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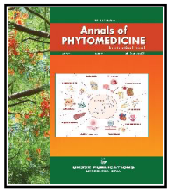

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Medicinal application and industrial utilization of Veldt grape (*Cissus quadrangularis* L.): A review

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Abstract

This review examines the medicinal uses and industrial applications of *Cissus quadrangularis* L., emphasizing its historical and therapeutic significance. Widely recognized for its bone-healing capabilities, *C. quadrangularis* is a key herb in Ayurveda and other traditional medicine systems, often used to treat fractures, osteoporosis, and joint pain. Native to tropical regions such as India, the plant contains a variety of bioactive compounds, including flavonoids, triterpenes, and phytosterols, which offer antioxidant, anti-inflammatory, and pain-relieving effects. Recent studies highlight its potential to support bone health, address metabolic disorders, and serve as a food fortifier to improve nutritional value. Although, *C. quadrangularis* has long been used traditionally and shows promising pharmacological properties, further clinical research is needed to confirm its safety and effectiveness. This review consolidates existing research on *C. quadrangularis*, exploring its chemical makeup, traditional uses, and potential as a functional food ingredient, promoting its broader recognition in both medical and industrial sectors.

1. Introduction

India boasts a vast biodiversity and a deep-rooted tradition of using flora and fauna for both nutritional and medicinal purposes. Of the estimated 250,000 higher plant species worldwide, over 70,000 are medicinal, with India itself hosting more than 45,000 plant species, positioning it as the 12th global biodiversity hub (Nagori *et al*., 2011). Traditional systems like Siddha, Ayurveda, Unani, Naturopathy, and Homoeopathy reflect a long-standing and safe reliance on herbal remedies (Vaidya and Devasagayam, 2007). Research indicates that India contributes approximately 8,000 medicinal plant species, including 700 from Ayurveda, 600 from Siddha, and 700 from Unani, with additional plants cited in the Rigveda and Yajurveda. Beyond traditional medicine, millions of Indians commonly use plants as health foods, spices, home remedies, and over-the-counter treatments (Nagori *et al*., 2011). The World Health Organization estimates that almost 80 per cent of people worldwide rely on traditional medicinal practices (Palbag *et al*., 2013). India possesses an extensive array of indigenous plants, offering a rich source of therapeutic potential.Veldt grape (*C. quadrangularis*) is a prominent medicinal plant in India. Its name is derived from its effectiveness in mending bone fractures, combining “Had” for bone and “Jod” for setting. *C. quadrangularis* is widely spread in hotter Indian, Sri Lankan, Malaysian, Java and West African regions (Chopra *et al*., 1986). It is referred to by various regional vernacular names specific to the languages of different regions around the world. In India, it is commonly called Bonesetter, Adamant Creeper, Veldt-grape, Asthisamadhani, and Hadsanka. In Bangladesh, it is known as Hathisur, while in Sri Lanka, it is called Heeressa. In West Africa, names such as Treebine, Zarnazaru, Banddiagra, and Oongoonujaara are used. In Thailand, it is referred to as Khankho, phet sangkhaat, and san cha khuat (Bafna *et al*., 2021). *C. quadrangularis* is a perennial climbing herb with a thick, quadrangular, green stem that is fleshy, angular, and bears long tendrils. Young stems are sharply angled and winged, but as they age, they lose most of their leaves. The plant’s leaves are simple, ovate or kidney-shaped, with 3-7 lobes and a smooth surface on both sides, measuring approximately 3-5 × 5-3 cm, and have deciduous stipules. Its small flowers, around 2 mm, are pink to white with four ovate-oblong petals, a green, cup-shaped hypanthium, and a smooth ovary. The fruit consists of red, single-seeded berries (6-10 mm in diameter) with smooth, obovoid seeds (4-8 mm), with flowering and fruiting taking place from June to July (Robert *et al*., 2001). *C. quadrangularis* (Veldt grape), a fleshy plant from the Vitaceae family, is widely distributed across India, thriving in warm tropical climates. Recognizable by its smooth, buff-colored stems with hints of green and reddish-brown along its angular sections, *C. quadrangularis* produces small, greenish-white, bisexual flowers from June to December. The plant forms aerial roots in the rainy season and yields single, ellipsoid or pear-shaped seeds (Shahand Unnati, 2011). Propagation is efficiently achieved using stem cuttings, particularly in June and July. Healthy, mature, 30 cm cuttings are taken from the mother plant and placed in beds with a supportive climbing substrate and moderate watering. As a succulent, it requires controlled watering to avoid excess moisture. New buds appear within days, eventually

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growing into fully developed plants that resemble the original. These young plants are easily relocated as needed, facilitating rapid multiplication and wide distribution of the species (Sundaran *et al*., 2020).

C. quadrangularis, known as 'Asthi Samharaha' in Sanskrit, signifies its bone-healing properties and is recognized in Ayurveda for treating various ailments. According to Kirtikar and Basu, the stem is characterized as hot, dry, sweetish, bitter, laxative, anthelmintic, aphrodisiac, stomachic, and analgesic. It is used for conditions like blindness, epilepsy, and loss of appetite (Senand Dash, 2012). In Siddha medicine, it is regarded as a tonic and analgesic, promoting the healing of broken bones. The stem is antiscorbutic; its paste is used for asthma, and its juice is administered both internally and externally to aid fracture healing. The juice is also beneficial for epistaxis when applied in the nostrils, for otorrhea as eardrops, and for irregular menstruation. The powdered ashes of its shoots are given internally for dyspepsia, while the root powder effectively unites bone fractures and serves as a remedy for constipation and gout (Mukherjee *et al*., 2016). In Ayurveda, the stem of *C. quadrangularis* is also known to have alterative, antibacterial, dyspeptic, gastrointestinal, tonic, and soothing effects in the treatment of arthritic eye and ear conditions, irregular menstruation, asthma, and back and spinal problems. Research has shown that the extract from *Cissus* has androgenic and cardiotonic properties (Chopra *et al*., 1986). The plant is also utilized for treating conditions such as epilepsy, convulsions, hemorrhoids, anorexia, indigestion, and asthma. Traditionally, it has also been employed to manage menstrual issues and menopause. *C. quadrangularis* offers a variety of benefits, including pain-relieving analgesic properties, regenerative capabilities for wound healing, and a reduction in body fat by decreasing adipose tissue. It is also known for its antioxidant, anti-inflammatory, and antibacterial effects (Yoon *et al*., 2023). Furthermore, the plant may help lower cholesterol levels, relieve menstrual discomfort, boost immune function, and assist in treating skin diseases, colic, epilepsy, chronic ulcers, and metabolic syndrome (Malathi, 2014). Traditionally, in Africa, it has been used to address ailments such as syphilis, sickle cell anaemia, malaria, and gonorrhea, and in Cameroon, it is utilized for oral rehydration (Mate *et al*., 2008). Phytochemical screening of *C. quadrangularis* has identified various compounds, including iridoids, stilbene derivatives, sterols, triterpenes, alkaloids, fatty acids, methyl esters, and flavonoids. Leaf analysis revealed ecosyl eicosanoate, tetratriacotanol, tetratriacontanoic acid, αβ-amyrin (a), and β-sitosterol (b), along with polyphenols like quercetin, daidzein, and genistein. Lupeol, known for promoting melanin production, was also detected (Singh *et al*., 2007; Rao *et al*., 2011). Additionally, two new iridoids (6-O-[2,3-dimethoxy]-trans-cinnamoyl catalpol and 6-O-meta-methoxy-benzozyl catalpol) were identified, along with the known iridoids picroside-1 and pallidol. Three new marker constituents were found in the aerial parts, including δ-amyrin and 3,3',4,4'-tetrahydroxy biphenyl (Mehta *et al*., 2001).

