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REVIEW ARTICLE

PHARMACOLOGY

Pharmacognostic and traditional properties of Cissus quadrancularis Linn -An overview

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ABSTRACT

Cissus quadrangularis, a medicinal plant indigenous to Asia and Africa. It is used in indigenious system of medicine like ayurveda, siddha, unani and homoeopathy. The active compounds isolated form this plant are considered to be very effective in various treatments, such as osteoporosis, asthma, cough, hemorrhoids, and gonorrhea. The paper reports on its traditional, phytochemical and pharmacognostic properties such as antioxidant, anticancer, analgesic, anti-inflammatory and antipyretic activities of *Cissus quadrangularis.*

KEY WORDS

piceatannol, resveratrol, flavonoids, quadrangularins, antioxidant, anti tumour, *Cissus quadrangularis.*

INTRODUCTION

Cissus quadrangularis is the most common species, belonging to the family Vitaceae, commonly known as "Hadjod." The leaves are simple or lobed, cordate, broadly ovate or reniform, serrate, dentate, sometimes 3-foliate and glabrous. Flowers small, greenish white, bisexual, tetramerous, opposite to the leaves. Fruit globose or obovoid fleshy berries. The stem and leave of *C. quadrangularis* is used for the treatment of hemorrhoid, menstrual disorder, scurvy and as antioxidant, anti-flatulence, antibacterial, antifungal. In India it is used for many diseases[1-4]. The extract of the plant exhibit cardiotonic and androgenic property. Phytochemical studies of *C. quadrangularis* found several phytochemical constituents such as ascorbic acid, carotene, anabolic steroidal substances, calcium,. β-sitosterol, δ-amyrin, δ-amyrone, flavonoids, triterpenoids[5-7] and various secondary metabolites.[8-10] Pharmacological studies showed the bone fracture healing property[11] and antiosteoporotic[12] effect of this plant. Two capsules of 500 mg dry powder of *C. quadrangularis* taken twice daily were very effective in the treatment of hemorrhoidal pain and inflammation as well as reducing the size of hemorrhoids[13]. It has been investigated that methanolic extract of *Cissus quadrangularis* possesses antiulcer and cytoprotective property in indomethacin induced gastric mucosal injury. The aqueous extract also shows acetylcholine like activity on isolated ileum of rabbit and uterus of rat. *Cissus quadrangularis* has been reported to include antioxidant, anti-flatulence, antibacterial, antifungal, anti-inflammatory, analgesic, antibacterial, and cancer suppressive. This study was aimed to present an overview of traditional, phytochemical and pharmacological investigations of bioactive compounds present in this plant.

Cissus quadrancularis

Taxonomy:

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Vitales
Family : Vitaceae
Genus : Cissus
Species : *quadrangularis*

Habit and habitat:

Cissus quadrangularis is a herb, reaching a height of 1.5 m and has quadrangular-sectioned branches with internodes 8 to 10 cm long and 1.2 to 1.5 cm wide. Cissus quadrangularis grows natively in hot, dry regions of India, such as the Deccan peninsula. It is also found on the lower slopes of the Western Ghats, and is widespread across drier areas of Arabia and Africa.

Morphological characters:

Cissus quadrangularis is a low-growing shrub with a characteristic, four-sided stem. It is a climbing plant, often found growing over lower-growing vegetation. Cissus' thick stem is glabrous and fleshy, with constrictions at its nodes. Its alternate, simple leaves are also thick and ovate, with serrated margins. The leaves measure about 8 cm long and 6 cm broad. Numerous tendrils grow out of the plant's nodes.

Traditional properties:

Cissus quadrangularis is an ancient medicinal plant native to the hotter parts of Ceylon and India. It 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. Cissus quadrangularis is used for obesity, diabetes, a cluster of heart disease risk factors called "metabolic syndrome," and high cholesterol. It has also been used for bone fractures, weak bones (osteoporosis), scurvy, cancer, upset stomach, hemorrhoids, peptic ulcer disease (PUD), painful menstrual periods, asthma, malaria, and pain. Cissus quadrangularis is also used in bodybuilding supplements as an alternative to anabolic steroids. Cissus quadrangular stem resembles the shape of bones and joints in the body. And in deed it is very effective in strengthening the bones and joints. It is explained as Asthi samharaka, Ashti Shrunkhala and Vajravalli. Modern research has shed light on Cissus' ability to speed bone healing by showing it acts as a glucocorticoid antagonist[14]. Cissus possesses anabolic and androgenic properties[15]. In addition to speeding the remodeling process of the healing bone, Cissus also leads to a much faster increase in bone tensile strength. In clinical trials Cissus has led to a fracture healing time on the order of 55 to 33 percent of that of controls. Cissus exerts antiglucocorticoid properties is suggested by a number of studies where bones were weakend by treatment with cortisol, and upon administration of Cissus extract the cortisol induced weakening was halted, and maintain the healing process. It has been prescribed in Ayurveda as an alterative, antihelmintic, dyspeptic, digestive, tonic, analgesic in eye and ear diseases, and in the treatment of irregular menstruation and asthma. In Cameroon, the whole plant is used in oral re-hydration, while the leaf, stem, and root extracts of this plant are important in the management of various ailments. Various formulations now contain extracts of *Cissus quadrangularis* in combination with other compounds, used for the purpose of management of overweight and obesity, as well as complications resulting from these

