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Therapeutic potential of *Cissus quadrangularis* L.: An evidence-based review of Ayurvedic claims

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Cissus quadrangularis L. (Hadjod or Harjor), which belongs to the family Vitaceae, is one of the most significant medicinal herbs/plants used in Ayurveda and folk medicine since primaeval times. It is used in Ayurvedic medicine. The entire herb is utilized to treat a variety of illnesses and conditions. Ayurveda recommends it to reinforce bones, relieve constipation, improve digestion, and act as an aphrodisiac. In Unani medicine, it is employed to alleviate gastritis. The entire plant is used to cure asthma, while the powdered root is administered specifically to treat bone fractures. It may also help calm the stomach when gastrointestinal problems occur. According to different studies, scurvy and irregular menstruation can also be treated with *C. quandrangularis*. A lot of work, including taxonomy, ethnobotany, pharmacology, pharmacognosy, phytochemistry, and clinical aspects, has been done on different parts and aspects of *C. quadrangularis*, and different activities have been proven on the basis of experimental research studies carried out by different workers across the world. The details of the comprehensive review are presented in the present paper.

Keywords: *Cissus quadrangularis* L., Clinical trials, Pharmacognosy, Pharmacology, Phytochemistry, Taxonomy

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Introduction

India is one of the pioneers in the development and practices of well-documented indigenous systems of medicine. Several hundred plant species are used medicinally, most of them in herbal remedies and in indigenous systems of medicine where either the whole plant, or plant parts are used and thus the importance of 'medicine-men' or '*Vaidyas*' grew enormously. In this way, 'Ayurveda' attained its highest position of medical knowledge and wisdom, crossing the boundaries of India and reached to different parts of the world[1]. In the modern era, the plant constituents have been investigated, the pharmacological activity of the active principles figured out by animal experimentation, and formulations created from the plant medications have been clinically tested, ensuring the validation of ayurvedic claims[2].

The present review is an effort made for re-establishment of legacy of ayurvedic medicinal claims validated through modern tools and techniques used by various researchers. The review is focused on substantiation of claims of *C. quadrangularis* given in ayurvedic textbooks. Among the 750 most used plants in ayurveda, *C. quadrangularis* which is commonly known as 'Hadjod' in Indian system of medicine (AYUSH) is also considered as promising plant for fractured bone healing. In ayurvedic medicine system, the plant is used for six classical formulations of ayurveda[3] and fifteen herbal formulations[4] sold in various market of the Country.

The generic term *Cissus* L. is taxonomically situated within the genus *Cissus* of the family Vitaceae commonly known as the grape family. The species is recognised for its unique succulent, quadrangular stem and the plant is native to a wide geographical range spanning tropical Africa, Arabian Peninsula and parts of Southern and South East Asia. POWO currently acknowledges several heterotypic synonyms for the species such as *Vitis quadrangularis* and *Cissus succulenta* while maintaining *C. quadrangularis* L. as the accepted botanical name[5]. This is known as *Granthiman,*

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Asthisanghari, Vajrangi, Asthishrankhala, Asthisanharaka[6], *Asthisamhrita, Vajravalli*, and *Caturdhara* in Sanskrit; Hadjod, Harjor in Hindi, and Bone setter, Cactus vine, Climbing cactus, Edible stemmed vine, Kangaroo vine, Succulent-stemmed wild grape, Veld grape, Winged tree vine, Adamant creeper in English. *C. quadrangularis* has been evaluated for potential medical uses. In India, it is frequently used to make traditional soups, dals, and chutneys. Furthermore, Ayurveda has established its enormous healing powers. Scholarly sources on this ancient Indian medical practice claim that *C. quadrangularis* has strong healing capabilities for bone fractures and is an immense natural cure for flatulence, indigestion, weight loss, epilepsy, diminished sexual drive, and haemorrhoids[7].

Methodology of literature review

A literature review was conducted to gather data on *C. quadrangularis*, utilising both contemporary and traditional sources. Traditional claims were recorded using classical Ayurvedic texts, such as the Ayurvedic Pharmacopoeia of India (API), the Compendium of Indian Medicinal Plants, and Bhavaprakasha Nighantu. The aforementioned were subsequently verified using contemporary scientific databases and national portals, including One Nation One Subscription (ONOS), Google Scholar, PubMed, ScienceDirect, Scopus, SpringerLink, and Web of Science. Relevant articles published between 1960 and 2025 were identified using keywords linked to *C. quadrangularis*, including phytochemistry, pharmacological activities, including preclinical and clinical trials, toxicity and safety studies, and therapeutic uses. The literature was assessed for relevance, and only peer-reviewed English-language research publications and reviews were included. To provide contemporary scientific evidence to support traditional wisdom, data from selected studies were systematically examined.