1.1 Traditional uses

In Ayurveda, the *C. quadrangularis* (CQL) stem is described as hot, dry, and sweet-bitter. Recognized for its anthelmintic, laxative, digestive, stomachic, analgesic, tonic, and aphrodisiac properties, it is traditionally applied in managing piles, visual impairment, tumors, muscle pain, disorders of vata and kapha, loss of appetite, epilepsy, constipation, chronic ulcers, and bone fractures. Similarly, the Unani system of medicine highlights its use in bone healing, recommending both internal intake and external application. Additionally, it is employed for spine and back issues and to help eliminate pus (Kirtika and Basu, 2005). *C. quadrangularis* (CQL) does not appear in ancient classical Ayurvedic texts, with its earliest known mention in the 16th Century text Bhavprakasha. In Bhavprakash Nighantu (Vaidya, 1968), Sanskrit sources describe CQL's therapeutic properties. Known as Asthisamhaaraka, it is believed to balance vata and kapha (shleshman), promote bone healing, and possess a warm (ushna) nature. CQL is also recognized for its laxative (sara) action, ability to expel worms, treat piles (durnaaman) and eye ailments (aksi), induce dryness, taste pleasant, have a light (laghu) quality, function as an aphrodisiac (vrsya), aid digestion, and enhance pitta levels (Bafna *et al*., 2021). *C. quadrangularis* is traditionally, utilized for treating insect bites and sores on animals like camels and horses, typically applied as a paste (Valli and Vaseeharan, 2012). In India, traditional medical systems like Siddha and Ayurveda have widely utilized this plant for managing "Asthi" or bone-related conditions, including fractures, pain, inflammation, osteoporosis, and rheumatoid and osteoarthritis (Nagori *et al*., 2011). The Unani medicine system recommends internal use and topical application for bone fracture healing. In Siddha medicine, the stem is recognized for its stomachic properties and is commonly used for digestive issues. A paste made from the stem is used in asthma treatment and applied both internally and externally to aid in bone healing (Chatterjee and Prakashi, 1994). Additionally, powder from the shoots is administered for indigestion, while powder derived from the roots is applied as a bone plaster and in treating gout and constipation (Kumbhojkar *et al*., 1991; Singhand Maheshwari, 2013). Although, this herb is associated with numerous traditional claims, these assertions have yet to be validated through human clinical trials.

1.2 Utility of the plant

C. quadrangularis is utilized for various health issues, including diabetes, obesity, high cholesterol, bone fractures, allergies, cancer, stomach upset, painful menstrual periods, asthma, malaria, wound healing, peptic ulcer disease, and conditions associated with weak bones, such as osteoporosis. It is also employed as a bodybuilding supplement as an alternative to anabolic steroids. The herb is commonly used to address osteoarthritis, rheumatoid arthritis, and osteoporosis. The roots and stems are applied in the treatment of bone fractures, while a paste made from the stem boiled in limewater is used for asthma. The powdered herb is administered for hemorrhoids and certain bowel infections. Stem juice is used to treat scurvy, debilitating menstrual disorders, otorrhea, and epistaxis. Additionally, the herb is given to cattle to enhance milk production. The robust, fleshy quadrangular stem has been traditionally used to treat acid reflux, gastritis, eye disorders, piles, and anaemia (Sundaran *et al*., 2020).

1.3 Bioactive components of *C. quadrangularis*

The therapeutic effects of *C. quadrangularis* largely depend on its diverse bioactive compounds, which exhibit synergistic interactions. Key active phytochemicals found in CQ include categories like steroids, flavonoids, terpenoids, stilbenes, iridoids, tannins, and vitamins. Advanced phytochemical analyses, such as HPLC, GC-MS, and NMR, have identified various compounds in CQ. Notably, several steroids such as β-sitosterol, β-sitosterol glycoside, amyrin, friedelin, and friedelan-3-one have been successfully isolated from

CQ (Mehta *et al*., 2001; Aswar *et al*., 2010; Adesanya *et al*., 1999). The primary flavonoids isolated from *C. quadrangularis* include quercetin, resveratrol, trans-resveratrol-3-O-glucoside, piceatannol, stigmasterol, kaempferol, and rutin. Among these, quercetin and resveratrol are the most extensively studied for their significant therapeutic potential. Additionally, catalpol is the most therapeutically potent iridoid in CQ, known for its bone-stimulating effects (Jain and Shaikh, 2016; Singh *et al*., 2007). *C. quadrangularis* includes numerous enzymes and minerals, such as calcium, iron, magnesium, potassium, phosphorus, and zinc, which enhance its various therapeutic properties. The extraction and fractionation solvents used significantly influence the types of compounds isolated from CQ, as each solvent interacts differently with compounds based on polarity. Consequently, key constituents that promote bone healing and stimulate bone growth are separated according to their distinct polarity profiles in different solvents (Nawghare*et al*., 2017; Kumar *et al*., 2010). Figure 1. depicts the bioactive compounds found in Veldt grape (*C. quadrangularis*), emphasizing the key constituents linked to its therapeutic effects. At the centre of the diagram are four main bioactive compounds: Alpha amyrin, beta amyrin, beta-sitosterol, and friedelin, all known for their positive impact on bone health and various other conditions. Furthermore, the diagram highlights daidzein, genistein, and quercetin, which are acknowledged for their antioxidant and anti-inflammatory properties. Together, these compounds enhance the plant's standing in traditional medicine, especially in terms of supporting bone healing and promoting overall health (Sundaran *et al*., 2020). Despite its medicinal and nutritional benefits that could contribute to food and nutrition security, *C. quadrangularis* is not widely recognized among young adults (Inglehart and Baker, 2000).

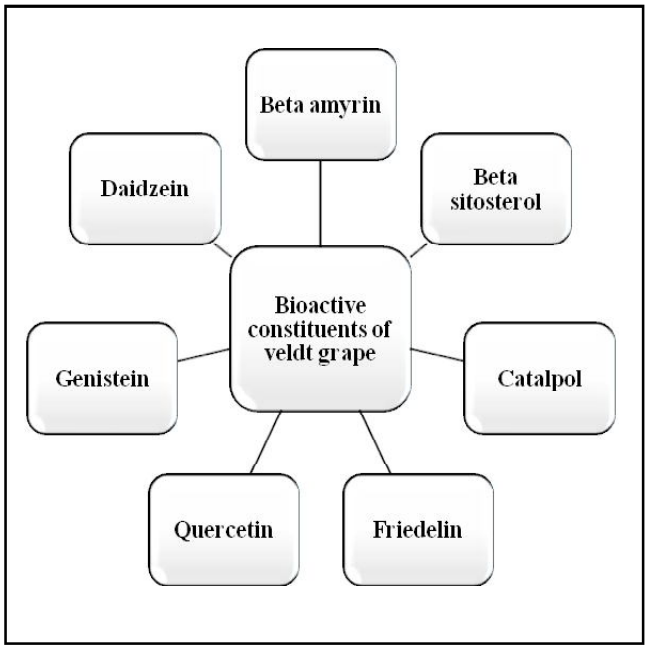

Figure 1: Bioactive constituents of Veldt grape.
Source: Sundaran *et al*. (2020).

Although, *C. quadrangularis* is widely used in Ayurveda and complementary medicine, its safety, efficacy, and effects remain uncertain due to the lack of comprehensive systematic reviews and meta-analyses. While some controlled studies on *C. quadrangularis* have been conducted in humans, most research has been carried out using animal models and cell culture systems. Recently, several applications involving *C. quadrangularis* (either alone or combined with other components) have been submitted by researchers, with most studies focusing on its potential to treat obesity, diabetes, osteoporosis, and bone fractures (Sharan *et al*., 2021).

