

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

<u>Review Article</u> ISSN 2394-3211 EJPMR

A REVIEW ON TRADITIONAL APPLICATION OF CISSUS QUADRANGULARIS LINN.

Poulami Ghosh¹, Nikhil Gupta¹ and Soham Mandal*

¹School of Pharmacy, The Neotia University, Sarisha, Diamond Harbour Road, 24 Parganas (South), West Bengal-743368.

*Usha Rani Institute of Pharmacy, Sabang, Paschim Medinipur, West Bengal -721166.



*Corresponding Author: Soham Mandal

Usha Rani Institute of Pharmacy, Sabang, Paschim Medinipur, West Bengal -721166.

Article Received on 29/10/2023

Article Revised on 19/11/2023

Article Accepted on 09/12/2023

ABSTRACT

Cissus quadrangularis Linn. is an indigenous medicinal plant grown which belongs to the Vitaceae family. It was found in India, Sri Lanka, and Africa. It is a shrub, with a slender, fleshy fibrous and smooth stem, with fourwinged internodes. Almost all of its parts are used in traditional systems of medicine as seeds, stem, roots, and shoots are the most important partswhich are used medicinally. The plant is also known as Harishankar or Hadjod in Hindi and Asthisanghata, Kandavalli, Vajrangi, etc., in Sanskrit. It contains a high amount of Vitamin C,Vitamin A, anabolic steroidal substances, and calcium. The phytochemical constituents which have been isolated from the plant C. quadrangularis possess activities like anti-inflammatory, anti-tumor, gastroprotective, antioxidant, antimicrobial, and various other important medicinalproperties. The extracts from the stem of this plant have been used widely for the early repair of fractures, gout, back pain, and irregular menstruation. In ancient Ayurveda, it has been prescribed as a general tonic, especially for the fractured patient which had written by Bhava Prakasha and Chakra Dutta. Since then, it has been used as an external application and as an internal medication by bonesetters. C. quadrangularis comes in the form of a capsule, tablet, and syrup. This review is based on C. quadrangularis uses at ayurveda.

KEYWORDS: C. quandrangularis, Medicinal properties, Ayurvedic uses.

INTRODUCTION

The nature has provided a complete store-house of remedies to cure all types of diseases of mankind. The nature provides us drugs in the form of herbs, plants and algae's to cure the incurable diseases without any toxic effect. Cissus qudrangularis L.(Hadjod) belongs to Vitaceae family is an indigenous medicinal plant of India.^[1,2,5] It is famous by different names in various vernacular languages. It is called as as Hadjod in Hindi, it is famous as Vajravalli, ashtishrunkhala in Sanskrit. It is known as Kandvel in Marathi, Haddjor in Punjabi, in Orissa it is called as Hadbhanga, known as Vedhari in Gujrati, Perandi in Tamil, Nalleru in Telagu, and Veldgrap, Edible Vine in English. The use of this plant is to promote fracture healing process which is an old practice.^[4,40,34] It has been prescribed in ancient Ayurvedic texts by Bhava Prakash and Chakra Dutta as a general tonic especially for the fractured patient. It has been taken with milk by bone setters for internal medicine as well as external application.^[8,9,7,35] The stem of *Cissus* qudrangularis is also reputed in Ayurveda as alterative, anthelmintic, dyspeptic, digestive, tonic, analgesic in eye and ear diseases, in the treatment of irregular menstruation and asthma, and in complaints of the back and spine. Scientific studies have revealed the Cissus extract to possess cardiotonic and androgenic property.

The plant extracts also exhibit cardiotonic property. The *Cissus quadrangularis* Linn. is a rich source of carotenoids, triterpenoids and ascorbic acid and is proved to have potential for medical effects, including "Gastro protective activity" in conjugation with NSAID therapy and in "Lipid metabolism and oxidative stress". The *Cissus quadrangularis* L. plant contain high amount of vitamin C, Carotene A, anabolic steroidal substances and calcium. Stem contains two asymmetric tetra cyclic triterpenoids; Onocer-7-ene-3b-21a diol & Onocer-7ene 3a, 2,1 diol.^[3,6,12]

