

Cissus quadrangularis: A medicinal plant with diverse pharmacological activity

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ABSTRACT

Cissus quadrangularis, commonly known as hadjod, is a plant native to Tropical Asia and much of Africa which have been known for years to show medicinal properties. This medicinal plant can attain a height to about 4.9ft that can grow on any type of soil (ranging from light to heavy soil) and can survive in wide range of temperature and pH. Cissus quadrangularis has a wide range of pharmacological application in bone fracture healing, tissue repair, osteoporosis prevention, weight loss, blood sugar regulation, digestive disorder, menstrual irregularity, cholesterol and triglyceride lowering, anti-microbial, analgesic, vitamin C supplement, anti-oxidant, anti-cancerous, anti-pyretic, anti-inflammatory, joint health, muscle mass increase and wound healing. The extracts of methanol, ethyl acetate, ethanol and water were taken in different experiments to record the activity of the plant for different disease and it could be used for the treatment of all these diseases.

Keywords: Cissus quadrangularis, pharmacological application, plant extracts, treatment, anti-cancerous

I. INTRODUCTION

Cissus quadrangularis Linn. is an indigenous medicinal plant of India which belongs to the Vitaceae family. In Sanskrit, it is known as asthisanghara, which means "the plant will strengthen the bone". There are other common names for the plants, such as, Veldt grape, Devil's backbone, adamant creeper, hadjod and pirandai. Cissus quadrangularis (CQ) is a native plant of Arabia, Tropical Asia and parts of Africa. This tendril-climbing shrub can go up to a height of 1.5m (4.9ft) which have a fleshy and stout quadrangular sectioned branches with internodes of length of 8-10cm and width of 1.2-1.5cm, which make up the most of the plant. It has toothed trilobe leaves which are at 2-5cm at nodes and constitutes around 5-8% of the aerial parts of the plants. There are many people in the parts of the World where they consume the young leaves and tendril shoots

[1]. The raceme of this plant is small, having white, yellow or green flowers and sometimes also carries globular red colour berries.

C. quadrangularis has a divergent tolerance for the environmental conditions around it. It can grow in well drained sandy soil, loamy soil as well as clayey soil. It has also shown its growth in nutritionally poor soil of acidic, alkaline and neutral pH. The plant did not show growth in shade but showed in draught prone soil. There are primitive uses of this plants in Thailand, where the stems and leaves are exploited to treat scurvy, dyspepsia and haemorrhoids. There are several other very common applications, which are common in India, Africa and Sri Lanka, like bone fracture treatment, skin infection treatment and weight control by hadjod.

Like other medicinal plants, there are various phytochemicals present in hadjod that serve as an important feature for the treatment of diseases. The major constituents are Carotene A, Ascorbic acid, Ketosteroid, Triterpenoids, β -sitosterol and Calcium. Other phytochemicals includes calcium oxalate, flavonoids, resveratrol, phytosterols, pallidol, δ -amyryn, piceatanmol, δ -amyron, parthenocissine and water soluble glycosides [2]. The pharmacological properties of this plant, comes from these components which have the potential to act as anti-inflammatory, anti-hemorrhoid, analgesic, anti-ulcer, bone fracture healing, androgenic, gastro-protective and anabolic agent [3]. Cissus quadrangularis, is also used as a potent agent to lower cholesterol, triglyceride levels and blood glucose levels.

Though Cissus is used widely in Ayurveda and complementary medications but the safety, effects and its efficiency still remains unclear, due to lack of systemic review and meta-analysis. There are various studies that are carried out on Cissus in a well-controlled manner with humans is limited, but a greater number of studies has been executed in animal and cell culture system. There are quite a few applications that have been submitted by many researchers in recent years

on *Cissus quadrangularis* (either single or combined with other constituents). The major studies were conducted in the treatment of obesity, diabetes, osteoporosis and bone fracture [4].

