

Cissusquadrangularis and its medicinal applications - A Review

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Abstract:

Plant-based medicinal products are evolving trends currently in all research areas. Traditional systems of medicine such as Ayurveda and Siddha prefer *Cissusquadrangularis* for various therapeutic purposes such as fracture healing, colic, malaria, epilepsy, fever, piles, gout, skin diseases, etc., It is a perennial climbing herb called Devil's Backbone or Veldt Grape, traditionally known as "Asthisamharaka" or "Hadjod" (Bone setter) which belongs to Vitaceae family extensively distributed throughout the tropical areas, especially Asia and Africa. It has diverse pharmacological actions like antibacterial, antioxidant, anti-inflammatory, antiepileptic, antiulcer, anthelmintic, etc., The present review emphasizes the taxonomy, morphology, distribution, and medicinal uses of this plant with more updated information on its scientific research and results available in various aspects of this plant including pharmacology and its phytochemical features. This review also focuses on the up to date information on dental applications of this plant.

Keywords; *Cissusquadrangularis*, phytochemicals, pharmacology, herbs

Introduction:

Plants are the significant natural resources for traditional medicines in India. It is said that more than 2000 tons of medicinal plants are required as raw materials per year in which more than 7800 manufacturing units are involved in the production of Plant-based health products and herbal medicines in India (1). More than 1500 herbal products are sold as traditional medicines (2). In the current status, there has been increasing research interest in natural resources, especially plants. Nearly all parts of plants act as an important source for the formation of new drugs (3). *Cissusquadrangularis* is a commonly used medicinal plant having enormous therapeutic potential and is most often used in Ayurvedic and Siddha medicines.

Ecological background:

Cissusquadrangularis is a succulent perennial medicinal herb widespread throughout the tropical countries of the world. It favors warm tropical climate and is distributed throughout the hotter parts of Philippines, Ceylon, Bangladesh, Thailand, India, West Africa and Java (4). However it is extensively found in tropical forest areas of Africa and Asia (5,6,7)

Taxonomic hierarchy(8,9): Table no.1

| | |
|---------------|------------------------|
| Kingdom | Plantae |
| Subkingdom | Viridiplantae |
| Infrakingdom | Streptophyta |
| Superdivision | Embryophyta |
| Division | Tracheophyta |
| Subdivision | Spermatophytina |
| Class | Magnoliopsida |
| Superorder | Rosanae |

| | |
|---------|----------------|
| Order | Vitales |
| Family | Vitaceae |
| Genus | Cissus |
| Species | Quadrangularis |

Vernacular names: Table no.2

| | |
|---|----------|
| Pirandai | Tamil |
| Vajravalli,Asthisamaraka, Asthisamharaka | Sanskrit |
| Hadjod | Hindi |
| Kandvel | Marathi |
| Hadjor | Punjabi |
| Hadbhanga | Oria |
| Vedhari | Gujarati |
| Nalleru | Telugu |
| Veldtgrape,Edible Stemmed Vine | English |

Morphological characteristics:

Cissusquadrangularis is a succulent perennial,climbing herb of height up to 1.5 m with simple tendrils. It has leaves of 2.5-5 cm length and ± 5 cm width which are lobed (3-7), either in kidney shape or ovate,glabrous,serrate, and their base is rounded (8,9). It consists of small,bisexual greenish-white flowers and a deciduous,short calyx which is in cup shape and petals are 4-5 in number (10). It has one-seeded succulent obovoid or globose dark purple or black berries which are pyriform or ellipsoid in shape(8). Its stem is buff-colored with a greenish tinge and branching dichotomously where there are the presence of nodes and internodes with lengths of 8-10cm and widths of 1-1.5 cm(9).

Phytochemical features:

Literature has shown that there are various studies revealed that *Cissusquadrangularis* has many phytochemical constituents such as Vitamin C, triterpenoids, stilbenederivatives, flavonoids, phytosterols, phenols, carotene, β -sitosterol, alpha and β -amyrins, etc(11-15) and these constituents are responsible for various therapeutic purposes in medical and dental fields. Among all those, the major constituents are β -sitosterol, ketosteroid, triterpene, two asymmetrical tetracyclic triterpenoids, calcium, and ascorbic acid(16,17).