conditions, notably metabolic syndrome (syndrome X). Phytochemical analyses of *Cissus quadrangularis* revealed high contents of ascorbic acid, carotene, anabolic steroidal substances, and calcium. The stem contains two asymmetric tetracyclic triterpenoids, and two steroidal principles. The presence of β-sitosterol, δ-amyrin, δ-amyrone, and flavanoids (quercetin) has also been reported,[16] all these components having potentially different metabolic and physiologic effects. The typical recommended daily dosage of Cissus extract is between 100 and 500 mg, depending on the concentration of the extract and the severity of symptoms. For the powder of the dried plant, the ayurvedic texts recommend a dosage of 3 to 6 grams to accelerate fracture healing. Safety studies in rats showed no toxic effects at dosages as high as 2000 mg/kg of body weight. So not only is Cissus efficacious, it is also quite safe, in either the dried powder form or the commercially available extract. Cissus also possess analgesic properties on a mg per mg basis comparable to aspirin or anti-inflammatory drugs like ibuprofen. Cissus quadrangularis constitutes one of the ingredients of an Ayurvedic preparation, `Laksha Gogglu', which has been proved to be highly effective in relieving pain, reduction of swelling and promoting the process of healing of the simple fractures as well as in curing the allied disorders associated with fractures[17]. The mechanism through which Cissus exerts its analgesic and anti-inflammatory properties has not been well characterized. It may act centrally, but the anti-inflammatory features suggest that it acts by preventing the conversion of arachidonic acid to inflammatory prostaglandins. With studies showing that hormone replacement therapy in postmenopausal women may increase the risk of breast cancer and heart disease, many women are looking at alternatives to estrogen to help prevent osteoporosis. Although there appears to be no published research showing that Cissus increases bone density in osteoporosis, or helps prevent the disease, the fact that the herb speeds recovery of fractures suggests that may increase bone density as well. It would almost certainly help speed the recovery of fractures that are a common occurrence with osteoporosis. Chronic glucocorticoid therapy is a high risk factor for the development of osteoporosis. Glucocorticoids are believed to interfere with the action of osteoblasts, the cells that are responsible of the deposition of new bone material. Cissus seems to be devoid of side effects and may prove to be a viable compound in osteoporosis treatment. Cissus quadrangularis stem is fried in ghee and administered with milk as for the treatment of fractures and osteo arthritis. The stem is processed in sesame oil is very useful to treat Sandhivata. Cissus quadrangularis can be cooked by the salt, dried and deep-fried food and Lay caused by chromosome aberrations, sperm deformation and generate micro-organisms have antagonistic effects, thus demonstrating the role of genetic toxicity[18.] Besides the above-mentioned properties of Cissus, the plant is also rich in the vitamins/antioxidants vitamin C and beta-carotene. Cissus quadrangularis is a succulent vine from Africa and Asia. It is one of the most commonly used medicinal plants in Thailand, and is also used in traditional African and Ayurvedic medicine. All parts of the plant are used for medicine.

Phytochemical properties:

Cissus quadrangularis have numerous bioactive compounds such as alkaloids, resveratrol, piceatannol, pallidol ,parthenocissin , quadrangularins, ascorbic acid, carotene, phytosterol substances ,calcium, flavinoids, vitamins, enzymes, nicotinic acid, tyrosin, and triterpenoids , Cissus quadranguaris contains a variety of terpenoid components, such as the balsam

ketone , amyrin, onocer 7 ene 3 a 21diol[19], taraxerol, acetyl taraxerol, friedelin ketone[20].The main chemical constituents are tetracyclic triterpenoids, onocer-7-ene-3alpha, 21 beta-diol and onocer-7-ene-3beta, 21 alpha-diol and two steriodal principles I and II, alpha-sitosterol, delta-amyrin. The stem contains two asymmetric tetracyclic triterpenoids, and two steroidal principles. The presence of β-sitosterol, δ-amyrin, δ-amyrone, and flavanoids (quercetin) having different potential metabolic and physiological effects has also been reported[21,22] and the stem has revealed unique stilbene derivatives, which are termed quadrangularins A, B and C[10]. Other lipids and several phytosterols like heptadecyl octadecanoate, icosanyl icosanoate, 4-Hydroxy-2-methyltricos-2-en-22-one, 9-methyl-octadec-9-ene, α-amyrin, α-amyrone taraxeryl acetate, friedelan-3-one, taraxerol, P-sitosterol and isopentacosanoic acid are identified in this plant.Cissus quadrangularis is rich in vitamin C and beta-carotene. Analysis showed that Cissus contained Ascorbic acid at a concentration of 479 mg, and carotene 267 units per 100g of freshly prepared paste, in addition to calcium oxalate[23.]

