
***Cissus quadrangularis* Linn and Bone Health: A Comprehensive Review**

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ABSTRACT

Cissus quadrangularis Linn. (CQL) is a fleshy plant found in major parts of the world, especially in Asia, Africa, and a few other warm tropical regions. It is one of the common food items in India. Apart from other pharmacological activities of CQL has been used by common folk in India for promoting the fracture healing process. It was prescribed in the ancient Ayurvedic texts as a general tonic and analgesic, with specific bone fracture healing properties. Hence, herein we aimed to document on traditional medicinal uses of CQL and its role and mechanism of action with special reference to one healing process. In conclusion, CQL is a climbing herb commonly known as Hadjod and Asthisamadhani in India and traditionally used in the management of many illnesses. The major pharmacological activities of the plant include bone healing, antimicrobial, anti-diabetic, anti-inflammatory, anti-obesity, anti-oxidant, cardiovascular and hepatoprotective. Therefore, *Cissus quadrangularis* appears worthy of pharmacological investigations for new drug formulations especially in bone and joint health formulations.

Keywords: *Cissus quadrangularis* L., Traditional uses, Bone healing, Mechanism of action

1. Introduction

Plants play a key role in the industry of drug discovery and the pharmaceutical industries are greatly dependent on natural products for the development of new drugs^[1]. WHO report reveals 80% world's population uses folk medicine for their chief health care^[2]. Clinical microbiologists have great delight in evaluating the medicinal plants for new drugs^[3]. India is blessed with great knowledge through legacy and heritage in the field of health care such as Siddha, Homeopathy, Unani and Ayurveda^[4]. In India, indigenous systems of medicine utilize Medicinal plants as the vital source and such plants have traditionally taken up a prominent position in the lives of tribal people in spiritual, medicinal and cultural activities^[5]. *Cissus quadrangularis* Linn. (CQL) serves as a common food source in India^[6]. The perennial plant CQL is well known as *Vitis quadrangularis*. The scientific nomenclature of CQL is as follows:

Kingdom: Plantae

Subkingdom: Tracheobionta

Super division: Spermatophyta

Division: Magnoliophyta

Class: Magnoliopsida

Subclass: Rosidae

Order: Rhamnales

Family: Vitaceae

Genus: *Cissus* L.

Species: *quadrangularis*

The vernacular names of CQL are as follows: Kannada: Mangarahalli; Tamil: Piranti, Vajravalli; Malayalam: Cannalamparanta, Peranta; Hindi: Cannalamparanta, Peranta; Bengali: Har, Harbhanga, Hasjora, Horjora; Marathi: Harjora, Hadsankal, Kandavel; Telugu: Nalleru, Nelleratiga, Vajravalli; Oriya: Hadavhanga; Urdu: Horjora, Harsankar; Gujarati: Chodhari, Hadsand, Hadsankal. The plant

comprises simple or reniform, serrate ± 5 cm wide leaf and four-angled stem connected at nodes, internodes which are up to 10 cm long, and dichotomously branched (Figure 1) [7].



Fig 1. Showing plant of *Cissus quadrangularis* L

CQL is extensively utilized in producing traditional medicines in India. Overall plant body assists in oral rehydration [14]. It is an abundant source of beta carotene and vitamin C [8]. Nanoparticles synthesized of CQL are studied for anti-cancer activity [9]. The CQL extract is proven as antiviral, free radical scavenger, antibacterial, anti-inflammatory, antioxidant and the mixture of sesame oil and CQL stem extract used to treat wheezing and skin issues [10]. CQL can reduce the body weight, serum lipid and serum glucose level [11]. The chemical components of this plant have been reported to contain phytosterols, keto-steroids, Indane and flavonoids which exhibit magnificent anti-oxidant properties [12]. Traditionally this plant has different medicinal uses in leucorrhoea, piles, gout, tumours and peptic ulcers. It is also utilized for the production of biochar and hydrocarbonaceous bio-oil [13].

