



A review on *Cissus quadrangularis* L. as herbal medicine

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Received 21 February 2020; Revised 08 May 2020

Cissus quadrangularis L. is a fleshy plant found in major parts of the world, especially in Asia, Africa, and a few other warm tropical regions. It is one of the common food items in India. Ayurveda uses the whole plant for digestive aid (Pachana) and directed as palliative and roborant. *C. quadrangularis* also serves as a good source of triterpenoids ascorbic acid, carotenoids, flavonoids, and steroids. *C. quadrangularis* is also used for various treatments like fracture healing, anti-ulcer, antihelmintic, antifungal, antihemorrhoidal, analgesic, antibacterial properties, etc. It also serves in the best way to treat various infirmities such as hemorrhoids, leprosy, epilepsy, dyspepsia, skin burns, dysentery, bowel complaints, to increase appetite, etc. This article throws light on various recent knowledge of scientific research in various aspects of this plant, which mainly incorporate remarkable pharmacological activities such as anti-ulcer, anti-bacterial, anxiolytic, antipyretic, antidiabetic, bone healing, antioxidant and anti-inflammatory properties, and phytochemicals studies.

Keywords: Antimicrobial, Antioxidant, Antiulcer, Bone healing, *Cissus quadrangularis*, Phytochemical composition.

IPC code; Int. cl. (2015.01)- A61K 36/00, A61K 36/87

Introduction

Plants play a key role in the industry of drug discovery and the pharmaceutical industries are greatly dependent on natural products for the development of new drugs¹. WHO report reveals 80% world's population uses folk medicine for their chief health care². Clinical microbiologists have great delight in evaluating the medicinal plants for new drugs^{3,4}. India is blessed with great knowledge through legacy and heritage in the field of health care such as Siddha, Homeopathy, Unani and Ayurveda^{5,6}. In India, indigenous systems of medicine utilize Medicinal plants as the vital source and such plants have traditionally taken up a prominent position in the lives of tribal people in spiritual, medicinal and cultural activities⁷. *Cissus quadrangularis* L. (CQ) serves as a common food source in India⁸. The perennial plant CQ is well known as *Vitis quadrangularis*. The scientific nomenclature of CQ is as follows: Kingdom: Plantae; Subkingdom: Tracheobionta; Superdivision: Spermatophyta; Division: Magnoliophyta; Class: Magnoliopsida; Subclass: Rosidae; Order: Rhamnales; Family: Vitaceae; Genus: *Cissus* L.; Species: *quadrangularis*. The vernacular names of CQ are as follows: Tamil:

Piranti, Vajjavalli; Malayalam: Cannalamparanta, Peranta; Hindi: Cannalamparanta, Peranta; Bengali: Har, Harbhanga, Hasjora, Horjora; Marathi: Harjora, Hadsankal, Kandavel; Telugu: Nalleru, Nelleratiga, Vajravalli; Oriya: Hadavhanga; Urdu: Horjora, Harsankar; Gujarati: Chodhari, Hadsand, Hadsankal; Kanada: Mangarahalli. The plant comprises simple or reniform, serrate ± 5 cm wide leaf and four-angled stem connected at nodes, internodes which are up to 10 cm long, and dichotomously branched^{9,10}. It is extensively utilized in producing traditional medicines in India. It helps to decrease pain and bone brawny, because of its bone healing/joining ability, which is referred to as "*Hadjod*"^{11,12}. Toxicological studies on CQ reveals that there is no toxic effect in its extract¹³. Overall plant body assists in oral rehydration¹⁴. It is an abundant source of beta carotene and vitamin C¹⁵. Nanoparticles synthesized of CQ are studied for anti-cancer activity¹⁶. The CQ extract is proven as antiviral, free radical scavenger, antibacterial, anti-inflammatory, antioxidant and the mixture of sesame oil and CQ stem extract used to treat wheezing and skin issues¹⁷. CQ can reduce the body weight, serum lipid and serum glucose level^{18,19}. The chemical components of this plant have been reported to contain phytoosterols, keto-steroids, Indane and flavonoids which exhibit magnificent anti-oxidant properties^{13,20}.