Botanical description and distribution

C. quadrangularis is a large perennial climber. Its stem is fleshy and much-branched like a cactus, jointed with quadrangular 4-winged, divided in nodes and internodes; tendril at some of the nodes, which are long, simple, and leaf-opposed. These tendrils are the modified terminal buds. *C. quadrangularis* plants are leafless when they are old. The 4-10 mm long petiole is profoundly canaliculated. Leaves are alternate, bright green, base cuneate or truncate; broadly ovate, ovate or reniform, 3-7 lobed, slightly denticulate, glabrous, petiole short; stipules small, obtuse. Flowers are greenish-white in shortly peduncled umbellate cymes. Calyx is cup-shaped with 4 obtuse fleshy lobes. Petals 4, ovate oblong, acute, hooded at the apex. Disk erect 4-lobed. Stamens are inserted beneath the margin of the disk; anthers are free. The ovary is habitually 2-celled, with a short style. Fruit is a globose or ovoid berry, red when ripe, 1-2-seeded. Flowering and Fruiting: July to September. An extensive climber found on hedges, shrubs, and trees. The indigenous range of this species is Tropical and mostly found in South Africa, Madagascar, the Arabian Peninsula, and the Indian Subcontinent to the Myanmar regions[7] (Fig. 1).

Vernacular names[7,8]

C. quadrangularis is an important herb used by Indian systems of medicine (AYUSH). The plant is known through its various vernacular names in different regional languages of the country, which are given in Table 1.

Classification[5]

According to the Plants of the World Online (POWO) database curated by the Royal Botanic Garden, Kew; the taxonomic situation of *C. quadrangularis* is given in Table 2.

C. quadrangularis in ayurveda[6]

In the famous textbook of single ayurvedic medicinal plants viz. '*Bhavprakash Nighantu'*,

Fig. 1 — a) *Cissus quadrangularis* L. (Hadjod) plant, b) Stem of *C. quadrangularis* L, and c) Leaves of *C. quandrangularis* L.

Table 1 — Vernacular names of *C. quadrangularis* in different regional languages of India

S. No.	Regional Languages	Vernacular names
1	Assamese	Harjara, Harjora - lata
2	Bengali	Harbhanga, Harjora, Haadjodaa, Hadajora
3	English	Adament creeper, Bone setter, Edible Stemmed vine, Edible vine, Veld grape
4	Gujarati	Chodhari, Hadasankala, Haadsaankal, Vedhari
5	Hindi	Hadjod, Hadjora, Hadjoda, Harsankari
6	Kannad	Mangaraballi, Mangarvallee, Mangaroli
7	Malayalam	Changalam parande, Chanamparanda, Piranta
8	Marathi	Ghanasakande, Ghanasvel, Ghonasakande, Kandvel, Kaandvel
9	Punjabi	Haddjor, Hadajoda
10	Sanskrit	Asthisamharaka, Asthisanghari, Asthishrinkhala, Asthisamhrita, Caturdhara, Granthiman, Vajravalli and Vajrangi
11	Tamil	Changalaparanda, Perandai, Pirandai
12	Telgu	Nalleru, Nallerutige
13	Urdu	Hathjod, Harjora

Table 2 — Taxonomical classification of *C. quandrangularis*

S. No.	Taxonomical rank	Classification
1	Kingdom	Plantae
2	Phylum	Streptophyta
3	Class	Equisetopsida
4	Subclass	Magnoliidae
5	Order	Vitales
6	Family	Vitaceae
7	Genus	*Cissus*
8	Species	*Cissus quadrangularis*
9	Authors	Linn.
10	Rank	Species

C. quadrangularis is well defined for its various names with their meaning in ancient literature of Ayurveda, its uses for treatment of various ailments and its properties. The description is given hereunder:

Shloka in Roman English:

Granthimanasthisanghari
Vajrangivaasthishrinkhala ।
Asthisangharakah Proktovatshleshmaharoashthiuka ॥
Ushnah Sarah
Krimighnashradurnamghnoakshirogjit ।
Rukshaswadurlaghuvrishyah Pachnah Pittalah
Smiritah ॥

Meaning of shloka

Hadasahari - anti-phlegm, healing of broken bones, curing heat, essence and worms, piles and eye diseases, it is dry, tasty, small, vryshya, digestive and bile generating.