CQL also plays a vital role in the healing of bone fissure and osteoporosis. It helps to decrease pain and bone brawny, because of its bone healing/joining ability, which is referred to as “Hadjod” [14]. With this background, the present narrative review of literature we mainly aimed to describe and delineate comprehensively on traditional medicinal uses and role and mechanism of action of CQL specifically in bone healing process.

2. Chemical Composition

CQL consists of various constituents such as flavanoides like quercetin, daidzein and genistein, triterpenoids like friedelin, vitamin ‘C’, stilbene derivatives like quadrangularin-A, resveratrol and piceatannol, iridoids like 6-O-meta-methoxybenzoyl catapol, picroside and pallidol and phytosterols like β -sitosterol and calcium were identified as major constituents of the plant [15]. The stem parts of plant contain A and β -amyrins, β -sitosterol, ketosterol, phenols, tannins, vitamin, carotene, Calcium oxalate, 3- methyl tritriacontanoic acid, taraxeryl acetate, taraxeroliso-pentadecanoic acid, Calcium ions and phosphorus. The Aerial parts of the plant contain new asymmetric tetracyclic triterpenoid 7-Oxo-Onocer-8-ene-3 β 21- α diol. Leaves of CQL contain Resveratrol, piceatannol, pallidol, parthenocissus and alicyclic lipids. Root powder of CQL often provides a steady source of mineral resources including potassium 67.5 mg; calcium 39.5 mg, zinc 3.0 mg, sodium 22.5 mg, Iron 7.5 mg, lead 3.5 mg, cadmium 0.25 mg, copper 0.5 mg and magnesium; 1.15 mg [16].

3. Perspectives on Traditional Uses

As per the Ayurveda, the stem of CQL is stated as hot, dry, sweetish and bitter. As the stem is having anthelmintic, laxative, digestive, stomachic, analgesic, tonic, aphrodisiac properties, it is useful in the management of piles, blindness, tumors, muscular pain, vata and kapha, loss of appetite, epileptic fits, constipation, chronic ulcers and bone fractures. Unani system of medicine also mentioned the use of stem of this herb for broken bones where internal administration and external application of

the same is stated. With this it is also used in complaints of the back and spine and to remove pus^[17]. CQL is not described in the earlier classical texts and its first entry appears to be in the 16th century text Bhavprakash. As per the Bhavprakash Nighantu^[18], the literature mentioned in Sanskrit gave the properties and pharmacological potential of CQL as “Asthisamhaaraka mitigates *vata* and *kapha* (*shleshman*), joins bone fractures. It is hot (*ushna*) in potency, is laxative (*sara*), destroys worms, cures piles (*durnaaman*) and eye (*aksi*) diseases. It causes dryness, is tasty, light (*laghu*) is aphrodisiac (*vrsya*), digestive, and increases pitta”.

CQL is preferred for conditions such as bites of poisonous insects, sores of camel and horses (its stem is used in paste form)^[19]. Moreover, it is one of the commonly used food supplements in southern India as the root powder of the herb is a good source of carbohydrates (68.89 ± 1.16 mg/100 gm), crude proteins (7.5 ± 0.17 mg/100 gm) and fibres (5.97 ± 0.10 mg/100 gm) with a calorific value of 335.5 ± 3.43 kcal/100 gm^[20]. CQL also possesses anti-rheumatic properties, anti-allergic, anabolic, and androgenic properties^[21]. Juice of the stem is dropped in to ear in otorrhea and into the nose in the epistaxis^[22]. Despite of wide-ranging therapeutic applications mentioned above, CQL has been used in disease conditions such as malaria, leprosy, ophthalmopathy, otorrhea, epilepsy, swelling, various skin diseases^[23], and schistosomiasis^[24]. The roots and stems are most useful for healing of fracture of the bones. The stem is bitter. It is given internally and applied topically in broken bones. It is also used in complaints of the back and spine. A paste of stem is useful for muscular pains. The plant has been documented in Ayurveda for the treatment of osteoarthritis, rheumatoid arthritis and osteoporosis^[25].