It also plays a vital role in the healing of bone fissure and osteoporosis²¹. Traditionally this plant has

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different medicinal uses in leucorrhoea, piles, gout, tumours and peptic ulcers¹¹. It is also utilized for the production of biochar and hydrocarbonaceous bio-oil²². Scientific experiments reveal that (CQ) is used in bodybuilding as an augment²³.

Phytochemical studies

The screening of Phytochemicals leads to revealing the existence of alkaloids, steroids, tannins, saponins, phytoestrogen steroids, cardio glycosides and terpenoids. Flavanoids from CQ possess anti-microbial, anti-inflammatory, anti-diarrheal and anti-cancer properties²⁴⁻²⁶. Terpenoids are known to be used as anti-tumour drugs, it targets the lipoxygenase, phospholipases, and cyclooxygenase, and also plays a prominent part as anti-inflammatory agent²⁷. Various studies of Stilbenes reveal that they are anti-cancer, anti-inflammatory, an oestrogen receptor α agonist and efficient to stimulate apoptosis²⁸. In-plant to fulfil the fundamental requirements, primary metabolites are produced and self-defence is mainly because of the production of secondary phytometabolites⁹. The plant is rich in calcium, potassium, iron, copper, cadmium, calcium oxalate, zinc, lead, phenols, vitamins, carotenes, vitamins and other compounds²⁹. List of phytochemicals reported from CQ as mentioned in Fig.1. Quantitative analysis of basic elements and quantitative measurement of bioactive phytochemical components of CQ is tabulated in Table 1³⁰.

Chemical constituents in the stem

The stem extract of CQ has calcium ions (4 percentage by weight) and phosphorous. It also contains Calcium oxalate, 3-1-methyl tritriacontanoic acid, taraxerol acetate, taraxerol and isopentadecanoic acid¹. Phytochemical studies reveal the

presence of alpha and β -amyrins, β -sitosterol, ketosterol, phenols, saponins, tannins, vitamin, carotene, as shown in Fig. 1^{31,32}.

Chemical constituents in the leaves

The phytochemical studies of CQ leaves reveal the existence of parthenocissus, resveratrol, piceatannol, pallidol, alicyclic lipids, and other compounds shown in Fig. 1^{1,33}.

Chemical constituents in the ash of the plant

Ash of the plant shows the occurrence of Sodium, potassium, calcium, potassium tartrate and magnesium, as tabulated in Table 1³⁴.

Chemical constituents in the root

Phytochemical analysis Root reveals the presence of lead, iron, potassium, zinc, calcium, sodium, cadmium, copper and magnesium^{1,30}.

Other constituents

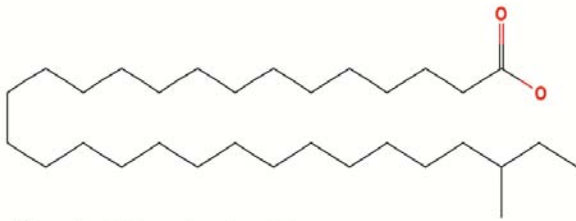
The aerial part of the plant shows the presence of 7-Oxo-Onocer-8-ene-3 β 21 α diol³⁵. The plant holds ascorbic acid of 479 mg and carotene of 267 mg per 100 g crisply made a paste³⁰. Additionally, the following compounds have also been found and reported such as perthenocissine, taraxeryl acetate, taraxerol, isopentacosanoic acid, friedelan-3-one, resveratrol, piceatannol, pallidol, phytosterols, two steroidal principles (C27H45O melting point 249-252 °C and C23H41O melting point 136-138 °C)^{30,36}, δ amyryl, δ amyryl, and 7-oxo-onocer-8-ene-3 β 21 α diol (C30H50O3) have been found³⁶. Ascorbic acid, two asymmetrical tetracyclic triterpenoid, triterpene, β -sitosterol, ketosteroid also has a high amount of anabolic steroidal substances, Calcium and Carotene A³⁰. quantitative HPTLC and HPLC methods determines the presence of asymmetric tetracyclic triterpenoids such as like 4'-tetra hydroxy biphenyl; d-amyryl; 21b-diol; d- amyryl; onocer-7-ene-3a; & 3,3',4, 3,3',4, 4'- tetrahydroxybiphenyl³⁶.

