupa KN (1963) Effect of *Cissus quadrangularis* on the healing of cortisone treated fracture. *Indian J Medical Res* 51: 667-676.
17. Potu BK, Rao MS, Nampurath GK, Chamallamudi MR, Nayak SR, et al. (2010) Anti-osteoporotic activity of the petroleum ether extract of *Cissus quadrangularis* Linn. in ovariectomized Wistar Rats. *Chang Gung Med J* 33: 252-257.
18. Muthusami S, Gopalakrishnan V, Stanley JA, Krishnamoorthy S, Ilangovan R, et al. (2016) *Cissus Quadranglaris* prevented the ovariectomy induced oxidative stress in the femur of adult albino rats. *Biomed Pharmacother* 81: 416-423.

Author Affiliations

[Top](#)

University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh, India

Submit your next manuscript and get advantages of SciTechnol submissions

- ❖ 80 Journals
- ❖ 21 Day rapid review process
- ❖ 3000 Editorial team
- ❖ 5 Million readers
- ❖ More than 5000 
- ❖ Quality and quick review processing through Editorial Manager System

Submit your next manuscript at • www.scitechnol.com/submission