4. Bone Healing and Mechanism of Action

The anabolic steroid from the CQL plant showed a marked influence in the rate of fracture healing by early generation of all connective tissue. CQL contains vitamins and steroids, which are found to have specific effect on bone fracture healing^[26]. CQL was tested for its bone protective properties and studied to discern the mechanism by which it is beneficial to bone^[27]. It had protected the microarchitecture of the long bones from ovariectomy-induced bone loss because of decreased inflammation and modulation through the bone morphogenetic protein and Wingless-related integration site (Wnt) signaling pathways. The results indicated that the plant is a potential therapeutic agent to treat postmenopausal osteoporosis with no side effects. Petroleum ether extract of CQL significantly increased the thickness of both cortical and trabecular bone suggesting the strong anti-osteoporotic activity of the plant. In addition, the extract reduced bone loss, as evidenced by the weight gain in femur, and also reduced the osteoclastic activity there by facilitating bone formation^[28,29]. Also, percentage of the total length of ossified cartilage (bone) in pups were higher suggesting that maternal administration of CQL petroleum ether extract during pregnancy can stimulate the development of fetal bone growth during the intra-uterine developmental period^[30]. In another study, ethanol extract showed significant restorative progress with mineralization along with fairly well distributed osteocytes as well as complete recovery with essential features of normal bone^[31].

Tasadduq, et al., examined the effectiveness of CQL in promoting osteoblast differentiation of the murine pre-osteoblast cell lines. The ethanolic extract augmented osteoblast differentiation, as reflected by a substantial increase in expression of the early osteoblast marker alkaline phosphatase activity^[32]. Osteogenic potential of CQL was studied by Toor, et al., and ethanolic extract of the plant accelerated fracture healing as well as early remodeling of fracture callus. The authors also studied the effect of hexane and dichloromethane fraction on the differentiation and mineralization of mouse pre-osteoblast cell line^[33,34]. According to Muthusami et al., CQL treatment has increased the DNA synthesis of human osteoblastic SaOS-2 cells indicating increased proliferation of these cells. Authors also revealed that the anabolic actions of ethanolic extract of CQL in human osteoblast like cells are mediated through increased mRNA and protein expression of Runx2, a key transcription factor involved in the regulation of bone matrix protein^[35]. Osteogenic potential of CQL on the mandibular

fracture healing was studied by various research investigators, and revealed that the plant helps in reducing pain, swelling, and fracture mobility and accelerate the healing of fracture jaw bones ^[36,37].

5. Conclusions

In conclusion, *Cissus quadrangularis* Linn is a climbing herb commonly known as Hadjod and Asthisamadhani in India and traditionally used in the management of many illnesses. The major pharmacological activities of the *Cissus quadrangularis* Linn include bone healing, antimicrobial, anti-diabetic, anti-inflammatory, anti-obesity, anti-oxidant, cardiovascular and hepatoprotective. Therefore, *Cissus quadrangularis* Linn appears worthy of pharmacological investigations for new drug formulations especially in bone and joint health care formulations.