Vernacular names

English: Edible stemmed vine, Adamant creeper, Bone setter Hindi: Hadjod, Hadjora, Hadsarihari, Harsankari, Kandvel Bengali: Har, Harbhanga, Hasjora, Horjora Gujarati: Chodhari, Hadsand, Hadsankal, Vedhari Kanada: Mangarahalli Malyalam: Cannalamparanta, Peranta Marathi: Horjora, Harsankar, Kandavel, NalllarTamil: Piranti, Vajjravalli Telugu: Nalleru, Nelleratiga, VajravalliOriya: Hadavhanga Urdu: Harjora, Hadsankal

Plantae
Tracheobionta
Magnoliophyta
Spermatophyte
Magnoliopsida
Rosidae
Vitales
Vitaceae
Cissus
quadrangularis

The scientific nomenclature of Cissus quadrangularis.

Description of the plant

The plant comprises simple or reniform, serrate wide leaf and four angled stem connected at nodes, internodes which are up to 10 cm long and dichotomously branched. *Cissus quadrangularis* reaches a height of 1.5m. The Toothed trilobe leaves 2 to 5 cm wide appear atthe nodes.

Each has a tendril emerging from the opposite side of the node. Racemes of small white, yellowish, or greenish flowers, globular berries are red when ripe.

All parts of plant –stem, root, leaves, shoot and dried ash are used for medicinal purpose.^[10,11,36]

History

Cissus quadrangularis is a succulent vine from Asia and Africa. It is one of the most commonly used medicinal plants in Thailand. It is traditionally used in African medicine as well as in Ayurveda. All parts of the plant are used for medicine.^[13,21]

Cissus quadrangularis is a traditional medicine usually said to come from Ayurveda but appears to have a wide range of locations which have used it medicinally due to its growing in numerous locations. Traditionally it was mostly used in treatment of female disorders (menopause, libido, and menstrual disorders) and treating bone disorders (increasing bone mass or accelerating fracture healing rates) which gives it the traditional name of the 'Bone Setter' (Hadjod), some other traditional usages are in regards to its supposed antiulcer properties, Antihemorrhoid properties, pain relieving properties and wound healing properties.

- Vrushya -aphrodisiac, improves vigor
- Pachana Digestive, relieves Ama Dosha
- Pittala -Increases Pitta Dosha

It is used in the treatment of obesity, gout, syphilis, Veneral diseases, leucorrhea, worm infestation, anorexia, diabetes, peptic ulcer, haemorrhoids and high cholesterol.

It is also used as a body building supplement. In North eastern states of India, its stem is used as a vegetable.

In Siddha system of medicine, it is used for healing bone fracture, piles, as an anti-aging herb, in Asthma, cough and gonorrhoea.^[31,38]

Traditional uses In Ayurveda

- Asthiyuk -strengthens bones.
- Sara-induces mobility, causes diarrheoa, purgation, relieves constipation
- Krumighna -Relieves worm infestation, useful in infected wounds
- Amaghna -Relieves ama a product of indigestion and altered metabolism.
- Vrushya -aphrodisiac, improves vigor
- Pachana Digestive, relieves Ama Dosha
- Pittala -Increases Pitta Dosha

It is used in the treatment of obesity, gout, syphilis, Veneral diseases, leucorrhea, worminfestation, anorexia, diabetes, peptic ulcer, haemorrhoids and high cholesterol.

It is also used as a body building supplement. In North eastern states of India, its stem is used as a vegetable.^[37,14,39]

In Unani

Cissus quadrangularis is a plant found in hotter parts of India. Powdered root is used as a specific for the fractures of the bones, with the same effects as plasters externally. Dose of the powder is 30-40 grains. Leaves and young shoots are frequently taken with curry in Southern India. In Madras, young shoots of the plant are dried and powdered, are burnt to ashes in a closed vessel and administered in dyspepsia and indigestion and certain bowel complaints. Leaves and young shoots are also considered as powerful alternatives. Juice of stem is dropped into the ear in otorrhoea and into the nose in epistaxis. It has also a reputation in scurvy and in irregular menstruation. Stem beaten into a paste is used to treat asthma. A preserve of stem prepared by boiling it in lime water is useful stomachic.