Properties and uses in Ayurveda

C. quadrangularis is highly useful to cure problems related to "*Vata*" and "*Kapha*" among the three bodily humours. It is hot in effect on the body and dry in nature, and light to digest. It is useful for the healing of fractured bones, as an anthelmintic, and as a very good remedy for haemorrhoids/piles. In addition, it is further reported for the treatment of eye complaints. *C. quadrangularis* possesses properties to treat antihelmintic, skin-related issues, and "Pitta doshas". The leaves are bitter in taste. *C. quadrangularis* is dry in nature. It is known for its various effects, such as an appetiser, to improve digestion (digestive), a blood purifier, and strengthening stamina and vigour. In Ayurveda, *C. quadrangularis* is commonly used in the healing of fractured bones, in cases of scurvy, dyspepsia, and bronchial asthma. It is also said to be a digestant. Tender leaves and ash of the stem are used for indigestion. In case of a bone fracture, it is used orally and externally (in paste form). The stem of *C. quadrangularis* is mashed into a paste for fractures and taken orally for asthma. Powdered leaves and shoots ease stomach issues, while stem juice aids scurvy and irregular menstruation[9].

Traditional and ethnobotanical uses

The stem, root, leaves, and whole plant of *C. quadrangularis* are used by Indian tribal and folk communities to treat ailments in humans and animals, including fractures, wounds, dysentery, indigestion, childbirth pain, joint pain, stomachache, and swelling. Fruits are edible or pickled, and the stems are used as a vegetable[10]. *C. quadrangularis* is used to treat various conditions in humans and animals, including fractures, sprains, arthritis, asthma, digestive issues, fever, gum bleeding, irregular menses, jaundice, ulcers, worms, wounds, and insect bites. It also aids fertility, skeletal strength, and appetite. In animals, it is used to treat bone fractures, fever, foot-and-mouth disease, swelling, and placenta expulsion, while its stem is consumed as a vegetable[11].

A lot of work has been done on different aspects of *C. quadrangularis*, and different activities have been proven based on experimental research studies carried out by different workers across the world. The details of a comprehensive review of *C. quadrangularis* are provided below.

Chemical constituents and phytochemistry

C. quadrangularis mainly consists of ascorbic acid, calcium oxalate, and carotene thriving in India's hottest regions[6]. It also has δ-amyrin, δ-amyrone, and sitosterol, along with novel tetracyclic triterpenoids like onocer-7-en-3α,21β-diol(I) and onocer-7-en-3β,21α-diol(II)[12]. Additional compounds such as 4-hydroxy-2-methyltricos-2-en-22-one, 7-oxo-onocer-8-ene-3β,21α-diol(I), 31-methyl-tritriacontanoic acid, and icosanyl icosanoate have been secluded[13]. Aqueous extracts exhibit acetylcholine-like action on rabbit, rat, and dog tissues, while a glucoside impacts the myocardium, with effects mitigated by calcium ions[14,15]. Sen *et al.* reviewed its distribution, morphology, taxonomy, tissue culture, and traditional uses[16]. Kumar BT identified high levels of alkaloids, flavonoids, terpenoids, glycosides, and saponins in methanol extracts, with tannins and steroids found in aqueous extracts[17]. Phytochemical studies of *C. quadrangularis* aerial parts revealed major compounds like ethan-1,1-diethoxy, n-hexadecanoic acid, and 9,12,15-octadecatrienoic acid-methyl ester[18].

Stem examination revealed raphides, intrafasicular cambium, and needle-shaped calcium oxalate crystals, with histochemical tests detecting alkaloids, tannins, phenols, and suberin. Aqueous, petroleum ether, and dichloromethane extracts contained alkaloids, phenols, steroids, and flavonoids[19]. Teware *et al.* found alkaloids, carbohydrates, glycosides, tannins, amino acids, flavonoids, saponins, and steroids in various extracts[20]. Pharmacological activities include analgesic, anti-inflammatory, antioxidant, antimicrobial, antiulcer, bone healing, and diuretic properties[21]. Studies also explore its taxonomy, morphology, tissue culture, and medicinal uses[22]. *C. quadrangularis* has been shown to possess pharmacological properties such as antioxidant, antimicrobial, anti-inflammatory, analgesic, bone healing, antiulcer, and diuretic activities[23]. Farmers in Benin use *C. quadrangularis* and *Acacia polyacantha* to treat gastrointestinal illnesses in livestock caused by salmonellosis, as both plants contain sterols, terpenes, flavonoids, anthocyanins, mucilage, and tannins[24]. Methanolic extracts of *C. quadrangularis* inhibit H^+/K^+-ATPase, with quantified phenolic and flavonoid content[25]. Compounds isolated from its stems include δ-amyrone, d-amyrin acetate, β-sitosterol, kaempferol, quercetin, and resveratrol, characterised using spectroscopy[26]. The plant's roots, stems, and leaves have been analysed for ash, minerals, and biochemicals. Stilbene derivatives such as resveratrol, piceatannol, pallidol, parthenocissin A, and new compounds *C. quadrangularis* A, B, and C have been identified[27,28,29]. Related species, such as *C. digitata*, yield apigenin, luteolin, and ampelopsin[30]. Furthermore, *C. quadrangularis* extract demonstrates CNS depressive and anticonvulsant activity through GABAA-benzodiazepine receptor binding[31].

