

Asthishrunkhala Drug Used in Ancient Indian Medicine- Phytochemical and Pharmacological Review

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Abstract:

Cissus quadrangularis L. is a succulent plant of family Vitaceae commonly found in tropical and subtropical xeric wood. It is a fleshy, cactus-like liana widely used as a common food item in India. The plant is prescribed in the ancient Ayurvedic literature as a general tonic and analgesic, with specific bone fracture healing properties. The plant is believed to be useful in helminthiasis, anorexia, dyspepsia, colic, flatulence, skin diseases, leprosy, hemorrhage, epilepsy, convulsion, haemoptysis, tumors, chronic ulcers, swellings. Following various folk claims for cure of various diseases, efforts have been made by researchers to verify the efficacy of the plant through scientific biological screening. The scrutiny of literature revealed some notable pharmacological activities of the plant such as antioxidant, free radical scavenging, anti microbial, anti bacterial, bone healing, anti ulcer, analgesic, anti inflammatory and diuretic, presented in this review such that the potential use of the plant either in pharmaceuticals or as an agriculture resource can be evaluated. The present review is an attempt to highlight phytochemicals, various traditional uses as well as pharmacological reports on *Cissus quadrangularis* L.

Keywords:

Introduction:

Cissus quadrangularis L. is commonly known as AsthiShrunkhala is a succulent plant of family Vitaceae commonly found throughout the hotter parts of India. It can be cultivated in plains coastal areas, jungles and wastelands up to 500m elevation. Plant is propagated using cuttings.^[1] Plant flowers in the month of June-December.^[2] Plant material occurs as pieces of varying lengths; stem quadrangular, 4-winged, internodes 4-15cm long and 1-2cm thick. The surface is smooth, glabrous, buff colored with greenish tinge, angular portion reddish-brown; no taste

and odour. 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 6-12mm long; stipules small broadly ovate, obtuse. Flowers are in shortly peduncle cymes with spreading umbellate branches. Calyx is cup shaped, truncate or very obscurely lobed. Petals are 4, ovate-oblong, short, stout. Berry is obovoid or globose, scarcely 6mm, long apiculate, red when ripe, 1- (very rarely 2) seeded.^[3] The whole plant including all parts such as stems, leaves, roots are documented to possess medicinal properties in ethnobotanical surveys conducted by

ethnobotanists in traditional system of medicine. The present review will possibly help to bridge between traditional claims and modern therapy on *Cissus quadrangularis* L. and also pinpoints unexplored potential of it.

Materials and Methods

Classification of the plant:

Kingdom: Plantae or green plants Subkingdom: Tracheobionta: Vascular plant

Super division: Spermatophyta: Seed bearing plants Division: Angiosperm(Flowering Plants) Class: Dicotyledoneae: Dicots; Angiosperms; Flowering plants; Subclass: Rosidae Order: Rhamnales Genus: *Cissus* L.: (Treebine) Trees with simple, entire leaves. Stems and branches are acutely angled or winged. Flowers are disposed in terminal panicles, small and polygamous. Calyx is short, entire and deciduous. Petals are 4-5, imbricate. Stamens are as many as the petals, with only 1 functional stamen. Ovary is unilocular, with a solitary ovule; style is filiform. Fruit is a large succulent drupe. Species: *quadrangularis* Linn. (Veldt-grape) Stems and branches acutely winged. Botanical name: *Cissus quadrangularis* Linn. Family: Vitaceae: Grape, Virginia creeper; usually lianas with alternate leaves, often palmately lobed or compound, sometimes pinnate. The leaf is opposed by a tendril (modified inflorescence developing from displaced bud) that attaches to support by twining or by forming adhesive discs; nodes usually swollen. The flowers are 4 or 5-merous, petals forming a cap that falls off when the flower opens; fruit a berry; seeds 4, with prominent cordlike raphe extending to a chalazas knot.