2. Phytochemical profile and principal constituents

The phytochemical profile of *C. quadrangularis* reveals a diverse range of bioactive compounds across various parts of the plant. The aerial sections, especially the stem, contain primary metabolites such as lipids (both cyclic and acyclic), fatty acids, methyl esters, proteins, amino acids, iridoids, gums, and mucilage. Additionally, secondary metabolites such as alkaloids, flavones, flavonoids, saponins, phytosterols, steroids, stilbenes, triterpenoids, tannins, carotene, cardiac glycosides, and vitamin C are also present (Josephand George, 2013; Prabhavati *et al*., 2016). Extracts from the underground parts show notable compounds, including alkaloids, saponins, tannins, flavonoids, and glycosides, further highlighting the plant's rich phytochemical diversity (Enechi and Odonwodo, 2003).The plant contains high levels of calcium, potassium, iron, copper, cadmium, calcium oxalate, zinc, lead, phenols, vitamins, carotene, and various other compounds (Mishra *et al*., 2010). The bioactive phytochemicals the mineral composition of *C. quadrangularis* demonstrate a high concentration of essential nutrients, with potassium recorded at 67.5 mg per 100 g of dry matter, followed by calcium at 39.5 mg per 100 g, sodium at 22.5 mg, and magnesium at 1.15 mg per 100 g. Trace elements like zinc, iron, copper, and cadmium are also present, with concentrations of 3.0 mg, 7.5 mg, 0.5 mg, and 39.5 mg per 100 g, respectively. In addition to these nutrients, *C. quadrangularis* contains naturally occurring compounds with potential toxic properties. Oxalate is present at a significant level of 135 mg per 100 g, while tannins, phytates, and saponins are found in smaller amounts, with concentrations of 0.3 mg, 20 mg, and 0.16 mg per 100 g, respectively (Ghouse, 2015).It is also an abundant source of beta-carotene and vitamin C. Analytical studies have revealed that it contains ascorbic acid at a concentration of 479 mg and carotene at 267 units per 100 g of freshly prepared paste, along with calcium oxalate (Chidambara, *et al*., 2003).The key bioactive components of *C. quadrangularis* (CQ) that contribute to its pharmacological properties include ascorbic acid, carotene, phytosterols, calcium, flavonoids, vitamins, enzymes, nicotinic acid, tyrosine, alkaloids, resveratrol, piceatannol, pallidal, parthenocissin, quadrangularis, and triterpenoids. Research has identified the presence of five known compounds, which include ecosyl eicosanoate, tetra triacontanoic acid, tetratriacotanol, αβ-amyrin (a), and β-sitosterol (b). Additionally, polyphenols such as Genistein (f), Quercetin (m), and Daidzein (c) have also been documented (Singh*et al*., 2007). Friedelin (e), a phytoestrogen present in *C. quadrangularis* (CQ) extract, has been associated with an increase in alkaline phosphatase (ALP) activity and a heightened rate of mineralization via estrogen receptors (Aswar *et al*., 2010). The stem contains two steroidal principles and two asymmetric tetracyclic triterpenoids. Additionally, β-sitosterol, δ-amyrin, δ-amyrone, and flavonoids (such as quercetin) with various potential metabolic and physiological effects have been identified. The stem has also shown the presence of unique stilbene derivatives known as quadrangularins A, B, and C (Jainuand Devi, 2004).

Table 1: The chemical constituents found in different parts of *C. quadrangularis*

S. No.	Part of the plant	Chemical constituents	Reference
1.	**Stem**	Calcium ions (4% by weight), phosphorus, calcium oxalate, 3-1-methyl tritriacontanoic acid, taraxerol acetate, taraxerol, isopentadecanoic acid, alpha and β-amyrins, β-sitosterol, ketosetosterol, phenols, saponins, tannins, vitamins, and carotene	Jainu *et al*., 2006
2.	**Leaves**	parthenocissus, resveratrol, piceatannol, pallidol, and alicyclic lipids	Gupta and Verma., 1991
3.	**Ash**	Sodium, potassium, calcium, potassium tartrate, and magnesium	Austin *et al*., 2004
4.	**Root**	Lead, iron, potassium, zinc, calcium, sodium, cadmium, copper, and magnesium	Ghouse, 2015

3. Toxicity studies of *C. quadrangularis*

Before exploring the pharmacological activities of any natural drug in animal studies, it is essential to determine its toxicity profile. Numerous studies have focused on establishing the toxicity profile of *C. quadrangularis* (CQL), detailing aspects such as the type of toxicity assessment, duration, animal models used, extract type, dosage, and resulting outcomes (Kothari *et al*., 2011; Attawish *et al*., 2002). This study aimed to assess any potential adverse effects of CQR-300 through subchronic toxicity and genotoxicity evaluations. Sprague Dawley rats received oral doses of CQR-300 (0, 100, 1000, and 2500 mg/kg/day) over 90 days. No treatment-related toxicity symptoms, mortality, weight changes, or alterations in food intake were observed, and functional assessments, eye examinations, and hematological, clinical chemistry, and organ weight measurements showed no significant adverse changes. Additionally, no abnormalities were found in histopathology. Mutagenicity tests (Amesassay, *in vitro* chromosomal aberration, and *in vivo* micronucleus assay) indicated no genotoxic effects. The no-observed-adverse-effect level (NOAEL) was established at 2500 mg/kg/day, suggesting that this dose is safe for use, translating to an estimated 150 g/day for a 60 kg human (Kothari *et al*., 2011). A study evaluated the subchronic toxicity of *C. quadrangularis* powder, traditionally used in Thailand for hemorrhoid treatment, over threemonths in Wistar rats. Five groups, including a control and recovery group, received doses up to 3.0 g/kg body weight per day, up to 100 times the therapeutic human dose. No significant differences in body weight, hematological parameters, serum chemistry, or internal organ histopathology were observed between the treated and control groups. These findings indicate that *C. quadrangularis* did not cause toxicity at the tested doses during the study period (Attawish *et al*., 2002). Contrary to the preclinical studies previously cited, a recent case report described a patient who developed thrombocytopenia after receiving a renal allograft. In a case study (Kulkarni and Bhat, 2020), a 65-year-old male renal transplant patient developed moderate to severe thrombocytopenia shortly after starting CQ capsules for back pain, while his immunosuppressive regimen remained unchanged. Upon discontinuation of CQ, his platelet counts rapidly normalized, suggesting a likely causative role of CQ in triggering thrombocytopenia, as no infection or other identifiable factors were present. This incident indicates that CQ could interact unfavorably with immunosuppressive drugs and may carry risks unaccounted for in traditional use, particularly for transplant patients or those with compromised immune systems. It underscores the need for comprehensive human trials to evaluate CQ's safety profile and caution against the unsupervised use of CQ or other herbal preparations in immunocompromised patients.

4. Relation with hormones

4.1 Estrogen

Estrogen is a crucial hormone involved in various physiological processes, including the regulation of the menstrual cycle, maintenance of bone density, and modulation of cardiovascular health. The ethanolic extract of *C. quadrangularis* appears to exhibit estrogenic effects by elevating serum estrogen levels rather than directly targeting estrogen receptors (Aswar *et al*., 2012).

4.2 Testosterone

Testosterone is a key androgen hormone responsible for the development of male secondary sexual characteristics, muscle mass, and overall vitality. Its role as a glucocorticoid antagonist suggests thatmay also possess anabolic and androgenic properties, potentially contributing to muscle growth and improved physical performance (Kaur and Malik, 2014).

