



A REVIEW- HADJOD A MAGICAL REMEDY

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ABSTRACT

Cissus quadrangularis is a very well know medicinal plant which is indigenous to Asia and Africa. Hadjod or bone setter; *Cissus quadrangularis* is a succulent herbal plant belonging to family Vitaceae. It is a fleshy, cactus which is widely used as a common food item in India. The whole plant including all parts such as stems, leaves, roots is documented to possess medicinal properties in ethnobotanical surveys conducted by ethnobotanists in the traditional system of medicine. *Cissus quadrangularis* contains ; Triterpenes i.e. - α - and β - amyryne, β - sitosterol etc , Unsymmetric tetracyclic such as triterpenoids- d- amyryn, 3,3',4,4'-tetra hydroxy biphenyl etc. and Flavonoids such as quercetin, kaempferol, quadrangularins A,B,C etc. Stem extract has high percentage of calcium ions and phosphorus, both of which is essential for bone growth. In Ayurveda this plant has been documented for the treatment of osteoarthritis, rheumatoid arthritis, and osteoporosis. The plant's stem juice is used to treat scurvy, menstrual disorders, and epistaxis. Shoots decoction along with dry ginger and black pepper is given for body pain. *Cissus quadrangularis* was found to be effective as antibacterial, antioxidant and free radical scavenging potential, Central nervous system depressant, and antiulcer. *Cissus quadrangularis* also effective as anthelmintic, analgesic, anti-inflammatory, anti-hemorrhoidal, anti-tumor, antipyretic, gastro protective, melanin promotion, bone healing, anti-obesity etc . Thus *Cissus quadrangularis* is a magic remedy in most of disease.

Keywords: *Cissus quadrangularis*, Flavonoids, Bone Healing, Osteoporosis

INTRODUCTION:

Hadjod (Had means bone, Jod means setter) or bone setter; *Cissus quadrangularis* is a succulent herbal plant belonging to family Vitaceae. Another names of Hadjod are Adamant creeper, Square stalked vine, veldt grape, devil's backbone, adamant creeper, athisamharaka, hadjod and pirandai, Sannalam, Nalleru, Vajravelli, Mangara valli [1]. It is a fleshy, cactus which is widely used as a common food item in India. Cultivation of Hadjod is done in plains coastal areas, jungles, and wastelands up to 500 m elevation. The plant is propagated using cuttings. Plant flowers in the month of June-December. Plant material contains pieces of varying lengths; stem quadrangular, 4-winged, internodes 4-15 cm long and 1-2 cm thick [2, 3]. The surface is smooth, glabrous, buff colored with a greenish tinge, angular portion reddish-brown; no taste and odor. Leaves are simple 2.5-5cm long, broadly ovate or reniform, sometimes 3-7 lobed, denticulate, glabrous, cordate, rounded, truncate or cuneate at the base; petioles 6-12 mm long; stipules small broadly ovate, obtuse. Flowers have short peduncle cymes along with spreading umbellate branches. Cup-shaped, truncate or very obscurely lobed Calyx is seen. Petals are 4, ovate-oblong, short, stout. Berries are of obovoid or

globose shaped and has long apiculate. Berries are red in colored when ripe, 1- (very rarely 2) seeded [4, 5]. The whole plant including all parts such as stems, leaves, roots is documented to possess medicinal properties in ethnobotanical surveys conducted by ethnobotanists in the traditional system of medicine. The stem is useful as 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 [6].