References

1. Sen MK, Dash BK. A review on phytochemical and pharmacological aspects of *Cissus quadrangularis* L. International Journal of Green Pharmacy (IJGP). 2012;6(3).
2. EL-Kamali HH, EL-Amir MY. Antibacterial activity and phytochemical screening of ethanolic extracts obtained from selected Sudanese medicinal plants. Current Research Journal of Biological Sciences. 2010;2(2):143-6.
3. Ramar K, Ayyadurai V. Evaluation of antimicrobial activity of medicinal plants and phytochemical analysis of *Cissus quadrangularis*. L., World J Pharm Res. 2015;4(5):2484-94.
4. Rathinam P, Sekhar KC, Sekhar DS. Antimicrobial activity and phytochemical constituents of combined extracts of *Cissus quadrangularis* and aegle marmelos. Int J Res Pharm Sci. 2012;3(1):135-9.
5. Ruskin RS, Kumari VP, Gopukumar ST, Praseetha PK. Evaluation of phytochemical, antibacterial and anti-cancerous activity of *Cissus quadrangularis* from South Western Ghats regions of India. Int J Pharm Sci Rev Res. 2014;28(1):12-5.
6. Ayyanar M, Ignacimuthu S. Pharmacological Actions of *Cassia auriculata* L. and *Cissus quadrangularis*. Journal of Pharmacology and toxicology. 2008;3(3):213-21.
7. Shukla R, Pathak A, Kambuja S, Sachan S, Mishra A, Kumar S. Pharmacognostical, Phytochemical and Pharmacological Overview: *Cissus quadrangularis* Linn. Indian Journal of Pharmaceutical and Biological Research. 2015;3(3):59.
8. Joseph B, George J, Mohan J. *Cissus quadrangularis* in the treatment of osteoporosis. World Journal of Pharmaceutical Research. 2013;2(3):596-605.
9. Kumar M, Rawat P, Dixit P, Mishra D, Gautam AK, Pandey R, Singh D, Chattopadhyay N, Maurya R. Anti-osteoporotic constituents from Indian medicinal plants. Phytomedicine. 2010;17(13):993-9.
10. Luseba D, Elgorashi EE, Ntloedibe DT, Van Staden J. Antibacterial, anti-inflammatory and mutagenic effects of some medicinal plants used in South Africa for the treatment of wounds and retained placenta in livestock. South African Journal of Botany. 2007;73(3):378-83.
11. Oben JE, Enyegue DM, Fomekong GI, Soukontoua YB, Agbor GA. The effect of *Cissus quadrangularis* (CQR-300) and a *Cissus* formulation (CORE) on obesity and obesity-induced oxidative stress. Lipids in Health and Disease. 2007;6(1):1-8.
12. Talreja T, Goswami A, Sharma T. Preliminary phytochemical analysis of *Achyranthes aspera* and *Cissus quadrangularis*. Journal of Pharmacognosy and Phytochemistry. 2016;5(5):362.
13. Tiwari M, Gupta PS, Sharma N. Ethnopharmacological, Phytochemical and Pharmacological review of Plant *Cissus quadrangularis* L. Research Journal of Pharmacognosy and Phytochemistry. 2018;10(1):81-90.
14. Sarkar BK, Kumar R, Kumar P, Mandal P, Bhusan V. Formulation and evaluation of anti-inflammatory herbal topical formulation of *Cissus Quadrangularis*. World Journal of Pharmaceutical Research. 2016;5(3):681-9.
15. Day NL. Alcoholism: Clinical and Experimental Research. 2002; 26:1584.