Cellulosic fibre extraction

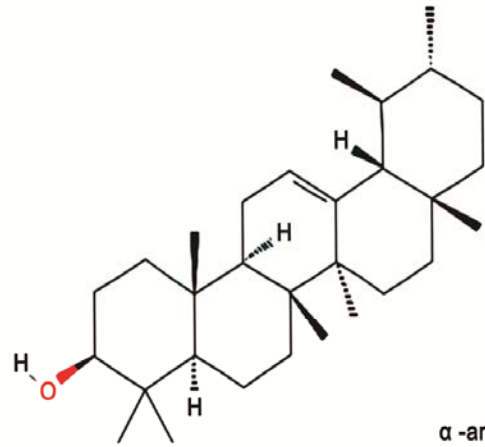
The energy-efficient technologies in aero and automotive industries are mainly contributed by polymer composite. As an alternative for artificial fibre which is carcinogenic and cost-effective in polymer composite natural cellulosic fibre from CQ is a great retrofit. Because of its cellulose - 82.73% and wax 0.18% gives copious specific strength and high bonding properties in composite

Table 1 — Quantitative composition of *C. quadrangularis*³⁰

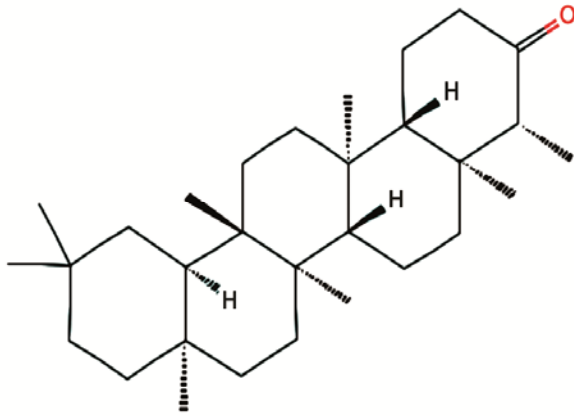
Elements	mg/100 g dry matter	Toxicants	mg/100 g of dry matter
Potassium	67.5	Oxalate	135
Calcium	39.5	Tannin	0.3
Zinc	3.0	Phytate	20
Sodium	22.5	Saponin	0.16
Iron	7.5		
Lead	3.5		
Cadmium	39.5		
Copper	0.5		
Magnesium	1.15		