SYNONYM:

Marathi: Horjora, Harsankar, Kandavel

Urdu: Harjora, Hadsankal

English: Edible stemmed vine, Adamant creeper, Bone setter

Hindi: Hadjod, Hadjora, Hadsarihari, Harsankari, Kandvel

TAXONOMY: CISSUS QUADRANGULARIS:

Kingdom: Plantae

Subkingdom: Tracheobionta

Super division: spermatophyta

Division: Magnoliophyta

Class: Magnoliopsida

Subclass: Rosidae

Order: Vitales

Family: Vitaceae

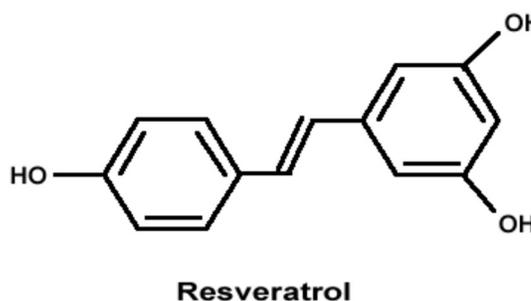
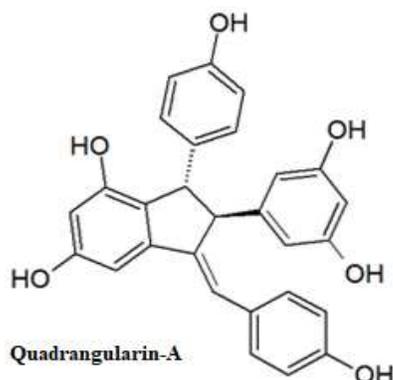
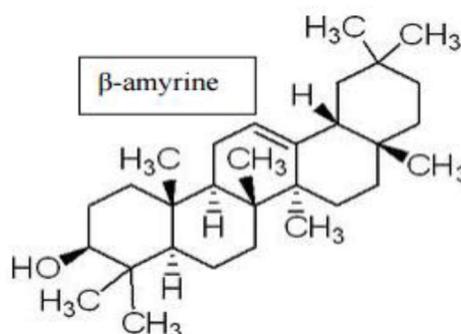
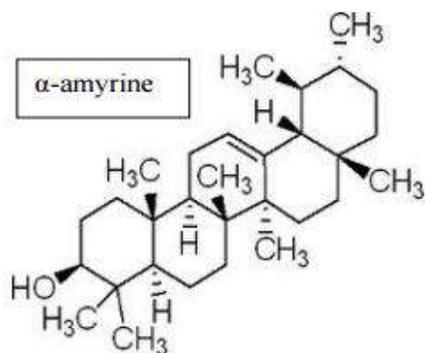
Genus: *Cissus*

Species: *quadrangularis*

PHYTOCONSTITUENTS:

Triterpenes - α - and β - amyrine, β - sitosterol, phenol, tannins, carotene and vitamin C. Unsymmetric tetracyclic triterpenoids- d-amyrin, and 3,3',4,4'-tetra hydroxy biphenyl.

Flavonoids- quercetin and kaempferol, and stilbene derivatives, quadrangularins A,B,C, resveratrol, pallidol, and phytosterols. **Stem extract contains a high percentage of calcium ions and phosphorus, both essential for bone growth [6].**



TRADITIONAL USES:

For healing of a fracture of the bones the roots and stems of Hadjod are most useful. The stem has bitter taste; in broken bones it is given internally and applied topically on affected area, and also used in patient who complains of the back and spine pain. In muscular pains a paste of stem is most useful. In Ayurveda this plant has been documented

for the treatment of osteoarthritis, rheumatoid arthritis, and osteoporosis. The plant's stem juice is used to treat scurvy, menstrual disorders, and epistaxis.

A stem paste is effective in asthma, burns and wounds, bites of poisonous insects and for saddle sores of horses and camels. Shoots decoction along with dry ginger and black pepper is given for body pain. The

infusion of the plant is anthelmintic. Leaves and young shoots are dried and powdered; then they are administered in certain bowel infections connected with indigestion.

The plant is effective in various diseases such as helminthiasis, anorexia, dyspepsia, colic, flatulence, skin diseases, leprosy, hemorrhage, epilepsy, convulsion, hemoptysis, tumors, and chronic ulcers. The traditional use of fleshy quadrangular stem in the treatment of gastritis constipation, eye diseases, piles, and anaemia. The stem is useful as a stomachic when boiled in limewater [7].