Cissus quadrangularis

Cissus quadrangularis is commonly known as devil's backbone, veldt grape, pirandai, asthisamhara and hadjod. This plant is native to Arabia, Tropical Asia and much of Africa. It is a perennial type of plant that belongs to the grape family [5].

Kingdom	Plantae
Class	Tracheophytes
Order	Vilales
Family	Vitaceae
Genus	Cissus
Species	<i>C. quadrangularis</i>

Table 1 *Cissus quadrangularis* classification

Hadjod attains a height of 1.5m (4.9ft) and has branches of quadrangular-sectioned with 8-10 cm long internodes with 1.2-1.5cm width. Every angle of each internode has a leathery edge. The trilobe is toothed with 2-5cm wide leaves that appear on the nodes. The nodes has tendril that emerge from its opposite sides. It carries small, white or yellowish or greenish flowers and the globular berries turn out red when ripe enough. Hadjod is also classified as an evergreen climber that grow to 5m by 5m at a very high pace. The soil that is suitable for best growth of this plant is sandy (light), loamy (medium) and clayey (heavy), well-drained soil is preferred and can also survive in very alkaline soil. The pH that is suitable for its growth could be acid, neutral or alkaline but also has the potential to survive in very acid and very alkaline soils. This plant cannot grow in shade and prefers dry or moist soil primarily and has the potential to tolerate drought.



Figure 1 *Cissus quadrangularis*

Pharmacological activity Reported

Joint Pain Reduction and Anti-inflammation

Inflammation and joint pain are mostly caused by the strenuous, high volume exercise [6,7], particularly in the case of people involved in exercises like running, powerlifting and bodybuilding [8,9]. Inflammation is the main cause of the joint pain as it produces interleukin-1 β and TNF- α . These two cytokines also promote the process of cartilage degradation and chondrocyte apoptosis which accelerates osteoarthritis. During all these years, there are various isolated ingredients and nutritional supplements have been observed to lessen the joint pain. In recent years, Aspirin is used which is a potent Nonsteroidal anti-inflammatory drug (NSAID) for the treatment of rheumatoid arthritis and related diseases [10], but it eventually lead to ulcer, which remains a major clinical problem and could be solved by the alternative use of CQ extracts.

Cissus quadrangularis has many active chemical compounds which may have the activity against it, mainly the ethanol, polyphenols and triterpenoids. Jainu et al., pre-treated the aspirin-induced gastric ulcer affected rats with *Cissus quadrangularis* and observed the inhibition in enhancement in the interleukin-1 β and TNF- α (plasma tumor necrosis factor) [11]. They hypothesised that the inhibition of these two is due to the triterpenoids and polyphenols and the ethanol extract inhibits the production of cytokines and accumulates the neutrophils.

In recent studies of Panthong et al., edema formation in rats in both the ears, induced by Ethyl-phenylpropionate and paws, induced by carrageenan with arachidonic acid, were inhibited by the CQ extracts by down regulating the metabolism [12]. The results shown by CQ for EPP induced edema in ears were quite promising, as it showed 70% inhibition after 15min application upto 62% inhibition after 120 minutes. The result for edema induced by carrageenan and arachidonic acid showed inhibition ranging from 72% in 15min to 49% in 120 minutes.