According to a phytochemical study, *C. quadrangularis* has important components such as flavonoids, alkaloids, tannins, saponins, and cardiac glycosides, making it a safe substitute for anabolic steroids as a supplement for bodybuilding[31]. In addition to taraxeryl acetate and iso-pentacosanoic acid, seven novel compounds were identified, comprising icosanyl icosanoate and 31-methyltritriacontanoic acid[32]. The vegetative portions included flavonoids that were detected by ESI-MS/MS30 and liquid chromatography, including vitexin, kaempferol 3-O-rhamnoside, quercetin, and quercitrin[33]. The plant has immunomodulatory properties attributed to its significant polyphenolic and flavonoid content[34]. Aloe vera, along with *C. quadrangularis*, has comparable molecules with antibacterial activity, according to phytochemical screening[35]. Calcium oxalate crystals in *C. quadrangularis* serve as a diagnostic tool for detecting adulterants[36]. Further research explores its effectiveness in treating chronic diseases and the molecular mechanisms behind its phytoconstituents[37,38]. The ethnopharmacological, phytochemical, and pharmacological aspects of *C. quadrangularis* were explored by Mukherjee *et al.*, who reported that its stem juice is useful for menstrual disorders, dyspepsia, and wound healing. The plant's aerial parts have antimicrobial, anti-inflammatory, antitumor, hepatoprotective, and gastroprotective properties[39]. Phytochemical studies of its stems isolated new phenolic and lignan glycosides, along with 12 known compounds identified through NMR and mass spectrometry. A novel triterpenoid, 7-oxoonocer-8-ene-3β,21α-diol, was also discovered[40]. GC-MS studies on related *Cissus* species identified β-sitosterol as a common compound[41]. Two new tetracyclic triterpenoids, onocer-7-en-3α,21β-diol and onocer-7-en-3β,21α-diol, along with other compounds, were isolated[42]. *C. quadrangularis* ethanol extract demonstrated protective effects on endothelial cells injured by hydrogen peroxide, restoring ROS levels and up-

regulating enzymes like Cu/Zn-SOD and eNOS, partly due to resveratrol and quercetin[43].

Pharmacological and clinical activities of *C. quadrangularis*

In Ayurveda, *C. quadrangularis* is used to treat fractured bones, scurvy, dyspepsia, bronchial asthma, indigestion, and as a gastroprotective tonic. It enhances bone healing, callus formation, and cartilage regeneration, providing bioavailable calcium, phosphorus, vitamins, and amino acids for healthy bone growth and strong teeth. Scientific evidence supports the traditional claims of *C. quadrangularis* found in ancient Ayurvedic literature.

Analgesic/anti-inflammatory activity

Studies on *C. quadrangularis* revealed significant analgesic effects in mice using methods such as Eddy's hot-plate and Haffner's clip tests[44]. The methanol extract showed positive results for haemorrhoid pain, inflammation, and size reduction, supporting its traditional use[45]. Additionally, a combination of *C. quadrangularis* and Lepidium sativum (LS) showed analgesic effects[46]. Pain and inflammation were effectively treated using topical treatments made from a variety of herbal ingredients[47]. In studies on osteoarthritis, *C. quadrangularis* and *Withania somnifera* together demonstrated promise in lowering gene transcription disruption[48]. Rats exhibited decreased oedema and anti-inflammatory, analgesic, and antipyretic effects from the ethanolic extract of *C. quadrangularis*[49]. Jain and Kohli identified five compounds in *C. quadrangularis* with anti-inflammatory properties[50]. Furthermore, *C. quadrangularis* has antibacterial, antidiabetic, anti-obesity, antioxidant, and cardiovascular properties[51]. Extracts of *C. quadrangularis* also inhibit enzymes such as COX-1, COX-2, and 5-LOX[52]. A preclinical study in rats demonstrated the anti-inflammatory effects of *C. quadrangularis* and LS[53].