Classical name: Asthisamhari

Sanskrit names: Asthisamhari, Vajravalli, Asthishrunkhala, Asthisamhara, Kandavalli, Vajrangi, Asthisamyojaka

Distribution Found throughout the hotter parts of India alongside hedges, neighboring countries like Pakistan, Bangladesh, Shrilanka and

Malaysia. It can be cultivated in plains coastal areas, jungles and wastelands up to 500m elevation. Plant is propagated using cuttings

Vernacular names

Hindi: Hadjod, Hadjora, Hadsankari, Hadsarihari, Kandvel Guj: Hadsankal, Hadsand, Chodhari Tam: Pirantai, Vajjravalli Tel.: Nalleru, Nulleratiga, Vajravalli Urdu : Hrajora, Hadsankal Oriya: Hadabhanga Beng: Har, Harbhanga, Hasjora, Horjora Eng.: Edible stemmed wine, Bonesetter, Adamant creeper Kan.: Mangarahalli Mal.: Peranta, Cannalamparanta *Powder characteristics* The colour of powder is brown; shows fragments of vessels, fibers, parenchymatous cells and few rosette crystals of calcium oxalate, starch grains and idioblasts containing raphides and isolated acicular crystals of calcium oxalate.

Phytochemistry:

Phytochemical studies of *Cissus quadrangularis* have shown the presence of various versatile constituents such as flavanoids, triterpenoids, Vitamin C, stilbene derivatives and many others, e.g. resveratrol, piceatannol, pallidol perthenocissin and phytosterols. Out of which ascorbic acid, triterpene, β -sitosterol, ketosteroid, two asymmetrical tetracyclic triterpenoids and calcium were identified as major constituents of this plant. The *Cissus quadrangularis* contains high amount of Carotene A, anabolic steroidal substances and Calcium. The plant contains ascorbic acid, 479 mg and carotene, 267 mg per 100 g freshly prepared paste, in addition to calcium oxalate. The stem of the plant contains two asymmetric tetracyclic triterpenoids, onocer - 7 ene 3 α , 21 β diol (C₃₀H₅₂O₂ m.p. 200 – 202 °C) and onocer - 7 ene – 3 β , 21 α diol (C₃₀H₅₂O₂, m.p. 233 – 234 °C). It also contains two steroidal principles –1. C₂₇H₄₅ O, melting point 249-252 °C. 2. C₂₃H₄₁ O, melting point 136-138 °C. Presence of β -sitosterol (Fig.3), δ amyirin and δ - amyrone is also reported. The aerial parts of *Cissus quadrangularis* is found to

contain a new asymmetric tetracyclic triterpenoid, 7-Oxo-Onocer-8-ene-3 β 21 α diol (C₃₀H₅₀O₃, m.p. 235-237 °C). Seven new compounds are also reported which are 4-hydroxy 2 methyl-tricos-2 ene -22- one, 9-methyloctadec- 9-ene, heptadecyl-octadecanoate, icosanylicosanoate, 31-methyl tritriacontan-1-ol, 7- hydroxy- 20- oxo- docosanyl cyclohexane and 31-methyl tritriacontanoic acid. Small amount of taraxeryl acetate, friedelan-3-one, taraxerol and isopentacosanoic acid is also present. Presence of 3, 3', 4, 4'-tetrahydroxybiphenyl is also reported. [20, 21, 22] Analysis of the air-dried *Cissus quadrangularis* plant reported to contain moisture 13.1, protein 12.8, wax 1.0, fiber 15.6, carbohydrate 36.6, mucilage and pectin 1.2 and ash 18.2%. The root powder also contain a rich source of mineral elements (mg/100g dry matter): potassium 67.5, calcium 39.5, zinc 3.0, sodium 22.5, iron 7.5, lead 3.5, cadmium 0.25, copper 0.5 and magnesium 1.15. [23, 24, 25, 26] Analysis of the toxicants also revealed the presence of oxalate, tannin, phytate, saponin contents (135, 0.3, 20, 0.16 mg/100g of dry matter) respectively. The ash formed from the *Cissus quadrangularis* contains mostly carbonates and to a smaller extent phosphates of sodium, potassium, magnesium and calcium. Presence of potassium tartarate is also reported. [27, 28] The *Cissus quadrangularis* stem is also reported to contain a water-soluble glycoside, which produces a fall in blood pressure in anaesthetized cats. Fresh stems of *Cissus quadrangularis* produces irritating action on the skin, which may be attributed to the presence of calcium oxalate and 31 methyl tritriacontanoic acid along with taraxeryl acetate, taraxerol and iso-pentacosanoic acid. [29, 30] Recently three new stilbene derivatives, quadrangularins A, B and C were isolated from *Cissus quadrangularis* together with resveratrol, piceatannol, pallidol and parthenocissine A. The