PHARMACOLOGICAL USES:

Antibacterial activity:

The dry stems of fresh ethyl acetate and methanol extracts have antibacterial activity, particularly against Gram-positive bacteria, such as *Bacillus subtilis*, *Staphylococcus aureus* [8]. The alcoholic extract of aerial part shows antiprotozoal activity against *Entamoeba histolytica*. Alcoholic extract of the stem is effective against *E. coli*. On in vitro screening; methanol and dichloromethane extract of whole plant show as it possess antiplasmodial activity [9].

Antioxidant and free radical scavenging potential:

Methanol extract of *Cissus quadrangularis* were studied using the model of

hepatotoxicity induced by carbon tetrachloride (CCl₄) in rats. CCl₄ administration exhibited significant inhibition in DPPH free radical formation, superoxide radical production and lipid peroxide production in erythrocytes associated with a marked elevation in the activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT) alkaline phosphatase (ALP) and decrease in superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and reduced glutathione (GSH), which was reverted by *Cissus quadrangularis* pretreatment. As a result *Cissus quadrangularis* inhibits lipid peroxidation, free radical production and thus increase in antioxidant enzymes activities, which reveal its antioxidant property. It can be concluded that the free radical scavenging activity of the plant extract may be responsible for the therapeutic action against tissue damage [10].

Central nervous system activity:

Central nervous system depressant activity is possessed by the root extract which is indicated by decrease in exploratory behavior. Saponins which are present in methanol extract of roots shows potent sedative activity and also inhibit spontaneous motor activity in mice [11].

Antiulcer activity:

Administration of *Cissus quadrangularis* extract after the application of acetic acid (AA) to the stomach enhanced the reduction of ulcer area in a dose-dependent manner which was confirmed by histo-architecture. Moreover, *Cissus quadrangularis* significantly increased the 3H-thymidine incorporation and the levels of polyamines such as putrescine, spermine and spermidine in ulcerated rats. In addition to antiulcer activity, the extract also shows gastroprotection in the ulcerated area by increased expression of TGF-A and additionally also reversed the changes in the gastric mucosa of ulcerated rats with significant increased in mitochondrial tricarboxylic acid (TCA) cycle enzymes and PCNA levels. Based on these results, the healing effect of *Cissus quadrangularis* on acetic acid induced gastric mucosal injury in rats may be confirmed [12].

Anthelmintic activity:

Cissus quadrangularis root was prepared and the in vitro anthelmintic activity was evaluated. The results showed that the alcoholic and aqueous extract of *Cissus quadrangularis* root exhibited anthelmintic activity in dose dependent manner giving shortest time of paralysis (P) at 100(ml) and death (D) with 200 mg/ml concentration. 100

mg/ml *Cissus quadrangularis* root, caused paralysis and death at 17.00 and 30.67 minutes respectively while, 200 mg/ml, caused paralysis and death at 8.33 and 18.50 minutes respectively against earthworm *Pheretima posthuma*. The standard drug such as piperazine citrate showed the same at 19.26 and 63.25 minutes, respectively. This study has proved that *Cissus quadrangularis* root not only demonstrated paralysis, but also caused death of worms at both the dose levels tested, in shorter time as compared to reference drug Piperazine citrate.^{13,14} Additionally it confirmed that tannins binds to free proteins in the gastro intestinal tract of host animal and cause antihelminthic effect. Tannins bind to glycoprotein on the cuticle of the parasite and may cause death. Therefore previous studies suggest that presence of tannins in the plant extract may be the reason for paralysis and death in the earthworm *Pheretima posthuma* [15].