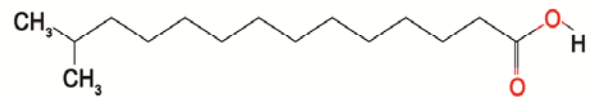
31 methyl triacontanoic acid



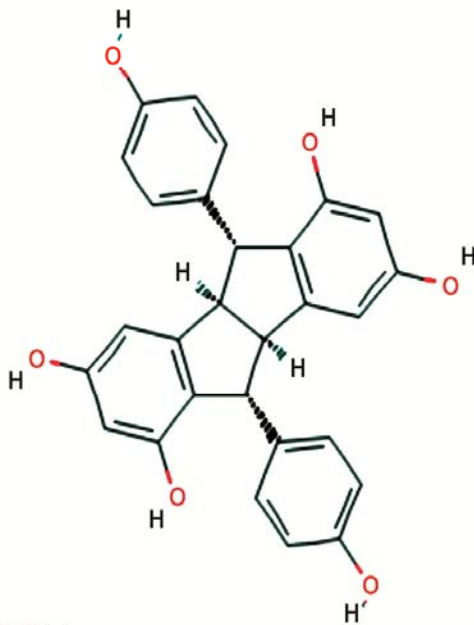
α -amyrin



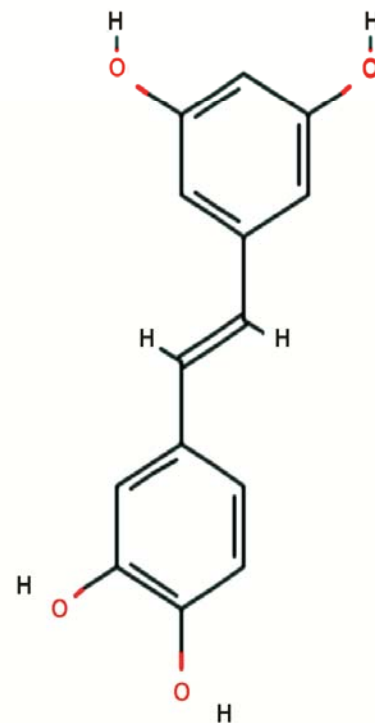
Friedelan-3-one



Iso-pentadecanoic acid



Pallidol



Piceatannol

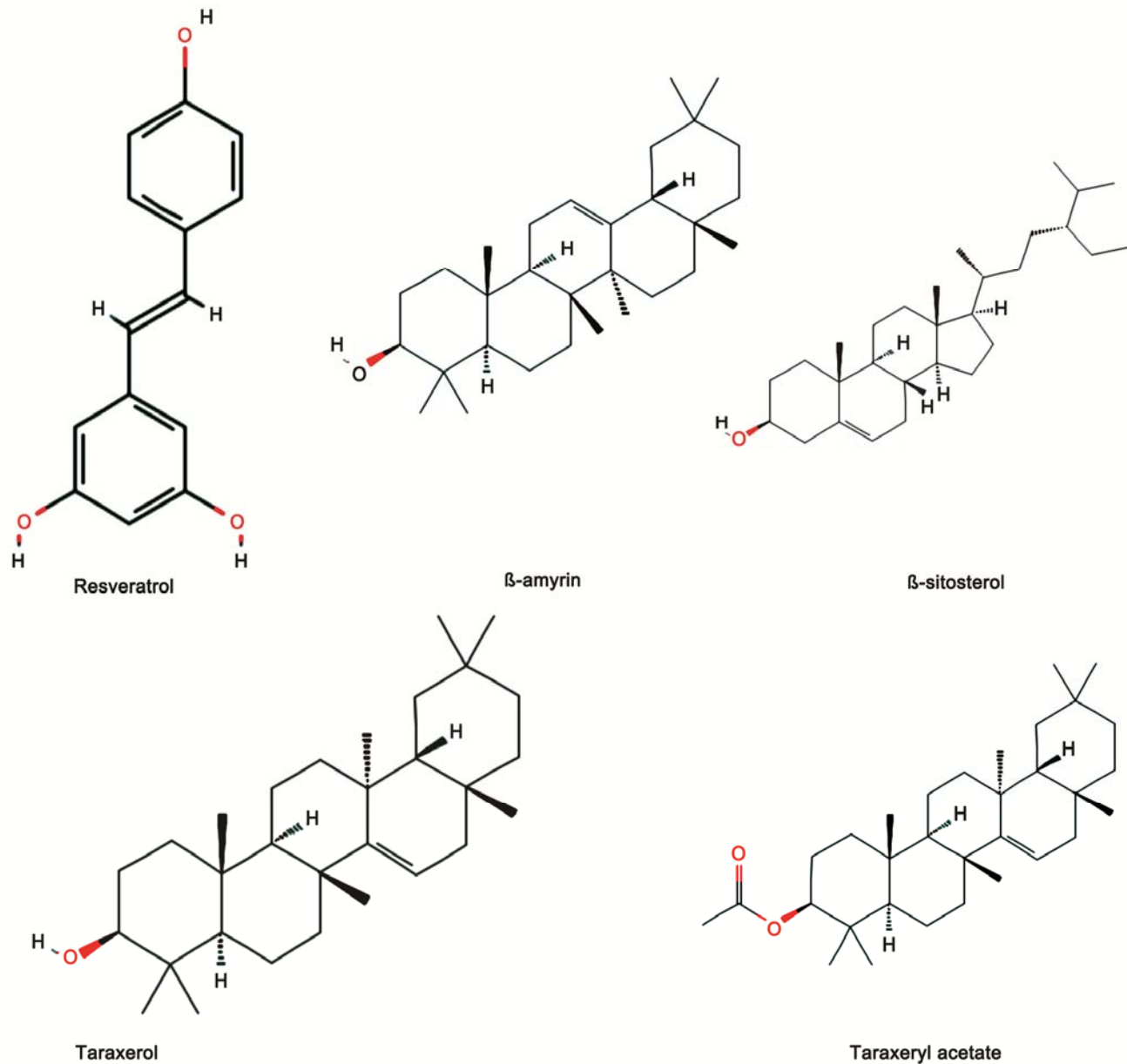


Fig. 1 — List of phytochemicals reported from *Cissus quadrangularis*

manufacturing and it shows lower density than carbon fibre, glass fibre, etc³⁷. It has thermal stability until 270 °C as it can withstand polymerization temperature.

Relationship of CQ with hormones

Testosterone

CQ can act as glucocorticoid antagonist it has been estimated to have androgenic activity⁹. Testosterone is a primary sex hormone and anabolic steroid which is vitally produced by the testes. It mainly responsible for male reproductive physiology and its development

and in addition to this, it plays a prominent role in regulating male behaviour.

Estrogen

CQ extract has an oestrogenic property by higher the blood oestrogen than acting on oestrogen receptors directly³⁸. Estrogen is a primary female sex organ and it plays a major role in the regulation and development of the female reproductive system. Experimental studies using estrogen deficiency rat models reveals that, in ovariectomized rats, 70% ethanolic extract (friedelin content-2.5%) is given as

an oral supplement which reveals that there is a statistical increase in estrogen concerning the ovariectomized control by 232% (100 mg/kg) and 94% (75 mg/kg). But this is lesser when compared with the reference drug 17 β -estradiol injections (568%), despite this difference, both were equivalent in protecting bone integrity³⁸.

Cortisol-C