In Medicinal plants-Germplasm of Peninsular India the *Cissus quadrangularis* uses is mentioned as the stem and whole plant is used in asthma, bowel complaints and as epistatic; stem is useful in piles, diseases of the ear and bleeding of nose, paste of the stem is useful in muscular pains, burns, wounds, bites of poisonous insects and for saddle sores of horses and camels; root used in fractures and cuts.

The stem of Hadjod or *Cissus quadrangularis* is used for the treatment of gastritis, bone fractures, skin infections, constipations, eye diseases, piles, anaemia, asthma. The stem juice is useful in scurvy and in irregular menstruation. The powder of dried shoot is useful in digestive problems and wound healing property. Stem paste is useful for muscular pains, burns, wounds, bites of poisonous insects and sores.

In case of bone fracture, the stem is fried in oil and apply on the site of fracture before application of splint/cast. Hadjod or Bone Setter has proven ability to join broken bones. Studies haves shown, the presence of vitamins and anabolic steroid, which may act on estrogenic receptors of the bone.

The plant helps in early ossification and remodelling of bones. The oral intake of plant, helps in quick healing of fracture by stimulation of metabolism and increased uptake of the mineralscalcium, sulphur and strontium by the osteoblasts in fractured bone.^[33,23]

Dosage of Hadjod or *Cissus quadrangularis* in Unani medicine

- Decoction of dried stem: 10-30 ml twice a day.
- Stem Juice: 10-20 ml twice a day.
- Stem powder/churna: 3-6 gm twice a day.^[32,25]

Chemical Constituents

Phytochemical studies on methanol extract revealed the presence of triterpenes including α - and β - amyrins, β sitosterol, ketosteroids, phenols, tannins, carotene, and vitamin C. Seven alicyclic lipids constituents have also been reported from Cissus quadrangularis. unsymmetric tetracyclic triterpenoids such as d-amyrin, onocer-7-ene-3a, 21b-diol, d-amyrone, and 3,3',4,4'- tetra hydroxy biphenyl, 3,3',4,4'-tetrahydroxybiphenyl have been isolated from plant and werequantitatively determined by HPTLC and HPLC methods in samples collected from five different geographic zones of India. Several other constituents such as flavonoids quercetin andkaempferol, stilbenederivatives, quadrangularins A, B, C, and many piceatannol, resveratrol, pallidol, others e.g. perthenocissi etc. and phytosterols have been isolated from the plant. Stem extract contains a high percentage of calcium ions and phosphorus, which is essential forbone growth and healing.^[17,20]

Pharmacological uses

Antioxidant and free radical scavenging activity

The methanol extract of *Cissus quadrangularis* exhibits strong antioxidant and free radical scavenging activity invitro and in-vivo systems mainly due to the presence of β -carotene.^[24]

Anti-microbial and antibacterial activity

The methanol extract (90%) and dichloromethane extract of stem possess antibacterial activityagainst S. aureus, E. coli, and P. aeruginosa and mutagenicity against Salmonella. Antimicrobial activity has also been reported from stem and root extract. The alcoholic extract of the aerial part was found to possess antiprotozoal activity against Entamoeba histolytica. The alcoholic extract of the stem showed activity against E. coli. Methanol and dichloromethane extract of the whole plant were screened for in-vitro antiplasmodial activity.^[22]

Bone healing activity

Paste of alcoholic extract of the plant was used locally as well as intramuscularly which facilitates rapid healing of fractures. Ethanol extract (95%) enhances the development of cortical bone and trabeculae in the foetal femur, which may be related to the rich content of calcium, phosphorous and phytoestrogenic steroids and shown to influence early regeneration and quick mineralization of bone fracture healing process. Ethanol extract (95%) of the whole plant possesses antiosteoporotic activity.^[32]

Anti-ulcer activity

The methanol extract showed significant antiulcer activity in experimentally induced ulcers in a rat model by decreasing gastric secretions and by enhancing glycoprotein levels. Methanol extract produces a healing effect on aspirin-induced gastric mucosal damage in rats through itsantioxidative mechanism.