Analgesic activity:

Haffner's tail flip and Eddy's hot plate methods were used to observe the analgesic effect of the drug at appropriate dose. Even a small dose as 1/40th cause increase in reaction time of the LD50, this effect lasted for about 4 hrs. As compare to aspirin; *Cissus quadrangularis* exhibited significant analgesic activity when tested by Haffner's

clip and Eddy's hot plate methods. The extract was effective by both oral and i.p. routes significantly ($P < 0.001$) and reaction time was found to be increased by both methods i.e. oral and i.p. routes. 2 to 4 hr is the duration of analgesic activity and at $1/20^{\text{th}}$ - $1/10^{\text{th}}$ optimum effect was observed of LD50 dose. The extract compared well with standard i.e. Acetylsalicylic acid [16, 17]. When this plant was used in bone fractures the analgesic effect may be of great value in relief of pain. As it shows same analgesic response like acetyl salicylic acid the nature of its chemically active phytoconstituents should be explored [18].

Anti-inflammatory activity:

Studies shows that inhibition of the paw edematous response induced by arachidonic acid injection was done by oral administration of phenidone. *C. quadrangularis* exerted inhibitory effect on the paw edema formation in the animal model. It has been observed that various phytoconstituents such as flavanoids, several flavones, flavonols, flavanols and flavanonols are inhibitors of lipoxygenase. Among them most active constituents such as luteolin is more effective as anti-inflammatory compounds. It has been previously shown that at least flavonoid, one of the major components of *C.*

quadrangularis, inhibits the inflammatory process. Further β sitosterol which is another active constituent of *C. quadrangularis* also shows antiinflammatory activity. The result of the study confirmed the finding that *C. quadrangularis* have an inhibitory effect on edema induced by both carrageenin and arachidonic acid. *C. quadrangularis* inhibits both cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolism. Hence it was suggested that *C. quadrangularis* is a dual inhibitor of arachidonic acid metabolism [19]. *Cissus* also possess anti-inflammatory activity on a mg per mg basis comparable to aspirin or ibuprofen. An Ayurvedic preparation, 'Laksha Gogglu' contains *Cissus quadrangularis*, which was found to be highly effective in pain relieving, reducing swelling and promoting the simple fractures healing process. It also cured the allied disorders which are associated with fractures. It prevents the conversion of arachidonic acid to inflammatory prostaglandins and thus show anti-inflammatory activity [20-22]. Recently anti-inflammatory activity assay of *Cissus* extract was performed. Key enzyme in the prostaglandin biosynthetic pathway is Cyclooxygenase, which is also important in the inflammatory process. *Cissus quadrangularis* extract shows the ability to

inhibit the COX-1 activity which was used to evaluate the anti-inflammatory activity. The anti-inflammatory activity of the extract was expressed as the percentage of inhibition of prostaglandin synthesis using a COX-1 assay. By using a scintillation counter the amount of (14C)-labelled prostaglandin synthesized was measured; the amount is measured after removing the unmetabolized (14C)-Arachidonic acid substrate by column chromatography. The percent inhibition of prostaglandin synthesis was calculated [23, 24].

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* shows that its major compounds are flavonoids. In the treatment of haemorrhoids and varicose veins the bioflavonoids, particularly diosmin, hesperidin and oligomeric proanthocyanidin complexes have demonstrated potential effective. Such bioflavonoids shows phlebotonic activity, vasculoprotective effects and antagonistic effect on the biochemical mediators of inflammation. The anti-inflammatory effect

which was observed from the crude extract of *C. quadrangularis* is due to the presence of the flavonoids especially luteolin, and by β -sitosterol.

Due to the presence of flavonoids in the extract of *C. quadrangularis* it show the venotonic effect which act in the same way as that of diosmin and hesperidin. To treat haemorrhoid diosmin and hesperidin are used in combination, the extract which produced the same activities (anti-inflammatory and venotonic) can also be used as Antihemorrhoidal drug. Besides these effects, As *C. quadrangularis* also possesses analgesic effect; it is very useful in painful haemorrhoid [25].

Anti-tumor activity:

Cissus quadrangularis through the whole water extract more than the methanol extract of antagonistic role of HepG2 cell proliferation, which as a traditional treatment for their cancer patients provide a scientific basis. In addition, Resveratrol is an effective anti-cancer agent of natural chemicals from *Cissus quadrangularis* that can trigger the human tumor cells, CD 95. This article can be downloaded from www.ijpbs.net P - 136 signaling-dependent cell death. Also has an entry that its anti-cancer activity attributed to its anti-cyclo-oxygenase activity [26].