Activity on fracture/wound healing and other bone-related disorders

Various investigations about *C. quadrangularis* demonstrate how effectively it functions in order to promote bone repair and fracture recovery. Knee osteoarthritis was found to respond well to an organic osteoseal herbal medicine containing *C. quadrangularis*, which provides vital minerals like calcium, vitamins, and amino acids to promote bone building[54]. In several animal studies, *C. quadrangularis* methanolic extract demonstrated accelerated bone fracture healing by 33% and resulted in positive effects in dogs with experimentally fractured bones[55-57]. Additionally, *C. quadrangularis* improved biomechanical, biochemical, and histological parameters by counteracting the anti-anabolic effects of cortisone on bone healing[58] and demonstrating anti-osteoporotic effects[59] in ovariectomized rats. In one clinical instance, a patient with leg fractures found that *C. quadrangularis* greatly accelerated their healing[60]. The calcium ion-rich bio-organic compounds in *C. quadrangularis*'s extract[61,62] promote the growth of calcite crystals and hasten fracture healing[63,64,65]. Furthermore, *C. quadrangularis* has been demonstrated to enhance osteoblast function in murine osteoblasts[66,67,68] and to stimulate osteoblast development and mineralisation in human osteoblast-like cells (SaOS-2)[69]. Additionally, its hexane and dichloromethane constituents influence differentiation and mineralization[70]. Nanofibers filled with *C. quadrangularis* have shown promise for bone regeneration, and the potential of *C. quadrangularis* for bone tissue engineering was further investigated[71]. *C. quadrangularis* increased bone density and sped up the growth of new bone in alveolar distraction, allowing for quicker implantation. *C. quadrangularis*'s involvement in healing and bone regeneration[72] is further supported by its widespread usage as an analgesic and tonic to treat broken bones, damaged ligaments, and tendons.

Effect on obesity

In a clinical investigation, the effects of *C. quadrangularis* preparations, such as CORE and *C. quadrangularis* R-300, on blood lipids, oxidative stress, and weight in obese and overweight people[73] were evaluated. When paired with a regular or low-calorie diet for 8 weeks, the study found that *C. quadrangularis* helped manage metabolic syndrome, namely by assisting with weight loss and reducing central obesity[74]. In addition, oxidative stress and obesity were well managed by mixing *C. quadrangularis* powder with rice flour, spices, wheat flour, and Bengal gram flour[75]. In addition to having antidiabetic, anti-inflammatory, anti-obesity, and antioxidant qualities, *C. quadrangularis* has demonstrated advantages in bone turnover and cardiovascular health[76].

Antiviral, antibacterial, and antimicrobial activity

The anti-plasmodial and GABA receptor binding properties of several medicinal plants, including *C. quadrangularis*, were examined *in vitro*[77]. *C. quadrangularis* extracts, using petroleum ether and ethyl acetate, demonstrated antibacterial properties against both Gram-positive (e.g., *Bacillus cereus*, *Staphylococcus aureus*) and Gram-negative bacteria (e.g., *Escherichia coli*, *Salmonella typhi*)[78]. Several plant extracts, notably *C. quadrangularis*, possess antimicrobial activity against *S. aureus*, *Pseudomonas aeruginosa*, and *E. coli*[79]. Secondary metabolites to facilitate supply en route for antimicrobial activities, such as flavonoids, alkaloids, and phenols, were identified using phytochemical screening[80]. The molecular consequences of *E. coli* inoculation on *C. quadrangularis* were examined at various doses (0.5, 1, 1.5 mL)[81]. Traditionally, *C. quadrangularis* was utilised to treat peptic ulcer disorders[82], and the production of silver nanoparticles[83] demonstrated its antibacterial activity. In addition to isolated triterpenes (lupenone, epifriedelinol, and isoarborenol) and phytosterol (β-sitosterol), alcohol-based extracts demonstrated antifungal[84] and antibacterial activity[85], with isolated triterpenes (lupenone, epifriedelinol, and isoarborenol) and phytosterol (β-sitosterol)[86]. *C. quadrangularis*-derived silver nanoparticles showed antibacterial activity against aquatic bacteria[87,88]. A methanolic extract of *C. quadrangularis* was evaluated for its antiviral activity against types 1 and 2 herpes simplex virus[89]. Furthermore, endophytic fungi from *C. quadrangularis* were identified by microscopical analysis, confirming the plant's therapeutic potential[90].