CQ decreases the catabolic effect by restraining the receptor which reveals the important role of a glucocorticoid antagonist³⁹. Cortisol is a steroid hormone and it belongs to the class of glucocorticoid. It is a catabolic hormone that is secreted by the adrenal cortex as a response to various physical and psychological stresses.

Pharmacological activities

Anti-ulcer activity

An ulcer is any disturbance in the biological membrane that acts as an obstacle for organ function to which that membrane belongs. CQ extract has a prominent activity towards peptic ulcer⁴⁰. Methanol extract shows great antiulcer activity which is evidenced by an experimentally persuaded ulcer in a rat model by improving glycoprotein level and reducing gastric secretions and through an anti-oxidative mechanism, it produces healing out-turn on aspirin persuade gastric mucosal destruction in rats⁴¹. Gastric juice and mucosal studies disclose that *Cissus* at a dose of 500 mg/kg given for ten days notably rises the mucosal defensive factors like mucin production, mucosal cell multiplication and life span of cells and the gastric damage is prevented by β -sitosterol and Triterpenoids³⁰. It has high potency for the healing of peptic ulcer^{42,43}.

Antibacterial activity

The stem and root of the CQ show significant antimicrobial activity⁴⁴. Antiprotozoal activity is seen in alcoholic extracts of aerial parts of the CQ against *Entamoeba histolytica* and also against *E.coli*^{4,45}. These are mainly reported against *S. mutans*, *Salmonella typhi*, *Bacillus subtilis*, *L. acidophilus*, *Streptococcus pyogenes*, *Escherichia coli*, *Proteus mirabilis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*¹⁴. The extracts of dichloromethane and (90%) methanol of the stem shows antibacterial activity against *E. coli* and *P. aeruginosa*. It shows the mutagenicity averse *Salmonella microsoma*. In alcoholic extracts, the aerial part shows antiprotozoal activity averse against *E. histolytica*⁴¹. The plant-