Antipyretic activity:

The various serial extract of the *Cissus quadrangularis* when orally administered in albino rats showed a reduction ($p \leq 0.01$) in hyperpyrexia induced by dried yeast injection with activity being pronounced in 18 hrs. This shows the antipyretic activity of *Cissus quadrangularis* [27].

Gastro protective Activity:

Well know traditional medicine for the treatment of gastric disorders is *Cissus quadrangularis*, which is the rich source of carotenoids, triterpenoids and ascorbic acid. Lots of studies have analysed and revealed the effect against gastric toxicity and the gastro protective effect of *Cissus quadrangularis* extract, against the gastric mucosal damage induced by aspirin. The studies on the experimentally induced gastric ulcer have investigated the effect of *Cissus quadrangularis* extract by analyzing the levels of tumor necrosis factor- α (TNF- α), interleukins, microvascular permeability, effect of nitric oxide synthase 2 (NOS-2), mitochondrial antioxidants effect, lipid peroxidation effect and DNA damage. In addition, the findings of the studies have shown that *Cissus quadrangularis* extract reversed the effect of aspirin administration such as increasing level of lipid peroxidation, xanthine oxidase (XO), myeloperoxidase and decreasing level of

superoxide dismutase (SOD), catalase (CAT) and selenium- glutathione peroxidase activities in the gastric mucosa, resulting in mucosal damage at both cellular and sub cellular level. In addition, oxidative damage of DNA is prevented by using *Cissus quadrangularis* extract which is done by reducing DNA fragmentation and thus indicates its block on cell death. Pre-treatment with *Cissus quadrangularis* extract ameliorated the observed effect significantly in the gastric mucosa of ulcerated rats [28].

Melanin Promotion activity: Exhaustively extraction of the powdered stems of *Cissus quadrangularis* were done with methanol (3.0 L) by using soxhlet apparatus for 8 hrs. After evaporation of the solvent under reduced pressure, 32.45 g crude extract was obtained and showed an excellent melanin promotion activity (380% at 50 μ g/ml) [29].

Bone Healing Activity:

Alcoholic extract of the plant facilitates rapid healing of fracture in albino rats when given locally as well as intramuscularly. Ethanol extract (95%) enhances the development of cortical bone and trabeculae in foetal femur, which may be related to rich content of calcium, phosphorous and phytoestrogenic steroids and as a result regeneration and mineralization process occurs faster i.e, bone fracture healing process takes place faster.

Antiosteoporotic activity was possess by ethanol extract (95%) of whole plant in ovariectomized rat model of osteoporosis at two different dose levels of 500 mg and 750 mg per kg per weigh [30].

The main constituent in *Cissus quadrangularis* is bioactive steroid which shows antiosteoporotic activity. Studies suggest that the steroid may act on estrogenic receptors of the bone and thus help in fracture healing. Also it has been observed that *Cissus quadrangularis* acts by stimulation of metabolism and increased uptake of the minerals calcium, sulphur and strontium by the osteoblasts in fracture healing [31, 32]. *Cissus quadrangularis* may be useful not only in building up bones but in improving functional efficiency [33]. The extract also neutralize the antianabolic effect of cortisone in healing of fractures, due to its high vitamin C content [34].