4.3 Cortisol

Cortisol, a glucocorticoid hormone produced by the adrenal glands, plays a vital role in regulating metabolism, the immune response, and stress management. *C. quadrangularis* may mitigate the catabolic effects of cortisol by inhibiting its receptor, indicating its potential as a glucocorticoid antagonist (Chopra *et al*., 1976).

5. Pharmacodynamics

5.1 Bone healing activity

C. quadrangularis is a well-recognized herb for treating bone-related conditions, with numerous studies utilizing various animal models and even human subjects to confirm its potential benefits. These studies collectively indicate that the plant plays a valuable role in managing bone fractures, and osteoporosis, and maintaining bone density. Central to these findings is the hypothesis that *C. quadran gularis* contains anabolic steroids, which may act through estrogenic receptors within bone tissue. Its effectiveness in promoting early bone ossification and remodeling appears to support enhanced metabolism and faster mineral uptake, particularly of calcium, sulfur, and strontium, by osteoblasts (Hamid and Patil, 2023). *C. quadrangularis* functions by stimulating metabolism and improving the absorption of minerals such as strontium, calcium, and sulfur. In an ovariectomized rat model of osteoporosis, the ethanol extract of the entire plant demonstrated anti-osteoporotic effects at dosages of 500 and 750 mg/kg (Siddiquaand Mittapally, 2017).The study investigated the daily use of *C. quadrangularis*. among 161 tribal individuals, including traditional healers and elders, through field trip conversations that documented local names, useful plant

parts, preparation methods, and dosages. The research identified 19 ethnomedical claims from various tribal communities in Andhra Pradesh, along with three dietary recipes. It concluded that *C. quadrangularis* is a widely available medicinal plant primarily used for bone healing, particularly in fractures, and is supported by traditional Ayurvedic texts as Asthishrinkhala. Furthermore, it serves as a dietary source of bio-calcium, indicating its potential benefits for bone health. The findings highlight the need for further pharmacological and clinical investigations to validate these claims and explore its use as a dietary supplement for conditions like osteoporosis and osteopenia (Prasad *et al*, 2018). *C. quadrangularis* is traditionally used for bone remineralization and fracture repair, a role supported by several studies. One study using a petroleum ether extract of *C. quadrangularis* examined its impact on bone cell proliferation and mineralization. In this experiment, mesenchymal stem cells (MSCs) from male Wistar rats were cultured with and without the extract. Results showed that MSCs treated with the extract exhibited significantly higher proliferation and differentiation into osteoblasts, as indicated by alkaline phosphatase (ALP) activity, while untreated cells showed no such differentiation. The treated groups also demonstrated a notably high mineralization rate (Potu *et al*., 2009). The fracture-healing potential of *C. quadrangularis* was demonstrated in a clinical study involving 16 patients with various types of fractures. An external paste of *C. quadrangularis* was applied, and radiological evaluations showed a significant reduction in healing time compared to the control group. Clinically, only one case showed minimal response; however, in most cases, the results were promising, with patients experiencing reduced fracture symptoms such as pain, swelling, and tenderness. This plant proved beneficial for bone injuries, likely promoting the early development of collagen fibers, which facilitates callus formation and faster calcification (Mishra *et al*., 2010). A clinical study demonstrated the beneficial effects of *C. quadrangularis* extract in patients with mandibular fractures, showing significantly faster healing compared to a placebo group. This acceleration in bone repair was attributed to the stimulation of mesenchymal-derived cells, including fibroblasts, chondroblasts, and osteoblasts. The anabolic steroid properties of *C. quadrangularis* were found to notably enhance the fracture healing rate, promoting early regeneration of connective tissues involved in the process and leading to quicker callus mineralization, ultimately reducing the healing time by approximately two weeks (Singh *et al*., 2011).

5.2 Antiosteoporosis activity

Reduced bone mineral density (BMD) leads to osteoporosis, which heightens the risk of fractures due to insufficient bone mass. Natural products that have demonstrated beneficial effects against osteoporosis primarily include phytoestrogens such as lignans, isoflavones, and flavonoids, which mimic estrogen's effects on various tissues in the body. In a 2010 experiment conducted by Manmeet Kumar and colleagues, the stem of *C. quadrangularis* was dried in the shade, and its ethanol extract was subsequently analyzed (Kumar *et al*., 2010). The spectrophotometric study revealed that this extract significantly enhanced alkaline phosphatase activity, approximately 1000 times greater than that observed with diazine (Yamaguchi and Sugimoto, 2000). Another study demonstrated the positive effects of the plant extract in treating induced osteoporosis. This study utilized ovariectomized rats to simulate postmenopausal bone loss associated with osteoporosis. Alkaline phosphatase (ALP) and tartrate-resistant acid phosphatase (TRAP) levels were measured through staining techniques, followed by analysis using microscopy and computer software to correlate staining intensity with the concentration of these biomarkers. The results indicated increased ALP levels, while TRAP levels, a well-established marker of bone resorption *via* osteoclast activity, decreased. Additionally, examining femur morphology corroborated these findings, showing a significant reduction in bone loss (Potu *et al*., 2009). Colle's fracture, frequently observed in individuals over 40, is especially prevalent among women due to osteoporosis following menopause. This fracture typically affects the distal radius at the corticocancellous junction. Siddara and his team conducted a study involving 30 patients with Colle's fracture, who were randomly assigned to one of three groups: Group A received an external application of *C. quadrangularis* Group B received an internal application, and Group C received both internal and external applications. Results showed that the combined internal and external treatment was the most effective among the groups (Siddara *et al*., 2012). Mandibular fractures often lead to significant morbidity and functional impairment, with typical healing times of 4-6 weeks. Nayak (2017) aimed to evaluate the osteogenic potential of *C. quadrangularis* (CQ) in expediting mandibular fracture healing. Thirty patients with mandibular fractures were included, with half receiving CQ in a randomized, open-label, parallel-group design. Serum biomarkers, clinical measures, and CBCT scans were assessed preoperatively and at one, three, and six weeks postoperatively. Results indicated significantly higher levels of alkaline phosphatase and serum phosphorus in the CQ group compared to the control, although changes in radiodensity and serum calcium levels showed no statistically significant difference. While CQ shows promise in enhancing certain healing markers, the findings suggest a need for larger studies to confirm its efficacy as a fracture-healing adjunct (Nayak, 2017). Patel and team. focused on creating a biocomposite treatment for osteoporosis by combining hydroxyapatite and chitosan to enhance calcium and phosphorus absorption in bones. Hydroxyapatite, chosen for its similarity to bone minerals, was synthesized through a chemical reaction and integrated with chitosan via co-precipitation to form hydroxyapatite-chitosan (HA/CS) composites. The HA/CS-drug composite was then prepared with a 12 h incorporation period and examined through XRD, FTIR, and TGA techniques to analyze structural and compositional characteristics. Out of six batches, batches F5 and F6 showed the most favorable properties in terms of porosity, Carr's index, and Hausner's ratio (Patel *et al*., 2024).