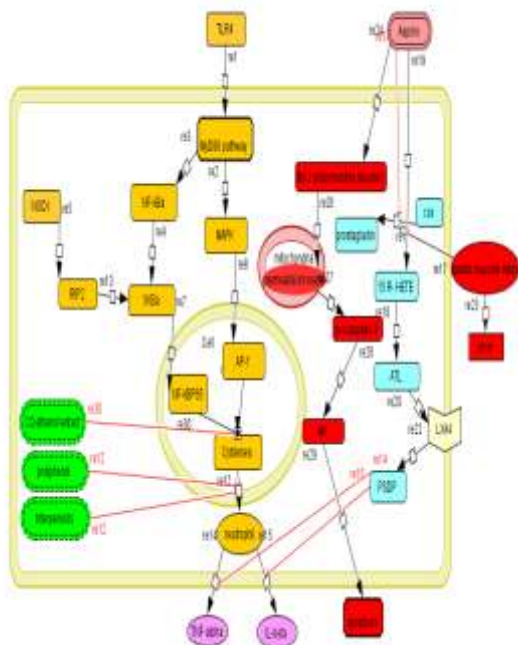


Figure 2 Molecular pathway of medicinal effect of *C. quadrangularis* and synthetic drugs 29 men (20- 46years) with strenuous exercise routine who experienced joint pain were given CQ-800, 4 times a day as capsules for 8 weeks. After the full course, it was observed that nobody had lethal side effects, blood pressure and heart rate was normal, overall pain was 33% less and overall stiffness was 23% less along with no change in CBC and decrease in exercise related pain and inflammation. The cartilage damage was also controlled due to inactivation of IL-1 but limitation was present due to the less number of subjects [13].

Fracture healing

Bone fracture healing is a time taking process, generally takes months or years that causes distress the patient as well as the surgeon. This long duration of healing results in economic loss and suffering to the patient and so faster healing is important for the fractures, especially of jaws and other delicate parts of the body. The study conducted by Shadab Mohammad et al. showed very promising results of faster bone fracture healing by the oral administration of extract of *Cissus quadrangularis*[14]. According to the study of Udupa and Prasad, the bones surrounded by thick muscles showed better results than the ones with thin muscle which contradicted the results of mandibular fracture, observed by Shadab

Mohammad [15]. When the tensile strength of the bones treated by the ethanol extract of *Cissus quadrangularis* were observed, it showed the maximum of all the others plants considered. In the fetal femur, the enhancement of development of the cortical bone showed quick mineralisation and early regeneration of the fractured bone, which is related to the rich content of the phytoestrogenic steroids, calcium and phosphorous [16].

Anti-osteoporotic

The decreased bone mineral density (BMD) causes osteoporosis which increases the fracture risk due to low bone mass. Osteoporosis is majorly an age-related issue that causes troubles in elders, especially in women after menopause, by decreasing mobility and increasing mortality. This disease with postmenopausal effects is often categorised under epidemic due to the limited choice for treatment. The hormone replacement therapy, which came out as an option to cure this but later discontinued as it showed side effects related to cardio-vascular system of body [17]. There are similar drawbacks for all approved therapies for osteoporosis which are all anti-resorptive. Agents which enhance the osteoblast functions are required for the bone formation stimulation.

Natural products which have shown positive results against osteoporosis, majorly belong to phytoestrogens; like lignins, coumestans, isoflavones and flavonoids, which exhibit estrogen like effects on various body tissues [18]. Plant derived chemical molecules are favoured over synthetic molecules due to the lesser amount of side effects and long term safety.

In an experiment performed by Manmeet Kumar and colleagues in 2010, along with many herbal plants, *Cissus quadrangularis* stem was taken and dried in shadow and later its ethanol extract was taken for the further analysis [19] and it was observed by spectrophotometric study that it stimulated the Alkaline Phosphatase activity around 1000 times more as compared to diadazine [20]. The osteogenic activities of the few isolated pure compounds of *Cissus quadrangularis* were acting positively as anti-osteoporotic by increasing the osteoblast mineralisation as assessed by the extraction of alizarin. The compounds showing positive effect for the anti-osteoporotic were extracted are mentioned in Table1.