mediated CaO nanoparticles reveal great inhibition on *E. coli* growth⁴⁶. Antibacterial nature against *Helicobacter pylori* is reported in the water extract of CQ³⁴. The aqueous extract of CQ proclaims antifungal and antibacterial activity against *Mucor sp.* and *Pseudomonas aeruginosa*⁴⁷. An experiment reveals that the ethyl acetate extract, ethanol and methanol extract of CQ possess high activity against *Klebsiella pneumoniae* bacteria and the zone of inhibition is 22, 11 and 10 mm respectively⁷. CQ reveals a great antibacterial tendency against cariogenic microorganisms¹⁴. The extracts of ethyl acetate and chloroform not producing significant results against *Penicillium sp* and *Proteus mirabilis*⁴⁷. The Gram-positive bacteria such as *Staphylococcus aureus*, *B. subtilis*, *Streptococcus* species and *B. cereus* were comparatively highly susceptible than the Gram-negative bacteria *E. coli* and *P. aeruginosa* which shows high resistance against the CQ extract⁴⁴.

Anxiolytic, antipyretic and antidiabetic properties

Status epilepticus is the preliminary manifestation of epilepsy. In animal (mice) model of epilepsy, the Aqueous extract of CQ reveals anticonvulsant, anxiolytic properties and it reduces the timing of and it multiplies pre and post-status epilepticus latency⁴⁸. On yeast induced hyperthermia in rats, CQ minimalizes fever at heavy doses within two hours which reveals its Antipyretic activity⁴⁹. The rhizome extract of CQ reveals a more useful anti-diabetic modulating effect in Alloxan-induced diabetic rats on blood sugar levels⁵⁰.

Bone healing activity

Osteoporosis is because of the lowering of bone mineral density and it leads to alteration of protein in bone and fracture⁴⁰. *C. quadrangularis* acts by vitalizing metabolism and enhanced take-up of the minerals strontium, calcium and sulphur. At two various dose levels (500 and 750 milligram/kg) the whole plant's ethanol extract has antiosteoporotic action in the ovariectomized rat model of osteoporosis⁴¹. The paste obtained from CQ stem is used to wrap the fracture spot and the total time required for fracture healing, pain, swollenness seems to be reduced significantly^{51,52}. An experimental study in the rat by the systemic usage of *C. quadrangularis* leads to full mending of normal make-up of bone, after fracture in 4 weeks on the other hand controls needed 6 weeks. This shows shortening by 2 weeks in bone healing^{30,41}. Structure and biochemical properties

of the bones in rats are fully restored by petroleum ether and ethanol extract of CQ^{12,53,54}. It is also reported that in gravid rat the CQ extract prompts the growth of the fetal bone⁵⁵. In the fracture healing CQ act by increased uptake of strontium, calcium, sulfur by osteoblasts and its efficacy in early ossification is reported and compared to cellular response CQ shows high influence osteoblastic proliferation²⁹. The aqueous extract of CQ after intramuscular injection to dogs promoted their fracture healing³⁹. Researches proved that CQ has a great effect on the components of the IGF system of Human osteoblasts such as SaOS-2 cells⁵⁶. CQ has the principles of anabolic steroids which reveal the fracture healing rate by formerly revitalization the connective tissues which play a prominent role in faster mineralization of callus and healing⁵⁷.

Fracture healing tendency of *C. quadrangularis* is revealed by this clinical study comprising 16 patients. A paste of the *C. quadrangularis* was applied externally to patients with different types of fractures. Radiological inspection reveals that there is a significant reduction in the healing time compared to the control group. Clinically it is apparent that in only one case there is no considerable effect however, the upshot is appreciable and in some cases symptoms of fractures like agony swelling and tenderness were absent. This plant is proven to be helpful to the wounded bones. It was contemplated that, it promotes the earlier development of collagen fibres which gives rise to the formation of callus and earlier calcification²⁹. The summary of patient trials with the observed reduction in healing time is tabulated in Table 2.