5.3 Reduction in joint pain and anti-inflammation

Diabetes, heart disease, and some kinds of cancer are among the many illnesses brought on by persistent inflammation (Shubham *et al*., 2023). *C. quadrangularis* is rich in phytochemicals and shows potential for treating various disorders. This study demonstrates its orexigenic, anti-inflammatory, antidiabetic, and antioxidant properties. Hemolysis inhibition ranged from 8.9 per cent to 25.6 per cent at concentrations between 12.5 and 200 µg/ml. The methanol extract of its stems inhibited porcine pancreatic α-amylase ($p<0.05$) at concentrations of 0.25 and 0.30 mg/ml. Its glucose adsorption capacity decreased with higher glucose concentrations, and increased food intake by *Drosophila* indicates an orexigenic effect. The stem extract exhibited protease activity of 975 U/ml and a specific activity of 3768 U/mg. Strong antioxidant activity was observed, with dose-dependent hydroxyl radical scavenging, suggesting *C. quadrangularis*

as a potential treatment for inflammation and diabetes (Zaki *et al*., 2021). Another study investigated the antihyperalgesic, immunomodulatory, antioxidant, and antiinflammatory properties of aqueous and ethanolic extracts of *C. quadrangularis*. *In vitro* assays assessed the extracts' ability to modulate immune responses (by inhibiting ROS, TNFα, IL-1β, IL-6, and stimulating IL-10), reduce inflammation (*via* protein denaturation and inhibition of 5-LOX, COX-1, and COX-2), and scavenge antioxidants (DPPH, ABTS, NO). *In vivo*, the extracts significantly alleviated hyperalgesia and allodynia in vincristine-induced Wistar rats at doses of 180 and 360 mg/kg. Treated rats also exhibited reduced levels of TNFα, IL-1β, and IL-6 in both serum and nerve tissue, while NGF and IGF levels increased. These results suggest that *C. quadrangularis* could be a promising natural therapeutic for managing neuropathic pain due to its multifaceted immunomodulatory, anti-inflammatory, and antioxidant properties (Feigni *et al*., 2022). Inflammation is a primary contributor to joint pain, as it leads to the production of interleukin-1 β and TNF-α. These cytokines further facilitate cartilage degradation and chondrocyte apoptosis, which exacerbates osteoarthritis. In recent years, aspirin, a potent nonsteroidal anti-inflammatory drug (NSAID), has been utilized for treating rheumatoid arthritis and related conditions. However, its use can result in ulcers, presenting a significant clinical issue that could be addressed through the alternative application of *C. quadrangularis* extracts (Nishida *et al*., 2004). In a pilot study conducted by Blossomer and his team, men aged 20 to 46, who reported chronic joint pain due to intense exercise, participated in the research. The participants were given a daily dose of 3200 mg of *C. quadrangularis* for approximately two months. The results indicated that *C. quadrangularis* was effective in reducing joint pain (Bloomer, *et al*., 2013). Another study demonstrated the anti-inflammatory properties of *C. quadrangularis* extract by assessing its capacity to inhibit COX (cyclooxygenase), 5-LOX (lipooxygenase), and TNF (tumor necrosis factor)-Alpha. The active fraction of the extract exhibited an IC_{50} value of 550 micrograms/ml. The inflammatory response was evaluated by pre-incubating RAW 264.7 cells with various concentrations of the active fraction, followed by an MTT assay. The results indicated a significant reduction in COX, inos (inducible nitric oxide synthase), and TNF-alpha levels in a dose-dependent manner (Bhajade *et al*., 2012).

5.4 Gastroprotective and antiulcer activity

C. quadrangularis is well-regarded in traditional medicine for treating gastric disorders, largely due to its rich composition of carotenoids, triterpenoids, and ascorbic acid, which enhance its nutritional value. Research demonstrates that aspirin use increases lipid peroxidation and elevates xanthine oxidase and myeloperoxidase levels in the gastric mucosa, resulting in cellular and subcellular damage. However, these harmful effects can be mitigated by the antilipid peroxidative effects of *C. quadrangularis* extract (CQE) (Viswanatha *et al*., 2010). Studies have investigated the influence of CQE on experimentally induced gastric ulcers by assessing levels of tumor necrosis factor-α (TNF-α), interleukins, microvascular permeability, nitric oxide synthase-2 (NOS-2) activity, mitochondrial antioxidants, lipid peroxidation, and DNA damage. The results indicate that aspirin causes an increase in lipid peroxidation, xanthine oxidase, and myeloperoxidase levels while reducing superoxide dismutase (SOD), catalase (CAT), and selenium-glutathione peroxidase activities in the gastric mucosa, leading to mucosal injury. CQE effectively counteracts this damage and protects against oxidative DNA damage by decreasing DNA fragmentation, thereby preventing cell death. Pre-treatment with CQE significantly improved the gastric mucosa's condition in ulcerated rats (Ayesha and Sirisha, 2017).

Studies on the ethanol extract of *C. quadrangularis* roots have shown antiulcer effects in rats with ethanol- and indomethacin-induced gastric ulcers. Pre-treatment with the extract significantly reduced ulceration in the gastric lining compared to the control. This protective effect was dose-dependent in both ulcer models, with a notable reduction ($p<0.05$) in the number of ulcer lesions observed in rats given varying doses of the extract or ranitidine (100 mg/kg body weight) relative to the control groups. These findings suggest that *C. quadrangularis* root extract has antiulcer properties (Enechi *et al*., 2013). Another study demonstrated that the methanol extract of *C. quadrangularis* has antiulcer properties in a rat model of experimentally induced ulcers. This effect was achieved by reducing gastric secretions and increasing glycoprotein levels. The methanol extract also promoted the healing of aspirin-induced gastric mucosal injury in rats, likely through its antioxidant mechanism. Compounds like triterpenoids and beta-sitosterol in the methanol extract exhibited antilipid peroxidation effects, thereby helping to prevent gastric damage (Somova *et al*., 2003). Aspirin consumption increases lipid peroxidation, xanthine oxidase, and myeloperoxidase activities, while lowering selenium-dependent glutathione peroxidase activity in the gastric mucosa, which results in cellular and subcellular mucosal damage.The gastroprotective effect of CQE appears to work through its antioxidant action, reducing oxidative processes, and lowering neutrophil infiltration (Devi *et al*., 2005).The methanol extract demonstrated notable antiulcer properties in a rat model with experimentally induced ulcers, primarily by reducing gastric secretions and increasing glycoprotein levels. It promoted healing in rats with aspirin-induced gastric mucosal injury *via* its antioxidative mechanism. The presence of triterpenoids and β-sitosterol in the methanol extract contributes to its antilipid peroxidative action, thereby preventing gastric damage (Perez Gutierrez and Vargas, 2006). In addition to preclinical studies, *in vitro* investigations have also been conducted to assess the ant helicobacter pylori activity of *C. quadrangularis* (CQL) extracts (Austin *et al*., 2003; Austin *et al*., 2004). These studies evaluated the anti-*H. pylori* potential of two CQL variants, variant II (round-stemmed) and variant I (square-stemmed), in both vegetative and flowering stages. Among the extracts tested, the chloroform extract of the flowering form showed the highest activity, with minimum inhibitory concentration (MIC) and minimum lethal concentration (MLC) values of 40 µg/ml for variant II and 30 µg/ml for variant I, demonstrating the significant antiulcer potential of the herb. Further studies are needed to explore the impact of seasonal variations on the constituents and corresponding anti-*H. pylori* effects of CQL.