Triterpenoids and beta-sitosterol present in methanol extract possess an anti-lipid peroxidating effect and thus prevent gastric damage.^[22,25]

Analgesic, anti-inflammatory, and stimulatory activity

Methanol extract possesses analgesic, anti-inflammatory, and venotonic effects associated with hemorrhoids, antiinflammatory activity is due to flavonoids especially luteolin, and β - sitosterol. β -sitosterol present in methanol extract can reduce the enzymes MPO indicating a reduction of neutrophils influx in the inflamed tissue. Ethanol extract exhibits a protective effect on neutrophilmediated tissue injury induced by aspirin. The methanol extract (90%) and dichloromethane extract of stems possess anti-inflammatory activity against COX-2.The stimulatory effect of the extract is probably due to vitamins and is greater than that of the anabolic hormone durabolin.^[15]

Anti-hemorrhoidal Activity

As the combination of flavonoids (90% diosmin and 10% hesperidin) used clinically for the treatment of haemorrhoid was reported to have anti-inflammatory and analgesic activities as well as venotonic effect which is not reported previously. Phytochemical study of C. quadrangularis revealed that its major compounds are flavonoids.

The bioflavonoids, particularly diosmin, hesperidin and oligomeric proanthocyanidin complexes have demonstrated potential in the treatment of haemorrhoids and varicose veins. These bioflavonoids exhibit phlebotonic activity, vasculoprotective effects and antagonistic effect on the biochemical mediators of inflammation. The anti-inflammatory effect which is already been observed from the crude extract of C. quadrangularis could be produced by the flavonoids especially luteolin, and by β -sitosterol.

The venotonic effect of C. quadrangularis may also be postulated to be due to the effect of flavonoids present in the extract which act in the same way as that of diosmin and hesperidin. As diosmin and hesperidin are used in combination to treat haemorrhoid, the extract which produced the same activities (anti-inflammatory and venotonic) can also be used as Antihemorrhoidal drug. Besides these effects, C. quadrangularis also possesses analgesic effect, which can be very useful in painful haemorrhoid.^[16]

Central nervous system activity

The root extract possesses central nervous system depressant activity indicated by the decrease in exploratory behavior. Methanol extract from roots contains saponins which show potent sedative activity and also inhibit spontaneous motor activity.^[18,19]

Antihemorrhoidal Activity

As the combination of flavonoids (90% diosmin and 10% hesperidin) used clinically for the treatment of haemorrhoid was reported to have anti-inflammatory and analgesic activities as well as venotonic effect which is not reported previously. Phytochemical study of C. quadrangularis revealed that its major compounds are flavonoids.

The bioflavonoids, particularly diosmin, hesperidin and oligomeric proanthocyanidin complexes have demonstrated potential in the treatment of haemorrhoids and varicose veins. These bioflavonoids exhibit phlebotonic activity, vasculoprotective effects and antagonistic effect on the biochemical mediators of inflammation. The anti-inflammatory effect which is already been observed from the crude extract of C. quadrangularis could be produced by the flavonoids especially luteolin, and by β -sitosterol.^[30]

The venotonic effect of C. quadrangularis may also be postulated to be due to the effect of flavonoids present in the extract which act in the same way as that of diosmin and hesperidin. As diosmin and hesperidin are used in combination to treat haemorrhoid, the extract which produced the same activities (anti-inflammatory and venotonic) can also be used as Antihemorrhoidal drug. Besides these effects, C. quadrangularis also possesses analgesic effect, which can be very useful in painful haemorrhoid.^[26,27,28,29]

CONCLUSION

It is important to understand the significance of traditional medicinal practices and the potential benefits of natural compounds. The example of *Cissus quadrangularis* highlights the need for scientific investigation into the efficacy and safety of traditional remedies. By conducting thorough screening and testing, isolated phyto principles can be evaluated and potentially used as lead molecules for the management of various diseases.

It is also important to acknowledge the rich history and knowledge of traditional medicine in ancient civilizations. The therapeutic efficacy of *Cissus quadrangularis* for wound healing, antioxidant and antimicrobial activity, as well as bone fracture healing, demonstrates the potential of natural resources in medicine. Furthermore, the plant's high mineral content exemplifies the importance of proper nutrition for the human body.