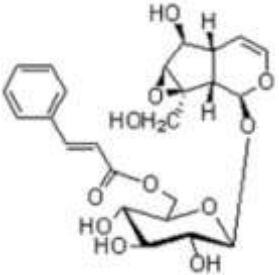
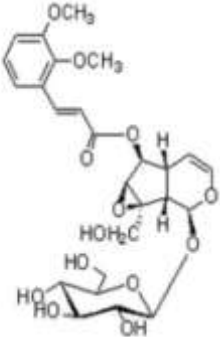
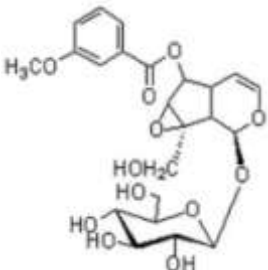
<p>6-O-trans-cinnamoyl-catalpol</p>	
<p>6-O-[2,3-dimethoxy]-t-cinnamoyl-catalpol</p>	
<p>6-O-m-methoxybenzoyl catalpol</p>	

Figure 3 Compounds of CQ showing positive effects on anti-osteoporosis [21]

Among Asian women, a lower prevalence of hip fracture was observed when their diets were made high in phytoestrogens [22]. The pure compounds isolated from *Cissus quadrangularis* has osteogenic activities with varying potency of the increasing ALP activity. The compounds isolated from the plant showed osteoblast mineralisation lead to promising use of these compounds in treatment of menopausal osteoporosis [19].

Control weight and obesity problem

The problem of obesity has become one of the most common cause behind the increased risk of strokes, diabetes, heart diseases and many forms

of cancer. The most common remedies for weight related issues are control of calorie intake and expenditure of it by exercise, but this attempt most of the time end in failure. There are many plant-derived substances which have reportedly assisted with weight management and loss but do not show promising long lasting effect. The non-stimulant and stimulant ingredients exist naturally, where the non CNS stimulation causing enhanced thermogenesis along with adverse effects on cardiovascular system like increase in blood pressure and heart rate. The extracts as well as isolated flavonoids and carotenoids of hadjod if consumed in combination with thermogenic agents have showed promising results in increasing the energy metabolism without any adverse effects [4]. The energy metabolism enhancement resulted in better sports performance, weight loss and management. Exercise when combined with intake of the extract resulted in higher thermogenesis than in sole intake. The cellular protein synthesis is stimulated by physical activity which could lead to increase in muscular mass and energy expenditure. The botanical product of non-stimulant nature showing thermogenic mechanisms could have a great potential in weigh management.

Anti-arthritis

Joint swelling, premature mortality, systemic complication and destruction of synovial joints are the characteristic feature of rheumatoid arthritis (RA). Genotype and environmental factors interaction is involved in rheumatoid arthritis [23]. Patients suffering from Rheumatoid arthritis have various macrophages present in the synovium like TNF- α , IL-6, IF-1 β which are directly incriminated in responses immunity in pathogenesis of RA [24]. The first line drugs for ceasing the progression of disease includes biochemicals that inhibit the cytokine responses [25]. *Cissus quadrangularis* effect against bone disorders and inflammation have been reported. When orally administered, the extract of hadjod inhibited joint swelling but was dose dependent in both induced and adjuvant arthritis. It also decreased the serum TNF- α level, synovial expression of inflammatory, angiogenesis marker, and also oxidative stress. Thus, indicating the potential of the extracts of hadjod for rheumatoid arthritis treatment.

Anti-diabetic

The altered metabolism of carbohydrates, protein and lipids along with hyperglycemia are the characteristics, indicating the onset of Diabetes

mellitus [26]. This untreatable disease has a complex etiology that works with equal participation of the lifestyle and genetic factors [27]. The therapeutic options that are available for the treatment for diabetes, have many limitations along with side effects. This makes the discovery of treatment of diabetes from plant based materials more necessary and important. The extracts of *Cissus quadrangularis* has free radical scavenging and hypoglycemic property [11, 28]. The extracts of CQ have been observed to show potent response against high cholesterol, triglyceride and blood glucose levels, accompanied by body weight reduction [4].