5.5 Antimicrobial and antibacterial activity

The methanol (90%) and dichloromethane extracts of *C. quadrangularis* stems exhibit antibacterial properties against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*, as well as mutagenic effects on *Salmonella microsome*. Additionally, both stem and root extracts have shown antimicrobial activity. The alcoholic extract of the aerial parts demonstrated antiprotozoal effects against *Entamoeba histolytica*, while the stem's alcoholic extract exhibited activity against *E. coli*. Moreover, the methanol and dichloromethane extracts of the entire plant were evaluated for *in vitro* antiplasmodial

activity. The dried stems, extracted with ethyl acetate and methanol, also displayed antibacterial activity, particularly against Gram-positive bacteria such as *Bacillus subtilis* and *Staphylococcus aureus* (Rajpal, 2005). An antibacterial compound (Cp) was extracted from the stem of *C. quadrangularis*, achieving a 5.39-fold increase in specific activity and an 8.67 per cent recovery. SDS-PAGE analysis estimated the enzyme's molecular weight at 39 kDa, and it appeared as a single band on Native-PAGE. The protease activity was optimal at pH 6.0 and 50°C, with stable activity across a pH range of 3 to 10, retaining over 90 per cent relative activity. Metal ions like $Mg^{2}z$ and $Ca^{2}z$ enhanced its protease activity. Cp displayed significant antibacterial effects, yielding inhibition zones of 21 mm and 20 mm against *Bacillus cereus* and *Bacillus megaterium*, respectively, at a concentration of 4.74 U/ml. Transmission electron microscopy confirmed Cp's ability to degrade the bacterial peptidoglycan layer (Muthu *et al*., 2017). Another study aimed to assess the antibacterial properties of *C. quadrangularis* (CQ) against *Porphyromonas gingivalis*, a key pathogen involved in periodontal disease. Aqueous and ethanolic extracts of CQ were prepared using a Soxhlet extractor, and their antibacterial activity was tested at various concentrations, with the minimum inhibitory concentration (MIC) determined through broth microdilution. The results showed that the ethanolic extract of CQ, when mixed with 10 per cent dimethyl sulfoxide (DMSO), exhibited greater inhibition of *P. gingivalis* compared to the aqueous extract. Both extracts showed MIC values of 500 µg/ml, but the ethanolic extract dissolved in DMSO demonstrated a stronger effect with a lower IC_{50} value of 194.36 µg/ml. These findings suggest that CQ has significant potential for the treatment of periodontal disease (Nair *et al*., 2024).

5.6 Antiobesity and antihyperlipidemic activity

An aqueous extract of *C. quadrangularis* leaves and stems, administered at a dose of 300 mg, demonstrated efficacy in reducing body fat and enhancing blood markers linked to metabolic syndrome (26). Additionally, this extract was shown to aid in weight reduction, improve blood metrics related to metabolic syndrome, and elevate serotonin levels in individuals who are obese or overweight (Kuate *et al*., 2015). It has been observed that *C. quadrangularis* inhibits lipid accumulation effectively in 3T3-L1 adipocytes without inducing cytotoxic effects. Additionally, it downregulated mRNA expression of genes related to adipogenesis and lipogenesis, including fatty acid binding protein, fatty acid synthase, lipoprotein lipase, stearoyl-CoA desaturase-1, and acetyl-CoA carboxylase. These findings indicate the plant's potential antiobesity properties, achieved by reducing key adipogenic and lipogenic gene and protein expressions (Lee *et al*., 2018). The antihyperlipidemic effects of *C. quadrangularis* (CQL) are believed to be attributed to its phytosterols (such as stigmasterol, β-sitosterol, and ketosteroid) and flavonoids (including kaempferol, quercetin, and daidzein) (Karri *et al*., 2019). Phytosterols may work by lowering LDL cholesterol levels or decreasing intestinal cholesterol absorption, which can lead to increased fecal excretion of cholesterol (Racette *et al*., 2010; Camil and Ravi, 2020). An aqueous extract from the leaves and stems of *C. quadrangularis* at a 300 mg dose proved effective in reducing body fat and improving blood markers linked to metabolic syndrome, it aided in weight reduction, enhanced blood parameters related to metabolic syndrome, and increased serotonin levels in individuals who were obese or overweight (Nash *et al*., 2019; Kuate *et al*., 2015). Another study investigated the impact of *C. quadrangularis* extract on lipid profiles in rats with hyperlipidemia induced by a high-fat diet. At dosages of 800 and 1200 mg/kg, the SGPT and SGOT levels in groups 5 and 6 showed significant changes ($p<0.05$), with a more pronounced effect seen in SGPT. However, none of the doses-400, 800, or 1200 mg/kg-produced statistically significant changes in SGOT, though both SGPT and SGOT levels decreased in a dose-dependent manner. In terms of renal function, statistical analysis revealed that urea levels in groups 5 and 6, which received 800 and 1200 mg/kg, differed significantly ($p<0.05$), while creatinine levels showed no significant change. When assessing HDL and LDL, groups 5 and 6 exhibited significantly increased HDL levels ($p<0.05$). Additionally, group 5, which received 800 mg/kg, displayed a statistically significant reduction in triglycerides ($p<0.05$), as well as in total cholesterol levels ($p<0.05$) (Haider *et al*., 2024).

5.7 Antidiabetic activity

According to the World Health Organization, around 422 million individuals globally are affected by diabetes, with an approximate annual mortality rate of 1.6 million. It has long been known that diet plays a significant role in managing diabetes mellitus (Jyoti *et al*., 2023). Thus, effective treatment options remain essential, encompassing conventional allopathic medications, lifestyle adjustments, Ayurveda, and other alternative medicine systems. *C. quadrangularis* formulations have demonstrated the potential in reducing blood glucose levels in studies involving obese individuals (Oben *et al*., 2006). Additionally, administering ethyl acetate and hydroalcoholic extracts of *C. quadrangularis* at a dose of 200 mg/kg significantly lowered blood glucose levels in alloxan-induced diabetic rats (Srivastava, 2011). Lekshmi and her team highlighted the antidiabetic potential of *C. quadrangularis* stem extract, which operates by enhancing the body's antioxidant defence mechanisms. The ethyl acetate fraction, abundant in quercetin, may offer benefits as a dietary supplement to help mitigate diabetic complications. Furthermore, the plant's antidiabetic properties are linked to strengthening the antioxidant system and reducing inflammatory responses (Lekshmi *et al*., 2015).The antidiabetic potential of *C. quadrangularis* stem extract operates through enhancement of the antioxidant defense system. The ethyl acetate fraction, which is high in quercetin, may be advantageous as a dietary supplement to help mitigate diabetic complications. Additionally, the plant's antidiabetic effects are linked to its ability to strengthen the antioxidant defense system and reduce inflammatory responses (Sibi *et al*., 2020). A study examined the antihyperglycemic effects of ethanol extract from *C. quadrangularis* (EtCQ) leaves on alloxan-induced diabetic rats. EtCQ and glyburide were administered to the rats, and glucose levels were measured over short-term (24 h) and long-term (28 days) periods. In the 28-day study, daily dosing of EtCQ and glyburide significantly lowered serum glucose levels compared to untreated diabetic rats, with the highest EtCQ dose (400 mg/kg) also preventing weight loss. In an oral glucose tolerance test (OGTT), EtCQ at doses of 200 and 400 mg/kg increased the glucose threshold shortly after glucose administration. Overall, EtCQ at 400 mg/kg showed the strongest antihyperglycemic effect, indicating that *C. quadrangularis* ethanol extract has significant potential for lowering blood glucose (Chaudhari *et al*., 2013). A study explored the protective effects of ethanolic extract of *C. quadrangularis* (EECQ) on steatohepatitis associated with type 2 diabetes (DM), specifically through the inhibition of NOX4. Steatohepatitis was induced in Sprague Dawley rats by feeding them a high-fat diet for 12 weeks, followed by

treatment with EECQ at a dose of 200 mg/kg for six weeks. Various tests, including glucose and insulin tolerance, along with liver histology, confirmed the presence of steatohepatitis in the DM rats, characterized by increased serum lipid levels, aminotransferases, and liver damage. However, EECQ treatment prevented these abnormalities, maintaining normal glucose and insulin tolerance. In addition, the expression of advanced glycation end products (AGEs) and its receptor (RAGE) was elevated in diabetic rats, alongside increased NOX4 expression, oxidative stress markers, and inflammatory cytokines. EECQ successfully mitigated the elevated levels of these markers. Overall, the study suggests that EECQ protects against steatohepatitis in DM rats by reducing oxidative stress and inflammation. Further research in humans is needed to confirm its potential as a treatment for DM-induced steatohepatitis (Syed *et al*., 2021). A study assessed the impact of *C. quadrangularis* (CQ) on fetal skeletal ossification delays caused by maternal diabetes. Female Wistar rats were induced with diabetes before mating and divided into three groups: normal control, diabetic control, and diabetic CQ treatment (PECQ 500 mg/kg). After delivery, pups were examined for skeletal ossification. The diabetic control group showed fewer ossification centers and less ossification compared to the normal group. However, PECQ treatment during pregnancy significantly improved ossification in the diabetic CQ group. The results suggest that PECQ can help alleviate diabetes-related delays in fetal skeletal ossification (Srinivasa *et al*., 2014).