16. Ghouse MS. A pharmacognostical review on *Cissus quadrangularis* linn. Int J Res Pharm Biosci. 2015;2(7):28-35.
 17. Kirtikar KR, Basu BD. Indian Medicinal Plants, 1. International Book Distributors and publishers, Deharadun. 2005:604–605.
 18. Vaidya BG., Nighantu Adarsrh (Purvardh). Chaukhamba Bhartee Academy, Varanasi. 1968:304.
 19. Valli JS, Vaseeharan B. Biosynthesis of silver nanoparticles by *Cissus quadrangularis* extracts. Materials Letters. 2012; 82:171-3.
 20. Malathi AN. Nutritive value of mangoravalli (*Cissus quadrangularis*) powder and its value addition. Curr Trends Technol Sci. 2014;3(2):223-5.
 21. Prasad GC, Udupa KN. Effect of *Cissus quadrangularis* on the healing of cortisone treated fractures. Indian journal of medical research. 1963; 51:667–676.
 22. Nadkarni AK. Indian Materia Medica, 1. Popular Prakashan, Mumbai. 1982.pp284.
 23. Ekpo BA, Bala DN, Essien EE, Adesanya SA. Ethnobotanical survey of Akwa Ibom state of Nigeria. Journal of Ethnopharmacology. 2008;115(3):387-408.
 24. Bah S, Diallo D, Dembele S, Paulsen BS. Ethnopharmacological survey of plants used for the treatment of schistosomiasis in Niono District, Mali. Journal of Ethnopharmacology. 2006;105(3):387-99.
 25. Paulsen BS, Sekou B, Drissa D, Anna JK, Adsersen A. Antiplasmodial and GABAA-benzodiazepine receptor binding activities of five plants used in traditional medicine in Mali, West. Africa. Journal of Ethnopharmacology. 2007; 110: 451-57.
 26. Chidambara Murthy KN, Vanitha A, Mahadeva Swamy M, Ravishankar GA. Antioxidant and antimicrobial activity of *Cissus quadrangularis* L. Journal of Medicinal Food. 2003;6(2):99-105.
 27. Guerra JM, Hanes MA, Rasa C, Loganathan N, Innis-Whitehouse W, Gutierrez E, Nair S, Banu J. Modulation of bone turnover by *Cissus quadrangularis* after ovariectomy in rats. Journal of bone and mineral metabolism. 2019;37(5):780-95.
 28. Potu BK, Nampurath GK, Rao MS, Bhat KM. Effect of *Cissus quadrangularis* Linn on the development of osteopenia induced by ovariectomy in rats. La Clinica terapeutica. 2011; 162: 307–312.
 29. Potu BK, Rao MS, Nampurath GK, Chamallamudi MR, Prasad K, Nayak SR, Dharmavarapu PK, Kedage V, Bhat KM. Evidence-based assessment of antiosteoporotic activity of petroleum-ether extract of *Cissus quadrangularis* Linn. on ovariectomy-induced osteoporosis. Upsala journal of medical sciences. 2009;114(3):140-8.
 30. Potu BK, Rao MS, Bhat KM, Chamallamudi MR, Nayak SR. Petroleum ether extract of *Cissus quadrangularis* (Linn) stimulates the growth of fetal bone during intra uterine developmental period: a morphometric analysis. Clinics. 2008;63(6):815-20.
 31. Shirwaikar A, Khan S, Malini S. Antiosteoporotic effect of ethanol extract of *Cissus quadrangularis* Linn. on ovariectomized rat. J Ethnopharmacol. 2003; 89: 245–250.
 32. Tasadduq R, Gordon J, Al-Ghanim KA, Lian JB, Van Wijnen AJ, Stein JL, Stein GS, Shakoori AR. Ethanol extract of *Cissus quadrangularis* enhances osteoblast differentiation and mineralization of murine pre-osteoblastic MC3T3-E1 cells. Journal of cellular physiology. 2017;232(3):540-7.
 33. Toor RH, Malik S, Qamar H, Batoof F, Tariq M, Nasir Z, Tassaduq R, Lian JB, Stein JL, Stein GS, Shakoori AR. Osteogenic potential of hexane and dichloromethane fraction of *Cissus quadrangularis* on murine preosteoblast cell line MC3T3-E1 (subclone 4). Journal of Cellular Physiology. 2019;234(12):23082-96.
 34. Toor RH, Tasadduq R, Adhikari A, Chaudhary MI, Lian JB, Stein JL, Stein GS, Shakoori AR. Ethyl acetate and n-butanol fraction of *Cissus quadrangularis* promotes the mineralization potential of murine pre-osteoblast cell line MC3T3-E1 (sub-clone 4). Journal of cellular physiology. 2019;234(7):10300-14.
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35. Muthusami S, Senthilkumar K, Vignesh C, Ilangovan R, Stanley J, Selvamurugan N, Srinivasan N. Effects of *Cissus quadrangularis* on the proliferation, differentiation and matrix mineralization of human osteoblast like SaOS-2 cells. *Journal of Cellular Biochemistry*. 2011;112(4):1035-45.
36. Singh V, Singh N, Pal US, Dhasmana S, Mohammad S, Singh N. Clinical evaluation of *Cissus quadrangularis* and *Moringa oleifera* and osteoseal as osteogenic agents in mandibular fracture. *National journal of maxillofacial surgery*. 2011;2(2):132.
37. Brahmshatriya HR, Shah KA, Ananthkumar GB, Brahmshatriya MH. Clinical evaluation of *Cissus quadrangularis* as osteogenic agent in maxillofacial fracture: A pilot study. *Ayu*. 2015; 36: 169-173.