Effect on the urogenital system

In Trinidad and Tobago, ethnobotanical investigations conducted between 1996 and 2000 confirmed the use of plants, such as *C. quadrangularis*, to treat high cholesterol, diabetes, and urinary problems[91]. According to a survey conducted in Mali, 55 plants, including *C. quadrangularis* and *Stylosanthes erecta*, were found to be frequently used to treat schistosomiasis, and nine plant combinations have been employed to treat the urinary form of the disease[92].

Gastroprotective effect

An aspirin-induced ulcer model was employed to assess the gastroprotective properties of *C. quadrangularis* extract, which revealed notable protection against gastric ulcers[93,94,95]. *C. quadrangularis* extract improved glycoprotein and NPSH levels, decreased gastric secretions, raised gastric mucin content, and decreased the ulcer index[96,97]. Its preventive mechanism included increasing mitochondrial antioxidants, decreasing TNF-alpha and IL-1beta levels, and enhancing microvascular permeability. Additionally, *C. quadrangularis* extract demonstrated its anti-inflammatory qualities by inhibiting the generation of proinflammatory cytokines, neutrophil infiltration, and lipid peroxidation[98]. Moreover, *C. quadrangularis* extract stimulated cellular proliferation, which improved mucosal resilience and ulcer healing. *C. quadrangularis* extract demonstrated stronger anti-ulcerogenic effects than ranitidine, lowering ulcer incidence and boosting mucin formation. Methanolic and ethanol extracts of *C. quadrangularis* also showed antiulcer activity, substantially reducing gastrointestinal ulceration caused by indomethacin and ethanol[99]. Additionally, *C. quadrangularis* extract has antioxidative characteristics and helps rats resist aspirin-induced gastrointestinal mucosal lesions[100].

General protective effect

An indigenous plant in India, *C. quadrangularis* is well known for its ability to heal bone fractures[101]. Analgesic, antibacterial, antifungal, antioxidant, anthelmintic[102], and hepatoprotective properties have been discovered and reported[103]. Strong antibacterial activity against both Gram-positive and Gram-negative bacteria is demonstrated by various extracts, including methanol and ethyl acetate[104]. Assays such as FRAP and ABTS[105] have been employed to assess the plant's antioxidant characteristics[106]. The distinctions between seasonal samples and variants have been highlighted by phytochemical analyses[107].

Additionally, the plant exhibits hepatoprotective properties, namely against liver damage caused by the drug isoniazid[108]. *In vitro* anthelmintic activity against *Pheretima posthuma*[109] has been demonstrated by the root extract of *C. quadrangularis*. Treatment of oedema and fever[110] is supported by the anti-inflammatory properties of the ethyl acetate stem extract. Furthermore, *C. quadrangularis* protects against isoniazid-induced hepatotoxicity, which is favourable to liver health. Additionally, several studies have demonstrated its anti-inflammatory and antipyretic properties[111], as well as its potential to

enhance insulin sensitivity and antioxidant balance in high-fat, high-fructose diet models[112]. The plant is used extensively in traditional medical systems such as Ayurveda, Siddha, Unani, and homeopathy for a variety of diseases, including hepatoprotective, antibacterial, antidiabetic, and antihypertensive disorders[113], due to its varied pharmacological effects[114].

Anticancer activity

In a research investigation exploiting normal skin cells, the carcinogenic potential and risk aspects were investigated. Additionally, the impact of *C. quadrangularis* extract on HeLa tumoroid growth was investigated using an *in vitro* spheroid HeLa culture model[115]. The anticancer properties of *C. quadrangularis* leaf extract against MG63 cells were demonstrated, and the properties may be further explored in future research to treat bone tumours[116]. The *in vitro* anticancer, antibacterial, and qualitative phytochemical properties of *C. quadrangularis* were assessed. Ethyl acetate extract has anticancer activity *in vitro*, but it still exhibits significant activity against cancerous cells[117]. The efficacy of *C. quadrangularis* stem extract against the A549 lung cancer cell line, including qualitative phytochemical analysis, antimicrobial activity, cell viability, and *in vitro* anticancer activity, was investigated[118]. The biologically active elements of the entire *C. quadrangularis* plant Endoplasmic Reticulum Export Sites (ERES) evaluated using Gas Chromatography-Mass Spectrometry (GC-MS), which revealed the presence of elements in the methanolic extract. The principal ingredient in the methanolic extract, n-Hexadecanoic acid, has been reported to exhibit strong carcinogenic properties[119].