5.8 Hepatoprotective activity

The liver plays a crucial role in metabolizing various drugs, with the CYP450 enzyme and its subclasses being primarily responsible for this function. However, when these enzymes are inhibited by drug metabolites, it can lead to liver diseases. To mitigate these effects, the use of natural products is strongly recommended. In our study, we investigated the hepatoprotective and antioxidant properties of *C. quadrangularis*. The results indicated that the ME-CQ extract demonstrated hepatoprotective effects by reducing liver tissue damage caused by isoniazid and rifampicin, as well as promoting hepatocyte regeneration. Further research is needed to explore its mechanism of action (Sameer *et al*., 2020). The hepatoprotective potential of *C. quadrangularis* extract was evaluated in a study involving rats that had been pre-treated with isoniazid to induce liver toxicity. The efficacy of the extract was assessed by monitoring biomarkers, including aspartate transaminase (AST), alanine transaminase (Alt), alkaline phosphatase (Alp), and bilirubin. Results from this analysis, conducted on liver samples of sacrificed animals with ERBA diagnostic kits, indicated elevated levels of these biomarkers. Additionally, the study observed a notable reduction in lipid peroxidation alongside enhanced antioxidant activity, as evidenced by reduced levels of glutathione (gsh), superoxide dismutase (SOD), and catalase (CAT) (Swamy *et al.,* 2010). A study aimed to evaluate the therapeutic effects of aqueous extracts of *C. quadrangularis* and *Jatropha gossypiifolia* on acetaminophen-induced liver damage in mice. The mice were treated with the plant extracts (50 and 100 mg/kg) and silymarin (50 mg/kg), a known hepatoprotective agent, four hours after acetaminophen administration (300 mg/kg). Treatment lasted for two days, and various liver function markers and histological assessments were performed. Results indicated that acetaminophen caused significant liver damage, including increased levels of alanine aminotransferase, bilirubin, and oxidative stress markers. However, the plant extracts significantly reduced body weight loss, normalized liver enzyme levels, and improved oxidative stress markers. Additionally, both extracts reduced liver cell damage and inflammatory cell infiltration. These results support the potential use of *C. quadrangularis* and *J. gossypiifolia* extracts in the treatment of liver diseases (Temdie *et al*., 2023).

5.9 Anticancer activity

The potential anticancer and antitumor activities of *C. quadrangularis* have been demonstrated across several types of cancers, including breast cancer (in MCF-7 cell lines and DMBA-induced models), leukemia (HL-60 cell lines), osteosarcoma (MG63 human cell lines), as well as Dalton's ascitic lymphoma and Ehrlich ascites carcinoma (Bafna *et al*., 2021). Numerous scientific studies have documented the *in vitro* anticancer effects of *C. quadrangularis* methanolic and ethanolic extracts, revealing that both extracts contain flavonoids, polyphenols, and other bioactive components. Flavonoids, a key class of compounds within these extracts, demonstrate anticancer properties across various body tissues. The proposed mechanisms include initiation of apoptosis, antiproliferative actions, enzyme detoxification, modulation of the immune system, estrogenic/antiestrogenic effects, and pro-oxidant activity (Mutha *et al*., 2021; Medzhitov, 2010). *In vitro* studies utilized three distinct cell lines: MCF-7 for breast cancer, HL-60 for leukemia, and MG-63 for human osteosarcoma. The compounds quercetin, kaempferol, and others present in *C. quadrangularis* (CQL) boost antioxidant activity by neutralizing free radicals and promoting apoptosis, which contributes to the inhibition of tumorigenesis in HL-60 leukemic cells (Gibellini *et al*., 2010). Therefore, CQL has the potential to be developed as a cancer protective agent, necessitating further studies to explore the detailed mechanisms of cancer cell inhibition.The study investigated the anticancer and antioxidant effects of ethanolic extracts of *C. quadrangularis* on ovarian cancer (PA1) cells. The plant was dried, ground, and extracted with ethanol using a Soxhlet device. Phytochemical analysis revealed the presence of bioactive compounds. The extract showed significant antioxidant activity in a dose-dependent manner, compared to ascorbic acid, as measured by DPPH. *In vitro* testing on PA1 cells showed strong anticancer effects, with an IC_{50} value of 482.057 ± 113.857 µg/ml. The extract induced apoptosis in the cancer cells, confirmed by DAPI and carboxy-H2DCFDA staining. Molecular docking studies identified binding interactions between quercetin-3-O-alpha-L-rhamnopyranoside and erucic acid with the threonine tyrosine kinase (TTK) enzyme, with quercetin-3-O-alpha-L-rhamnopyranoside showing a strong binding affinity. These findings support *C. quadrangularis* ethanolic extract as a promising chemotherapeutic agent for ovarian cancer, particularly due to its anticancer compound, quercetin-3-O-alpha-L-rhamnopyranoside (Zhao *et al*., 2024). Another study explored the antiproliferative effects of ethanolic *C. quadrangularis* (CQ) extract on human cervical adenocarcinoma (HeLa) cells and conducted in silico analysis of active compounds against the apoptosis enzyme caspase-3. The extract reduced HeLa cell viability in a dose-dependent manner (25-300 µg/ml), while showing no toxicity to normal kidney epithelial cells (NRK-52E). CQ extract increased reactive oxygen species (ROS), induced nuclear condensation, decreased mitochondrial membrane potential (MMP), and promoted apoptosis in HeLa cells, as indicated by annexin V-FITC positivity. It also arrested the cell cycle at G0/G1 and G2/M checkpoints and activated caspase-3. Molecular docking revealed strong binding of CQ phytocomponents to caspase-3. The drug-likeness and toxicity analysis indicated that these phytocomponents could be safe and effective drug candidates. This study supports the potential of CQ extract as a chemotherapeutic agent for cervical cancer treatment (Siddiqui *et al*., 2021).