Women health and osteoporosis

C. quadrangularis is prescribed in Ayurveda in the treatment of irregular menstruation and menstrual issues²⁹. Osteoporosis is a dreadful epidemic, which leads to low bone mass because it worsens the bone tissues. Nearly 2000 million of the world population suffered from osteoporosis in recent years. The major cause for osteoporosis is due to the absence of certain hormones, specifically in men it is an androgen and in women is estrogen. In women, post-menopausal-

osteoporosis is caused due to misbalance in the function of the osteoclasts and osteoblast cells. Lack of calcium level in the body leads to deterioration of bones. In women at the time of menopause, it is hard to maintain the level of the calcium due to decreased levels of hormones which significantly leads to mineral loss from the bones^{12,29}.

At the time of menopause, there is a loss of estrogen, this paves the way to osteoporosis in the Postmenopausal women. The treatment aims to cease or downgrade the mineral loss so that pain and bone fractures can be controlled. There are various chemical agents such as calcitonin, raloxifene, bisphosphonates, and droloxifene etc. that are attempted in the treatment of osteoporosis but resulted in misfires and lead to cause breast cancer, vaginal bleeding, thromboembolic events, and breast tenderness. *C. quadrangularis* shows recuperation in postmenopausal osteoporosis by enhancing bone mineral density and greatly inhibits antianabolic effects. Experimental studies are performed to find out the recovery for postmenopausal osteoporosis and the antianabolic effect using *C. quadrangularis*. For the ovariectomized rat model of osteoporosis, ethanol extracts of CQ were administered at two different dosages such as 500 and 750 mg/kg a day. For this experimental study albino rats were used. These rats were divided into 5 groups and each group consists of 6 rats. Except for the control group, all other groups are ovariectomized. The second group (ovariectomized control) were fed with an equal amount of saline. The groups, three to five, were orally administered with 5.4 mg/kg of Raloxifene and 750 mg/kg CQ ethanol extract. The histopathological, biochemical, and biomechanical parameters revealed that ethanol extract of CQ has significant Antiosteoporotic property in comparison to the control drug. These studies strongly suggest that the ethanol extract of CQ significantly plays role in women health and also greatly helps in reversing the effects of osteoporosis. Hence, it can be used in pharmaceutical applications of women health in general.

Antioxidant

Important phytochemicals such as carotenoids, steroids, calcium and the consumption of plant polyphenol antioxidants play a major role in oxidative stress-related pathologies^{29,58}. Antioxidants are the substances that rummage free radicals, they reveal a prominent role in the avoidance of free radical-

Table 2 — Study of bone healing using *C. quadrangularis* in patients

No. of cases	Reduction in the healing time (%)
6	40
8	53
1	7

induced illness by giving up hydrogen radicals to the primary radicals which get reduced to non-radical chemical compounds and then get changed to oxidized antioxidant radicals. Free radical scavenging property and anti-lipid peroxidative properties are revealed in CQ extract⁵⁹. The methanol extract of (CQS) reveals enormous antioxidant and free radical rummaging action *in vivo* and *in vitro* systems mainly because of the presence of β -carotene and also shows inhibition in lipid peroxide production in erythrocytes, and production of superoxide radicals and formation of DPPH free radicals^{29,41}. The presence of keto and photo steroids, indoles, flavonoids and which are efficient antioxidants¹³. Dry and fresh stem extract ethyl acetate reveals the antioxidant activity of 64.8% in the β -carotene linoleic acid system and 1, 1-diphenyl-2-picrylhydrazyl systems 61.6%⁶⁰.

Anti-inflammation

The anti-inflammatory effect of CQ could be due to the presence of flavonoids mainly by, Beta-sitosterol and by luteolin^{8,61}. Comparing to ibuprofen or aspirin CQ also possess anti-inflammatory property on a milligram per milligram basis. 'Laksha Gogglu' one of the essential additive in Ayurveda drug preparation which is also present in *C. quadrangularis* and possess the properties to reduction of swelling, relieving pain, curing the allied disorders related with fracture and enhance curing fractures^{43,62}. In the test of anti-inflammatory activity EPP-induced rat ear oedema formation model is used which is very useful for investigating the inflammatory activity and screening. There are several inflammatory mediators liberated in this model such as bradykinin, histamine, PGs and serotonin which are efficient in enhancing vascular permeability, support vasodilation and also producing oedema⁶³. Experiments prove that the CQ holdback effect on the ear oedema formation in EPP induced model⁶¹. CQ shows anti-inflammatory activity accompanying the hindrance of pro-inflammatory agents such as TNF α and iNOS⁵⁶.