REFERENCES

- 1. Guo S, Pietro LA. Factors Affecting Wound Healing, J Dent Res., 2010; 89(3): 219-229.
- Steven BL, DeGuzman L, Lee WP, Xu Y, Siegel MW, Amento EP. One Systematic Administration of Transforming Growth Factorbeta1 Reverses Age or Glucocorticoid-Impared Wound Healing, J Clinical Invest., 1993; 92: 2841-2849.
- Frank S, Hubner G, Breier G, Longaker MT, Greenhalgh DG, Werner S. Regulation of Vascular Endothelial Growth Factor Expression in Cultured Keratinocytes, The J Biological Chemistry, 1995; 270(21): 2607-12613.
- 4. Frank S, Madlener M, Werner S. Transforming Growth Factors $\beta 1$, $\beta 2$ and $\beta 3$ and their Receptors are differentially regulated during normal and impaired wound healing, J Biological Chemistry, 1996; 271(17): 0188-10193.
- 5. Palu A, Su C, Zhou BN, West B, Jensen J. Wound healing effects of noni (Morinda citrifoliaL.) leaves: a mechanism involving its PDGF/A2A receptor ligand binding and promotion of wound closure, Pythother Res., 2010; 24(10): 1437-1441.
- Iyu D, Juttner M, Glen JR, White AE, Johnson AJ, Fox SC, Heptinstall S. PGE1 and PGE2 modify platelet function through different psotanoid receptors, Prostaglandins & other Lipid Mediators, 2011; 94: 9-16.
- 7. Riccioti E, Fitzgerlad GA. Prostaglandins and Inflammation, Journal of the Amercian Heart Association, 2011; 31: 986-1000.
- 8. Dr. Nadkarni's KM. Indian Materia Medica, Volume one, Revised and Enlarged by A.K Nadkarni, Published by Popular Prakashan PVT.LTD, 1976; 1284.
- Varaprasad KS, Abraham Z, Pandravada SR, Latha M, Divya S Raman, Lakshminarayan Set al. Medical Plants Germplasm of Peninsular India, Published by National Bureau of Plant Genetic Resources, New-Delhi-110 012, India, 2006; 50.
- 10. Dr. Mohd. Ataullah Shareef, Kitabul Advia Mufarradaath. Best Printers and Publishers-Hyderabad, First edition, 2012; 511-512.
- 11. Anonymous. Indian Medicinal Plants. Orient Longman Ltd, 1992; 2: 112.
- Guhabakshi DN, Pal DC, Sersuma P. A Lexicon of Medicinal Plants in India. Naya Prokash, 2001; 1: 443-45.
- 13. Rajpal V. Standardization of Botanicals. Eastern Publishers, 2005; 1: 77-81.
- 14. Anonymous. Medicinal plants of India. Indian Council of Medical Research, 1976; 1: 242-45.
- 15. Deka DK, Lahon LC, Saikia J, Mukit A. Effect of *Cissus quadrangularis* in accelerating healing process of experimentally fractured Radius-Ulna of dog: A preliminary study. Indian Journal of

Pharmacology, 1994; 26: 44-48.