Table 2: Summary of animal model studies on *C. quadrangularis* extract

Study	Animal Model / Cell Line	Dose (mg/kg or µg/ml)	Route of Administration	Effects	References
Study on insulin resistance	Perimenopausal and postmenopausal rats	200 mg/kg (EECQ), 100 mg/kg (metformin)	Oral	Improved insulin sensitivity, reduced body fat, normalized APPL1, IRS1, Akt1, and GLUT4 expression	Syed *et al*., 2022
Anticancer and antimicrobial study	A549 Lung cancer cells	7.8 - 1000 µg/ml	*In vitro*	Significant decrease in tumor cell viability, IC_{50} at 65.2 µg/ml	Payani *et al*., 2023
Bone turnover and postmenopausal Study	Ovariectomized rats	2 g/kg	Oral (CQ in diet)	Protected bone mass, increased estradiol, decreased bone resorption markers	Guerra *et al*., 2019
Anti-hyperglycemic study	db/db mice	50, 100, 200 mg/kg	Oral (*via* gavage)	Reduced body weight, fasting glucose, HbA1c, and insulin levels; enhanced glucose tolerance	Kim*et al*., 2024
Osteoporosis and bone health Study	Ovx mice (estrogen-deficient)	500 mg/kg	Oral (twice daily)	Improved bone microarchitecture, enhanced BMD in femoral and tibial bones, no cytotoxic effects	Azam *et al*., 2023
Obesity and metabolic syndrome study	Overweight participants	300 mg	Oral (daily capsule)	Reduced body fat (8.9% via impedance, 12.8% via DEXA); decreased waist and hip circumference	Nash *et al*., 2018
Glioblastoma multiforme study	U87 MG glioblastoma cells	0.1-0.8 mg/ml	*In vitro*	Induced cytotoxicity, cell cycle arrest, cell death via ER stress, autophagy, and mitochondrial apoptosis; suppression of pro-survival ERK and STAT3 pathways, DMSO ≤ 0.8%	Cheng *et al*., 2023
Bone fracture healing study	Wistar rats	400 mg/kg (oral), topical	Oral (P.O.), topical (on-site)	Early recovery of damaged bones with oral administration; improved healing with topical application compared to untreated control	Yadav *et al*., 2024
Bone healing with combined extracts study	Wistar albino rats	100 mg/kg	Oral	Increased serum calcium levels, enhanced femur thickness, complete bone bridging on radiographs; safe for organs throughout study	Ramachandran *et al*., 2021
Wound healing efficiency study	Wistar albino rats	20% and 40% ethanolic extract	Topical	40% ethanolic extract ethosomal gel found to be the best for wound healing activity compared to standard mebo ointment	Siddiqua and Mittapally, 2017

6. Therapeutic actions of *C. quadrangularis* extracts

Several studies have documented the diverse biological actions associated with different extracts of *C. quadrangularis* (CQ). Each type of extract demonstrates distinct activities: the ethanol extract is noted for its anti-osteoporotic and osteoblastic properties, while the methanol extract exhibits antimicrobial, antioxidant, anti-ulcer, and osteoblastic effects. The ethyl acetate extract influences gene expression and shows antioxidant and antimicrobial activity. The aqueous extract has antimicrobial, antiparasitic, CNS depressant, and anti-epileptic properties. Additionally, the active acetone fraction offers antiinflammatory effects, the petroleum ether extract supports anti-osteoporotic activity, and the chloroform extract possesses antibacterial properties. Silver nanoparticles derived from CQ present antimicrobial, anti-inflammatory, immunomodulatory, and hypolipidemic benefits, demonstrating high potential with minimal adverse effects.

Table 3: Extracts of *C. quadrangularis* and their actions

Formulation	Actions
Ethanol extract	Anti-osteoporotic and osteoblastic activity
Methanol extract	Antimicrobial and antioxidant activity, antiulcer activity, osteoblastic activity
Ethyl acetate extract	Gene expression, antioxidant and antimicrobial activity
Aqueous extract	Antimicrobial activity, antiparasitic activity, CNS depressant activity, antiepileptic activity
Active acetone fraction	Anti-inflammatory activity
Petroleum ether extract	Anti-osteoporotic activity
Chloroform extract	Antibacterial activity
Silver nanoparticles	Silver nanoparticles from CQ displayed antimicrobial, anti-inflammatory, immunomodulatory and hypolipidemic activities

Source: Jain *et al.* (2020).

7. Utilization of Veldt grape

Indigenous plants, used traditionally for food and medicine, have gained popularity for enhancing nutrition and addressing food insecurity. *C. quadrangularis*, one such plant, was used in this study to develop an energy bite to increase awareness and acceptance among young adults in South Africa. Two energy bite versions, 4 g and 6 g of *C. quadrangularis*, were tested for sensory appeal, safety, nutrition, and shelf-life. Nutritional analysis showed the bites were low in fat and salt, with no significant sensory differences. A supporting video with recipes helped increase interest in using *C. quadrangularis*, suggesting that a trendy food product and educational tool can boost the acceptance of this indigenous plant (Pal *et al*., 2024). In another study Veldt grape stem powder was incorporated into refined wheat flour to create a bread product, with a control sample made from 100 per cent refined flour. Bread is a staple food in India, known for its soft texture, pleasant aroma, and moist mouthfeel. As consumer interest in functional foods grows, the addition of Veldt grape stem powder enhances the bread's nutritional profile, making it richer in protein, dietary fiber, and minerals compared to standard wheat flour bread. Sensory evaluations indicated that up to 4 per cent Veldt grape stem powder can be added without compromising acceptability. The high levels of beneficial phytochemicals in *C. quadrangularis* suggest its medicinal value. Overall, this fortified bread is both nutritionally advantageous and economically viable, making it a promising option for health-conscious consumers (Nawghare, 2017).

This study focused on fortifying rice and flour with *C. quadrangularis* (CQ) stem powder to address nutritional deficiencies and enhance bone health. Mineral analysis indicated that CQ stems contain sufficient calcium, magnesium, and moderate phosphorus levels to meet recommended dietary allowances (RDA). The fortification was achieved through vacuum impregnation and blending. The effectiveness of the fortified rice (CQFR) and flour (CQFF) was assessed in animal models of osteoporosis and osteoarthritis, revealing significant recovery from calcium deficiency and related physiological damage, as confirmed by hematology, radiology, and histopathological analyses. This research underscores the potential of CQ-fortified rice to improve skeletal health, particularly in regions where rice is a staple food and micronutrient deficiencies are prevalent, thus offering a practical solution for populations suffering from skeletal complications (Lakshmanan *et al*., 2021).This research aimed to develop and standardize nutraceutical products, specifically biscuits and cookies, according to FPO specifications, incorporating RF dried *C. quadrangularis* (Veldt grape) powder at 5 per cent, 10 per cent, and 15 per cent levels in biscuits, and Veldt grape extract in ghee for cookies. Nutritional analysis revealed the RF dried stem contained notable amounts of phytosterols, ascorbic acid, phenols, calcium, iron, and selenium. Sensory evaluations showed that biscuits with 10 per cent Veldt grape powder received the highest scores, despite causing slight throat irritation. Similarly, cookies made with 10 per centveldt grape powder extract were well accepted by trained panelists. Overall, both products demonstrated good consumer acceptance and satisfactory antioxidant and mineral content, although higher percentages of veldt grape powder may lead to throat irritation in sensitive individuals (Karadbhajne *et al*., 2014).

8. Conclusion

Veldt grape (*C. quadrangularis*) is a valuable medicinal plant with a wide range of therapeutic uses, particularly in promoting bone health and managing metabolic disorders. Its diverse phytochemical composition, rich in bioactive compounds, supports both its traditional and modern medicinal applications. Additionally, its potential as a functional food ingredient offers a promising solution for addressing nutritional deficiencies, especially in regions where the plant is native. While traditional uses and preliminary studies

show positive outcomes, comprehensive clinical trials are urgently needed to confirm its safety and efficacy for broader use. Integrating *C. quadrangularis* into modern nutraceutical and dietary practices could improve health, particularly in populations vulnerable to osteoporosis and similar conditions. Future research should aim to explore its mechanisms of action, refine extraction methods, and evaluate its long-term effects in humans to fully unlock its therapeutic benefits.

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Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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