Streptozotocin is a natural alkyl chemical, which has an anti-neoplastic characteristic that is toxic to mammalian insulin producing beta cells particularly. In a study conducted by RK Lekshmi on Streptozotocin-induced diabetic rats, it was observed that the ethyl acetate fraction of the *Cissus quadrangularis* stem has potential against hyperglycemia in those rats [29]. The doses at which this activity was observed to be 100 and 200 mg/kg. The glucose utilisation enhancement, limiting glucogenic formation, and impaired liver glycolysis correction are the ways by which *Cissus quadrangularis* show ameliorative effect on hyperglycemia. The chemical compounds characterised by the Gas chromatography and mass spectrometry techniques showed presence of phenols, acetophenons, aliphatic and carbonyl compounds, fatty alcohols. N-methyl-1-adamantane acetamide was one of the main compounds of hadjod showing anti hyperglycemic effect. The supplementation of stem of hadjod in everyday diet has the potential to manage diabetes mellitus.

Analgesic and Anti-inflammatory

In a study conducted by A Pathong in 2007, a rat was induced by EPP that resulted in edema that became a model for all investigation and screening of activity of inflammation of all test substances [12]. The mediators of inflammation that released in this model were serotonin, histamine, PGs and bradykinin. The mediators involved in this showed potential to promote vascular permeability and vasodilation [30]. When CQ was tested, it showed potential inhibitory effect on the edema formation in ear of the rat induced by EPP. The study suggested that CQ has probably anti-edematous action on the mediators of inflammation that has the potential to treat acute inflammation. The crude extract of CQ showed the

anti-inflammatory effect due to the types of flavonoids like beta-sitosterol, luteolin acting as hesperidin and diosmin. The combination of these two drugs are used to treat along with reducing pain to certain level in inflammation related diseases like haemorrhoid. Thus, *Cissus quadrangularis* has the potential to be used as anti-hemorrhoidal drug.

Anti-ulcer

Nonsteroidal Anti-inflammatory (NSAID) is the category of the drugs that include aspirin, widely used for the treatment of rheumatoid arthritis and other related diseases. Ulcer is a major clinical problem associated with use of NSAID. Aspirin causes inflammation followed by ulcer by inducing the gastric damage leading to multistage pathogenetic event. Ulcer leads to mucosal injury that is followed by the epithelial cell apoptosis, up regulation in nitric oxide synthase (NOS) and induction of TNF factor and Interleukin-1 beta, triggering the activation of Nuclear factor [31]. The modern antiulcer drugs are associated with severe side effects and show very limited efficiency against gastric diseases [32]. Thus, drugs with parameter attenuation of inflammation that can afford protection against free radical production is needed. Phytomedicines are considered to be the new generation of medicines. The stem of *Cissus quadrangularis* is widely used to treat ulcers and other treatments of fractures, tumors or scurvy [33]. The stem part includes phytochemicals like triterpenes including beta-amyrins, ketosteroid, vitamin C and beta-sitosterol [34] that showed has been observed to show potential against the damage of stomach caused by aggressors in many animal models [35,36].

Future aspects

Hadjod is native to Arabia, Tropical Asia and Africa. It is a perennial type of plant that belongs to the grape family. There are various studies that are carried out on *Cissus* in a well-controlled manner with humans is limited, but a greater number of studies has been executed in animal and cell culture system. There are quite a few applications that have been submitted by many researchers in recent years on *Cissus quadrangularis* that could be applied in the practical life to treat diseases more organically and lesser side effects when compared to the chemical drugs taken by humans.

II. CONCLUSION

Cissus quadrangularis is perennial by nature and can grow upto several meters in a small duration of time. It has the potential to grow in variety of soil as well as variety of pH. *Cissus* is commonly known as hadjod and could be treated as potential medicine source to treat various diseases along with maintaining healthy body of the humans. This plant has its own benefits in regulating weight, glucose levels in blood, cholesterol level and has also shown great results in dealing with ulcers and along with bone related human body problems like osteoarthritis, healing the bone fracture at a faster pace or reduction in joint pain. This plant has the potential to become a source of medicine to treat all these diseases without severe side effects.

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