Bone healing effects

Traditional Indian medicine extensively uses *C. quadrangularis* which has significant osteogenic potential and aids in the healing of bone fractures[120]. *C. quadrangularis* extracts stimulate extracellular matrix calcification, osteoblastogenesis, and mesenchymal stem cell proliferation[121]. *C. quadrangularis* inhibited bone loss in the femur and tibia bones in mice with ovariectomies[122]. Increased levels of alkaline phosphatase (ALP) validate its function in osteoblast differentiation[123]. Its roots, stems, and shoots support bone-related conditions such as fractures[124], osteoporosis[125,] and osteoarthritis[126]. For injuries to the back, spine, and bones, topical and internal applications of *C. quadrangularis* are effective[127,128]. Additionally, *C. quadrangularis* is used to treat anorexia, asthma, burns, colic, dyspepsia, flatulence, insect bites, obesity, and skin diseases. Its leaves and shoots were used by traditional healers to treat gastrointestinal issues; dried shoots are used as treatments for indigestion and dyspepsia. *C. quadrangularis* is used in Ayurvedic therapies, such as Majja Basti, to strengthen bones[129]. Research studies indicate that the anti-osteoporotic properties of *C. quadrangularis* and *Emblica officinalis* are enhanced[130]. Numerous extracts of *C. quadrangularis* in petroleum ether, chloroform, ethanol, and aqueous solutions have demonstrated strong pharmacological properties. Because it stimulates osteoblastogenesis, calcification, and differentiation, *C. quadrangularis* may be used as a natural treatment to prevent osteoporosis and restore bone health[131].

How safe is it?

The acute oral toxicity, anti-inflammatory, and venoconstrictive properties of a standardised ethanolic *C. quadrangularis* extract[132] were analysed in a rat study. Enteric film tablets were also coated with the extract, and their efficacy and safety were evaluated. *C. quadrangularis* greatly reduced bone pain[133], but had no effect on haemorrhoids, according to a study of papers up to November 2016. Over the course of three months of administration at the recommended dosages, *C. quadrangularis* had no adverse impacts on internal organs, haematological parameters, or serum chemistry[134]. A prominent vegetable in Nigerian diets, the dried root of *C. quadrangularis* also has significant nutritional value[135].

Multidisciplinary scientific evidence on *C. quadrangularis*

C. quadrangularis, a common perennial climber in India, is traditionally used to treat anorexia, colic, dyspepsia, epilepsy, flatulence, helminthiasis, haemorrhage, leprosy, skin diseases, swellings, tumours, and ulcers[136]. It affects the development of bones in fetuses[137]. The pharmacological and therapeutic properties of *C. quadrangularis* and *Cassia auriculata* against a range of illnesses have been demonstrated by studies[138,139]. In rats, methanolic extracts improve antioxidant defence and prevent free radical damage, whereas *C. quadrangularis* ethanolic extracts cause apoptosis and genomic instability in A431 cells[140,141]. Cracks and microvoids have been seen in the morphological and

physicochemical characteristics of *C. quadrangularis* stem fibre and other components[142]. HPTLC methods, pharmacognostic criteria[143], and chemical profiling[144] precisely identify and measure the hydrocarbons and phytoconstituents in *C. quadrangularis*. It is important to identify its bioactive components because 3-ketosteroids were discovered to have no connection to their benefits for bone. There are still potential uses for *C. quadrangularis* in medicine and pharmaceuticals[145,146]. Acetonitrile and water were isocratically eluted using a Cosmosil C8 column in a reliable RP-HPLC method for phytosterol measurement in plant extracts, yielding precise and reproducible results[147]. Using TLC, alkaloids in plants with a track record of curing ailments were found, and HPLC[148] was used to purify them. The leaves, stems, and roots of *C. quadrangularis* have notable flavonoid content, according to an advanced HPLC method for evaluating flavonoids, including quercetin and kaempferol[149]. Anatomical, chemical, and thermal investigations, such as FTIR, XRD, and SEM, were used in the thorough evaluation of *C. quadrangularis* root fibre to highlight its special qualities[150]. Significant anti-osteoporotic actions were demonstrated by a phytoestrogen-rich fraction (IND-HE)[151] from *C. quadrangularis* aerial parts in ovariectomized rats, and hexane extracts revealed five dammarane-type triterpenes with comparable advantages[152].

Significant anti-hyperglycemic potential was demonstrated by ethanolic *C. quadrangularis* extracts, which decreased hyperglycemia in diabetic rats[153]. Diosmin and bioflavonoids have been shown in clinical trials to be effective in treating hemorrhoidal crises, reducing discomfort, bleeding, and regional oedema[154,155]. Methanolic preparations of *C. quadrangularis* demonstrated antioxidant qualities by lowering free radicals, preventing lipid peroxidation, and increasing the activity of antioxidant enzymes[156]. *C. quadrangularis* ethanolic extracts decreased oxidative damage and apoptosis[157] caused by hyperglycemia in MG-63 osteoblast-like cells. Furthermore, *C. quadrangularis* ethanolic extract-containing topical and ethosomal gels were created and assessed for increased patient compliance, demonstrating better pH stability, diffusion, and spreadability. The results confirm that *C. quadrangularis* has broad medical potential for a range of therapeutic uses[158].