Pharmacognostic properties:

Antioxidant and free radical scavenging potential:

Methanol extract of *Cissus quadrangularis* (CQE) were studied using the model of hepatotoxicity induced by carbon tetrachloride (CCl_4) in rats. CCl_4 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 CQE pretreatment. The results obtained suggest that CQE showed inhibition of lipid peroxidation, free radical production and 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[24].

Antibacterial activity :

The dry stems of fresh ethyl acetate and methanol extracts have antibacterial activity, particularly against Gram-positive bacteria, such as Bacillus subtilis, Sin shadow boxing bacteria, Staphylococcus aureus [25.]

***Anti-osteoporosis activity** :*

Ethanol extract was evaluated for its anti-osteoporotic activity in ovariectomized rat model of osteoporosis at two different dose levels of 500 and 750 mg/kg per day. The rats were divided into five groups .First group served as control. All the remaining groups were ovariectomized. Group 2 was fed with saline and served as ovariectomized control. Groups 3–5 were orally treated with Raloxifen (5.4 mg/kg) and ethanol extract of *Cissus quadrangularis* (500 and 750 mg/kg), respectively. The biomechanical, biochemical and histopathological parameters showed that the ethanol extract had a definite antiosteoporotic effect[12.]

Anti-tumor activity:

Cissus quadranularis 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[26]. In addition, Resveratrol is an effective anti-cancer agent of natural chemicals from cissus quadrancularis that can trigger the human tumor cells, CD95

signaling-dependent cell death. Also has an entry that its anti-cancer activity attributed to its anti-cyclo-oxygenase activity[27].

Antiulcer activity:

Administration of *Cissus quandrangularis* extract (CQE) 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 histoarchitecture. Moreover, CQE significantly increased the 3H-thymidine incorporation and the levels of polyamines such as putrescine, spermine and spermidine in ulcerated rats. In addition, the extract offers gastroprotection in the ulcerated area by increased expression of TGF-a and also reversed the changes in the gastric mucosa of ulcerated rats with significant elevation in mitochondrial tricarboxylic acid (TCA) cycle enzymes and PCNA levels. Based on these results, the healing effect of CQE on AA induced gastric mucosal injury in rats may be confirmed[28].

Analgesic activity:

The analgesic effect of the drug as observed by Cissus quadrangularis exhibited significant analgesic activity compared to that of Aspirin when tested using Haffner's clip and Eddy's hot plate methods. The extract was found to be effective by both oral and i.p. routes significantly ($P<0.001$) and reaction time was found to be increased by both methods. The duration of analgesic activity was from 2 to 4 hr and optimum effect was observed at 1/20th-1/10th of LD50 dose. The extract compared well with Acetylsalicylic acid [29]. The analgesic effect of this plant when used in bone fractures may be of great value in relief of pain which is a constant feature in these cases[30].

Anti-obesity activity :

Obesity and obesity-related complications (such as metabolic syndrome) are a common problem around the globe. To investigate the usefulness of Cissus quadrangularis in metabolic syndrome, particularly for weight loss and central obesity a randomized, double-blind, placebo-controlled study was performed, 123 overweight and obese persons were treated with Cissus for eight weeks, while consuming a normal or calorie-controlled diet. At the end of the trial period, significant net reductions in weight and central obesity, as well as in fasting blood glucose, total cholesterol, LDL-cholesterol, triglycerides, and C-reactive protein levels. These results suggest that Cissus may be useful in the management of weight loss and metabolic syndrome[31].

Antipyretic activity :

The various serial extract of the *Cissus quadrangularis* when orally administred in albino rats showed a reduction ($p\leq0.01$) in hyperpyrexia induced by dried yeast injection with activity being pronounced in 18 hrs. This shows the antipyretic activity of *Cissus quadrangularis*[32].

Bone fracture healing activity:

Cissus quadrangularis is commonly known as the "Bone Setter," the plant is referred to as "Hadjod" in Hindi because of its ability to join bones. A bioactive steroid is believed to be the main constituent in *Cissus quadrangularis*. Studies on fracture healing suggest that the steroid may act on estrogenic receptors of the bone. 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 [7,9]. Cissus 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, possibly due to its high vitamin C content[34].

CONCLUSION

The present study shows the pharmacological properties of various bioactive compounds present in the plant. The whole plant is used in India for the treatment of various diseases. Ayurveda mentions it as a tonic and analgesic, and prescribes its use to help heal broken bones, thus its name *asthisamharaka* . It is used in the treatment of osteoporosis, asthma, cough, hemorrhoids, and gonorrhea. Cissus may be useful not only in building up bones but in improving functional efficiency. Cissus quadrangularis is rich in vitamin C and beta-carotene. The extract also neutralize the antianabolic effect of cortisone in healing of fractures, possibly due to its high vitamin C content. The antioxidant potential of the extracts can be assessed by employing different in vitro assays. Cissus quadrancularis possesses various phytochemical and pharmacological properties as discussed in present paper. However more Clinical and Pathological studies should be conducted to investigate the active potentials of bioactive compounds present in this plant.

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