stem extract of *Cissus quadrangularis* plant contains a high percentage of calcium ions (4% by weight) and phosphorous.

Strength as per ayurvedic pharmacopoeia of india: [39]

Foreign Matter: NMT 1% W/W, Total Ash: NMT 5% W/W, Acid insoluble ash: NMT 1% W/W Alcohol soluble extractive: NLT 3% W/W, Water soluble extractive: NLT 23% W/W, Fixed oil: NLT 3% W/W, Sulphated Ash content: NMT 5% W/W, Arsenic: NMT 1 ppm, Lead: NMT 5 ppm, Total bacterial count: NMT 800 CFU/g Total fungal count: NMT 500 CFU/g, Moisture content: NMT 5% W/W

Traditional uses

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, used in complaints of the back and spine. [20] A paste of stem is useful for muscular pains. [1] The plant has been documented in Ayurveda for the treatment of osteoarthritis, rheumatoid arthritis and osteoporosis. [21,22] The stem juice of plant is used to treat scurvy, menstrual disorders, otorrhoea and epistaxis. [1] The use of sap with tamarind has been reported in East Africa for the treatment of gonorrhoea. [23] The herb is fed to cattle to induce flow of milk. The ash of plant is useful as a substitute for baking powder. [1] A paste of stem is given in asthma, burns and wounds, bites of poisonous insects and for saddle sores of horses and camels. [1,24] Decoction of shoots with dry ginger and black pepper is given for body pain the infusion of plant is anthelmintic. [1] Leaves and young shoots are powerful alternatives, dried and powdered; they are administering in certain bowel infections connected with indigestion. [20] The plant is useful in helminthiasis, anorexia, dyspepsia, colic, flatulence, skin diseases, leprosy, hemorrhage, epilepsy, convulsion, haemoptysis, tumors, chronic ulcers, swellings. The stout fleshy quadrangular stem is traditionally used for treatment of gastritis

constipation, eye diseases, piles and anemia. The stem boiled in limewater it forms a preserve useful as a stomachic; The Rongas of east Africa apply the pounded stem to wounds.^[25, 26]

Pharmacological uses

Following the folk and traditional uses of the plant, it has been investigated scientifically in animal model to validate the potential of the plant in cure of variety of ailments.

Antioxidant and free radical scavenging activity

Methanol extract of *Cissus quadrangularis* exhibits strong antioxidant and free radical scavenging activity *in vitro* and *in vivo* systems mainly due to the presence of β -carotene.^[27,28]

Anti microbial and antibacterial activity

Methanol extract (90%) and dichloromethane extract of stems possess antibacterial activity against *S. aureus*, *E. coli*, and *P. aeruginosa* and mutagenicity against *Salmonella microsoma*.^[29] Antimicrobial activity has also been reported from stem and root extract.^[27] The alcoholic extract of aerial part was found to possess antiprotozoal activity against *Entamoeba histolytica*.^[3] Alcoholic extract of the stem showed activity against *E. coli*.^[30] Methanol and dichloromethane extract of whole plant were screened for *in vitro* antiplasmodial activity.^[21]