Complete restoration of normal composition of bone, after fracture in observed four weeks by using *Cissus quadrangularis* systemic in rats while the controls required six weeks. Which indicates the bone healing duration was shorten by about two weeks. Against the controls group; in the systemic use of *Cissus quadrangularis* the total weight of the fractured bone also came down towards

normal much earlier which indicates quickest bone remodeling. All the events were hastened by about 10 to 14 days in the treated group; events namely fibroblastic phase (first week), collagen phase (second week) and osteochondroital phase (third and fourth weeks). The stimulation of all the cells of mesenchyma origin, namely the fibroblasts, the chondroblasts and osteoblasts by *Cissus quadrangularis* mainly cause hastening in the fracture healing. Due to *Cissus quadrangularis* osteoblastic proliferation shows has greater impact on than other cellular responses. In both the models , histological and histochemical observations shows that the mucopolysaccharide and collagen levels of the bones in the treated group came down to normal at the end of only four weeks while in the control it will take 6 weeks [35-37].

The radioactive calcium (Ca^{45}) studies indicated that in the first week of bone healing process; *Cissus quadrangularis* treated animal's causes less lowering of calcium (Ca^{45}) uptake while greater decrease in the calcium (Ca^{45}) uptake is seen in the control animals. Which is followed by a gradual increase in the subsequent weeks and reached to its maximum in the 4th weeks. At the end of 5th week the calcium (Ca^{45}) uptake in the treated group came to normal as

compared to 6th - 8th weeks in controls. Hence based on this study it was concluded that *Cissus quadrangularis* caused less amount of tissue reaction in the fractured region leading to optimum decalcification in the early stage with minimum of callus formations. As deposition of calcium was just enough to join the two broken segments of bones because of which remodeling takes place much faster in the treated group as compared with controls. Early recovery of animals is due to the early completion of calcification process and earlier remodeling phenomenon. The tensile strength studies indicated that *Cissus quadrangularis* treated group gain in the tensile strength much early which leads to 90 % of gain of its normal strength at the end of 6th week while in the control it is only 60% of gain of tensile strength. Which indicates *Cissus quadrangularis* helps in functional efficiency of bone as well as building up the chemical composition of the fractured bone that its mucopolysaccharides, collagen, calcium, phosphorus and others [38-42].

Anti-obesity activity:

Aqueous extract of leaf and stem from *C. quadrangularis* at 300 mg dose was effective in reducing body fat as well as improving blood parameters associated with metabolic syndrome [43]. Similarly, it was

effective in reducing weight, improving blood parameters associated with metabolic syndrome, as well as serotonin levels in obese and overweight individuals [44]. Ross reported that *C. quadrangularis* is found to be effective in obesity management and other complications associated with metabolic syndrome. The plant also demonstrated efficacy in the control and lowering of triglyceride, total cholesterol, low-density lipoprotein cholesterol, and fasting blood glucose levels [45, 46]. *C. quadrangularis* inhibited lipid accumulation without showing cytotoxicity to 3T3-L1 adipocytes. Further, it decreased adipogenesis/lipogenesis-related mRNA expression levels of fatty acid binding protein, fatty acid synthase, lipoprotein lipase, stearoyl-CoA desaturase-1, and acetyl-CoA carboxylase. The results suggested that the plant have an anti-obesity effect by its ability to decrease expression levels of adipogenesis/lipogenesis-related genes and proteins [47].

CONCLUSION: Now a day, traditional uses of natural compounds, especially of plant origin generally believed to be safe for human use. Scrutiny of these drugs is necessary by modern scientific lines such as phytochemical investigation, biological evaluation on experimental animal models, toxicity studies, investigation of molecular

mechanism of action of isolated phytoprinciples and their clinical trials. By literature review it was found that *Cissus quadrangularis* is a popular remedy for a variety of ailments and a range of formulations has been marketed. Future study of this required the isolation of active principles from *Cissus quadrangularis* which can further be evaluated in scientific manner using specific experimental animal models and clinical trials. *Cissus quadrangularis* was found to be effective as antibacterial, antioxidant and free radical scavenging potential, Central nervous system depressant, and antiulcer. *Cissus quadrangularis* also effective as anthelmintic, analgesic, anti-inflammatory, anti-hemorrhoidal, anti-tumor, antipyretic, gastro protective, melanin promotion. *Cissus quadrangularis* is considered as a versatile medicinal plant in both Ayurvedic and modern drug development.

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