C. quadrangularis has been the subject of extensive study due to its pharmacological and therapeutic qualities. Using the solvent evaporation method[159], transdermal patches were developed with HPMC E-15, and phytochemical screening revealed the plant's antidiabetic potential[160]. Ovariectomized rats' sexual behaviour was enhanced by the estrogenic activity of IND-HE (friedelin-rich fraction), which decreased the latency to darting and hopping[161]. The widespread CAM characteristic that helps it transition from wet to arid tropics[162] was discovered through taxonomic studies[163,164], which also identified distinctive *C. quadrangularis* variants[165]. In Southern India, *C. quadrangularis* leaves and stems are consumed with curry, and young shoots are used to treat indigestion[166]. Environment-friendly synthesis of copper oxide nanoparticles (CuO NPs) using *C. quadrangularis* extract resulted in 30±2 nm spherical particles[167]. Pharmacognostic investigations[168,169] established quality control parameters, and fixed-bed pyrolysis at 550°C yielded bio-oil and biochar, revealing 15 distinct compounds[170]. *C. quadrangularis* extracts counter various pathophysiological effects[171], and Ayurvedic references highlight its role in treating osteoporosis and other ailments[172]. HPTLC and HPLC analyses quantified marker constituents across five Indian regions[173]. Additionally, *C. quadrangularis* demonstrated sedative and anticonvulsant effects in mice, supporting its traditional use in African therapies for epilepsy and insomnia[174]. The plant's versatility includes analgesic, anti-malaria, and anti-asthmatic uses[175], with green nanoparticles from *C. quadrangularis* stem extract showing potential for nanoparticle manufacturing under controlled physical and chemical parameters[176]. Folk claims by Gond tribes and pharmacological evaluations further validate *C. quadrangularis*'s therapeutic significance[177].

Conclusion

Ayurveda is science of life since time immemorial, in which so many evidences for the use of more than 750 potential medicinal plants for the treatment of various ailments. Since ayurvedic system of medicine evolved slowly in last five thousand years it has a great legacy of oral health tradition which further documented in the forms of transcript with the evolution of civilisation. In traditional practices of Indian System of Medicines (ISM), many herbs using either as single drug or in compound formulations which gives a leverage to ISM as safer medicines without any side-effects,

therefore ISM drug delivery system is considered as holistic system of medicine.

Every major ancient culture worldwide has its traditional methods for treating mental and physical illnesses. Undoubtedly, the root and stem extracts of plant *C. quadrangularis* are often used to hasten the healing of bone fractures and are recognised to have therapeutic efficacy as well as antioxidant and antibacterial properties. The phytochemical components and pharmacological activities of *C. quadrangularis* are highlighted in this review. Because of its numerous therapeutic benefits, the plant is regarded as a flexible medicinal herb in both Ayurvedic and contemporary drug research. It is a rich source of certain minerals the body needs to function properly.

C. quadrangularis is renowned for its medicinal properties, has been described in various ancient ayurvedic texts for the treatment of fractured bones. In addition, this plant is used for numerous other health issues such as anthelmintic purposes, piles, eye disorders, skin-related problems, treatment of bile disorders, increasing appetite, improving digestion, blood purification, enhancing strength and vitality, scurvy, and cases of bronchial asthma. It is also helpful in regulating irregular menstrual cycles. In this review article, an attempt has been made to verify the properties of this great ayurvedic medicine through research under modern science as well as pharmacological and clinical trials. This study incorporates numerous original research papers, textbooks, patents, reference texts, and proceedings of conferences and workshops. This review article confirms that the medicinal claims of *C. quadrangularis* described in ayurveda stand up to the tests of modern science, indicating that ancient Indian science was as advanced as contemporary scientific examinations. The article supports the ayurveda and ancient practices by describing role of *C. quadrangularis* in modern medicinal practices. The present article validates the scientific nature of ayurveda in the current situation and provides a new direction for future research to be carried out not only in the context of ayurveda but also in the research of novel drug designing. This article encourages the use of numerous medicinal plants described in Ayurveda for the treatment of many incurable diseases.

Conflict of interest

The authors declare no conflict of interest.

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