Miscellaneous activity

The dry powder obtained from the shoot can relieve digestive issues and the decoction with *Piper nigrum* and *Zingiber Officinale* relieves body pain. Stem paste is useful for muscular torment, wounds, insect bites, burns and also shows great cardiotoxic features⁶⁴. It also shows the properties to cure skin ailment leprosy, convulsion, epilepsy and saddle sores of camel and horses^{30,48,65}. In the case of reducing and

weight and obesity, it plays a prominent role and the mixture of stem powder pulses fried with sesame oil used to cure many 'Vata' diseases⁶⁶⁻⁶⁸. Dichloromethane and acetone decoction of the plant consists of healing activity in opposite to cysteine protease. The extracts also reveal the androgenic property and cardiotoxic properties⁴¹. The stem fibre reveals thermomechanical properties for polymer composite reinforcement⁶⁹. In India, CQ is used in the treatment of piles¹³. African traditional medicine reveals its uses to cure indigestion, asthma, haemorrhoids, and anorexia⁴⁸ and in eastern Africa to treat gonorrhoea it is mixed up with tamarind⁹. Muscle relaxation in CNS depressant is seen in the aqueous extract⁷⁰. The water-soluble glycoside in the stem extract leads to create fall in BP in the anaesthetized cat³⁶. Fresh stem creates itching action on the skin which is due to the presence of 31 methyl tritriacontanoic acid along with, taraxerol, isopentacosanoic acid taraxerol acetate and calcium oxalate³⁰. A recent study reveals that the plant extract when acted with carbon dioxide, conduct to the emergence of calcite crystals of great irregular morphology, shows that bioorganic molecules attune in the extract harmonize the crystal morphology³⁰. Research exposes that the repress NF-kB set off and rouse of heme oxygenase-1²¹. CQ stem boiled with lime water is used to increase the appetite⁷¹. The powdered stem extract of CQ is used by Rangas of eastern Africa to heal injuries¹⁵.

Discussion

Among all the valuable discoveries in the medicinal research, nearly 25% of the drugs are derived from the plants and about 122 active compounds are currently in use⁷². Physicochemical parameters help the researchers to set the standards of crude drugs. The standardizations of the crude extracts are in great demand for *C. quadrangularis* as it shows enormous utility in the medical field to cure various diseases. An important result is that side-effects are minimum-to-nil in the human consumption of CQ and a heavy dosage of CQ (5000 mg/kg b weight) in an animal model has been proven to not cause any side effects³¹. Various information and parameters summarised in this review will help in further research and standardisation of crude drug for CQ.

Conclusion

Plant-based natural compounds as medicine have higher demand at present. The plant

C. quadrangularis exhibits required therapeutic properties in both traditional and allopathic medicine. The curative property of the plant lies in the presence of secondary metabolites in a significant composition. The extracts from roots and stem of the plant consist of various medicinal efficacies and are known to have antioxidants, accelerate the process of bone fracture healing, wound healing, antimicrobial activity and antiulcer activity. Some minerals present in this plant play a significant role in proper functioning in human metabolism. Proper documentation is crucial for medicinal plants to know their potential in the refinement of health and enhances traditional knowledge of medicinal plants. Pharmacological and phytochemical analysis of CQ portrays its versatile usage. In the future, animal models and various scientific methods must be used to test isolated compounds from *C. quadrangularis*, which would reveal the mechanism of those compounds. CQ without a doubt is a valuable medicinal plant that could benefit the medicinal research field greatly.

Conflict of interest

No known conflict of interest.

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