Bone healing activity

Paste of alcoholic extract of the plant was locally as well as intramuscularly facilitates rapid healing of fracture in albino rats.^[31] Ethanol extract (95%) enhances the development of cortical bone and trabeculae in fetal femur, which may be related to rich content of calcium, phosphorous and phytoestrogenic steroids and shown to influence early regeneration and quick mineralization of bone fracture healing process.^[32] Ethanol extract (95%) of whole plant possess antiosteoporotic activity in ovariectomized rat model of osteoporosis at two

different dose levels of 500 and 750 mg per kg per weight.^[1]

Anti-ulcer activity

Methanol extract showed significant antiulcer activity in experimentally induced ulcer in rat model by decreasing gastric secretions and by enhancing glycoprotein levels.^[32] Methanol extract produce healing effect on aspirin induced gastric mucosal damage in rats through its antioxidative mechanism.^[34] Triterpenoids and β -sitosterol present in methanol extract possess anti-lipid peroxidating effect and thus prevent gastric damage.^[35]

Analgesic, anti-inflammatory and stimulatory activity

Methanol extract possess analgesic, anti-inflammatory and venotonic effects associated with hemorrhoids, anti-inflammatory activity is due to flavonoids especially luteolin and by β -sitosterol.^[36] β -sitosterol present in methanol extract has ability to reduce the enzymes MPO indicating a reduction of neutrophils influx in the inflamed tissue.^[37] Calcium oxalate, carotene, tetraterpenoids, β -sitosterol, amyryn and anabolic ketosteroids, which are responsible for acceleration of healing and possess anti-inflammatory and analgesic activity.^[31,38] Ethanol extract exhibit protective effect on neutrophils mediated tissue injury induced by aspirin in rats 34. Methanol extract (90%) and dichloromethane extract of stems possess anti-inflammatory activity against COX-2.^[29] The stimulatory effect of extract is probably due to vitamins and is greater than that of the anabolic hormone durabolin.^[39]

Central nervous system activity

The root extract possess central nervous system depressant activity indicated by decrease in exploratory behavior. Methanol extract of roots contains saponins which show potent sedative activity and also inhibit spontaneous motor activity in mice.

Miscellaneous activity

Acetone and dichloromethane extract of the plant possess proteolytic activity against cysteine protease. Extract of the plant have wound healing activity and molluscidal activity. The extract of plant exhibits cardiogenic and androgenic property. Ethanol extract (50%) of aerial parts possess hypotensive activity and stem extract possess diuretic activity.^[21] The plant formulation is used in the management of weight loss, metabolic syndrome and cardiovascular problems.

Toxicology

The *Cissus quadrangularis* extract does not produce any toxic effect on oral administration (1mg/Kg daily for 10 days) in mice, rats and guinea pigs. However, on intravenous administration, the animals developed convulsions and died in five minutes. The MLD worked out to be 15.5 mg/Kg in guinea pigs. Toxicological evaluation of the plant revealed that the drug is safe even at higher dose for a prolonged duration of treatment. *Formulation and preparations* The plant is incorporated in various formulations along with different herbs. These include Laksadi Guggulu, Asthisamharadi Churna, Asthisamhara Taila, Dasyadi Kwatha, Darvi Kwatha etc.^[4]

CONCLUSION

In recent years, ethnobotanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. They obviously deserve scrutiny on 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. Our thorough screening of literature available on *Cissus quadrangularis* depicted an interesting fact that though the plant is a popular remedy for a variety of ailments and

a range of formulations has been marketed, little effort have been made to verify its purity, quality and efficacy through scientific screening. In future study, the isolated principles from *Cissus quadrangularis* needs to be evaluated in scientific manner using specific experimental animal models and clinical trials to understand the molecular mechanism of action, in search of lead molecule from natural resources.

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