- Anitua E, Andia I, Ardanza B, Nurden P, Narden AT. Autologus platelets as a source of proteins for healing and tissue regeneration, Thromb Haemost, 2004; 91: 4-15.
- 17. Borzini P, Mazzucco I. Platelet-rich plasma (PRP) and platelet derivatives for topical therapy. What is true from the biologic view point?, ISBT Science Series, 2007; (2): 272-281.
- Grinnell F, Billingham RE, Burgess L. Distribution of fibronectin during wound healing invivo, J Invest Dermatol, 1981; 76: 181-189.
- 19. Noli C, Miolo A. The mast cell in wound healing, Vet Dermatol, 2001; 12: 303-313.
- Demling RH. Oxandrolone, an anabolic steroid enhances the healing of a cutaneou wound in the rat. Wound Repair and Regeration, 2000; 8: 97-102.
- Mallika J, Shyamala Devi CS. In vitro and In vivo evaluation of free radical scavenging potential of *Cissus quadrangularis*. African Journal of Biomedical Research, 2005; 8: 95-99.
- 22. Rao BS, Deshpande V. Experimental Biochemistry. International Pvt. Ltd, 2005; 273-74.
- 23. Udupa KN, Prasad GC. The effect of *Cissus quadrangularis* on healing of cortisone treated fracture. Indian Journal of Medical Research, 1963; 51: 667.
- 24. Rao MS, Bhagath KP, Narayana Swamy VB, Gopalan KN. *Cissus quadrangularis* plant extract enhances the development of cortical bone and trabeculae in the fetal femur. Pharmacology Online, 2007; 3: 190-202.
- 25. Gutierrez RMP, Vargas R. Evaluation of the wound healing properties of Acalypha langiana in diabetic rats, Fitoterapia, 2006; 77: 286-289.
- 26. Shirwaikar A, Khan S, Malini S. Antiosteoporotic effect of ethanol extracts of *Cissus quadrangularis* Linn on ovariectomized rat. Journal of Ethnophramacology, 2003; 89: 245-50.
- 27. Mallika J, Shyamala Devi CS. Potent antiulcerogenic activity of *Cissus quadrangularis* on aspirin-induced gastric ulcer by its antioxidative mechanism. Journal of Clinical Biochemistry and Nutrition, 2003; 34: 43-47.
- Sanyal, A., Ahmad, A., & Sastry, M. Calcite growth in *Cissus quadrangularis* plant extract, a traditional Indian bone-healing aid. Current science, 2005; 1742-1745.
- 29. Mishra, G., Srivastava, S., & Nagori, B. P. Pharmacological and therapeutic activity of *Cissus quadrangularis*: an overview. International journal of pharmtech research, 2010; 2(2): 1298-1310.
- Camil, R.M., Lokesh, R. A review of *Cissus quadrangularis* L. as herbal Medicine. Indian J Nat Prod Rsour, 2020; 11(30): 155-164.
- 31. Managutti, A., Shah, D., Patel, J., Puttanikar, N., Shah, D., & Managutti, S. Evaluation of clinical efficacy of *cissus quadrangularis* in pain management and bone healing after implant placement–a pilot study. Medico Research

Chronicles, 2015; 2(5): 618-625.

- Parisuthiman, D., Singhatanadgit, W., Dechatiwongse, T., & Koontongkaew, S. *Cissus quadrangularis* extract enhances biomineralization through up-regulation of MAPK- dependent alkaline phosphatase activity in osteoblasts. In Vitro Cellular & Developmental Biology-Animal, 2009; 45(3-4): 194-200.
- 33. 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 SaOS2 cells. Journal of Cellular Biochemistry, 2011; 112(4): 1035-1045.
- Muthusami, S., Ramachandran, I., Krishnamoorthy, S., Govindan, R., & Narasimhan, S. *Cissus quadrangularis* augments IGF system components in human osteoblast like SaOS-2 cells. Growth Hormone & IGF Research, 2011; 21(6): 343-348.
- Brahmkshatriya, H. R., Shah, K. A., Ananthkumar, G. B., & Brahmkshatriya, M. H. Clinical evaluation of *Cissus quadrangularis* as osteogenic agent in maxillofacial fracture: A pilot study. Ayu, 2015; 36(2): 169.
- Potu, B. K., Bhat, K. M., Rao, M. S., Nampurath, G. K., Chamallamudi, M. R., Nayak, S. R., & Muttigi, M. S. Petroleum ether extract of *Cissus quadrangularis* (Linn.) enhances bone marrow mesenchymal stem cell proliferation and facilitates osteoblastogenesis. Clinics, 2009; 64(10): 993-998.
- 37. Dhanasekaran, S. Phytochemical characteristics of aerial part of *Cissus quadrangularis* (L) and its invitro inhibitory activity against leukemic cells and antioxidant properties. Saudi journal of biological sciences, 2020; 27(5): 1302-1309.
- Shimada, K., Fujikawa, K., Yhara, K., Nakamura, T. Antioxidative properties of xanthone on the auto oxidation of soybean in cyclodextrin emulsion. J Agric Food Chem, 1992; 40(6): 945-948.
- Govindarajan, R., Vijayakumar, M., Rawat, A. K. S., & Mehrotra, S. Free radical scavenging potential of Picrorhiza kurrooa Royle ex Benth, 2003.
- Chidambara Murthy, K. N., Vanitha, A., Mahadeva Swamy, M., & Ravishankar, G. A. Antioxidant and antimicrobial activity of *Cissus quadrangularis* L. Journal of medicinal food, 2003; 6(2): 99-105.