Tableno.3

| Parts of plant | Leaves | Stem | Root | Aerial part | Plant's Ash |
|----------------------------|--|---|---|---|---|
| Phytochemical constituents | Piceatannol, alicyclic lipids,parthenocissus, resveratrol, pallidol(14,18) | 1. Phosphorus and calcium ions (4 % by wt). 2. Calcium oxalate, taraxerol,Taraxerol acetate, isopentadecanoicacid, and 3-1-methyl tritriacontanoic | Sodium,calcium, magnesium, potassium,cadmi um, lead, copper, zinc and iron(11,14) | 1.7-Oxo-Onocer-8-ene-3 β 21 α diol(21) 2.A 100 g of paste contains Ascorbic acid (479 mg) and | Sodium, calcium, magnesium, potassium and potassium tartrate.(11,14). |

| | | | | | |
|--------------------------|---|---|---|---|---|
| | | <p>acid.(14).</p> <p>3.β-sitosterol, ketosterol, alpha and beta-amyrin,tannins,saponins, phenols,carotene and vitamin.(19,20)</p> | | <p>carotene (267 mg)(11)</p> <p>3.Ascorbic acid, Calcium, β-sitosterol,triterpene, two asymmetrical tetracyclic triterpenoid,ketosteroid and Carotene A(11)</p> <p>4. Asymmetric tetracyclic triterpenoids such as d-amyrin; 4'-tetrahydroxy biphenyl; d-amyrone; 21b-diol; onocer-7-ene-3a; & 3,3',4,3,3',4,4'-tetrahydroxy biphenyl(22)</p> <p>5. Cellulose fiber from CQ - 82.73% cellulose and 0.18% wax provides good strength and low density than that of glass fiber and carbon fiber. (23)</p> | |
| Therapeutic uses | Indigestion, Dyspepsia, and irritable bowels. | <p>Wound, skin infections, eye diseases, piles, constipation, irregular menstruation, anemia(Scurvy) and otorrhoea</p> <p>Burns And wounds , Poisonous insect bites and Asthma. Bone fracture swelling.</p> | Lumpy skin diseases, Wounds, and Also as tick repellent | Bone fractures. | As a baking powder substitute . Dyspepsia Indigestion |
| Pharmacological activity | Antioxidant Analgesic | Anti oxidant Anti – inflammatory | Antioxidant Antimicrobial | Induced differentiation and Inhibit | Anti inflammatory Antioxidant |

| | | | | | |
|--|--|--|----------------|---|--|
| | | Anti diabetic activity Anti ulcer Antiobesity Analgesic Anti cancer Anti osteoporotic | Anticonvulsant | proliferation Antiosteoporotic Anti infertility Antimicrobial Wound healing Anti oxidant Anti inflammatory Anticonvulsant Anti diabetic Antiobesity | |
|--|--|--|----------------|---|--|

Medical uses:

1. Weight loss and Obesity (Antiobesity):

Obesity is a major world-wide health problem increasing in both developing and developed countries(24). It has been evaluated that worldwide obese population is 6 billion which can increase upto 10 billion by 2025 (25). It is a multifactorial disease associated with high caloric diet, genetic influence, unhealthy lifestyles etc.,(26,27). It acts as one of the potential risk factors in developing various metabolic syndromes like type II diabetes mellitus, dyslipidemia, atherosclerosis, varioustypes of cancer, hypertension, stroke, dyslipidemia, and cardiovascular diseases(24,26,28). Changes in waist circumference in obese patients with metabolic complications tend to be useful predictors of CVD risk factors(29,30).

Literature stated that *Cissusquadrangularis* has the potential of reducing obesity in humans, treatment with CQR-300 resulted in antiobesity effects by downregulation of expression levels of adipogenesis, inturn inhibition of accumulation of lipids and also shown no cytotoxicity against 3T3-L1 adipocytes(31). Presence of fiber extracts and phytosterols in *Cissusquadrangularis* are responsible for anorexiant and anti-lipase properties that inhibit the absorption of dietary fats and raise serum serotonin levels that augment satiation(32).

Julius Oben et al conducted the randomized, double-blind, placebo-controlled study involving 123 overweight and obese persons (47.2% male; 52.8% female; ages 19–50). Among those, 92 obese (BMI >30) patients were divided randomly into three groups; placebo, formulation/no diet, and formulation/diet. The 31 overweight participants (BMI = 25–29) acted as the fourth (no diet) group treated with formulation alone. The results of this study found that *cissusquadrangularis* significantly reduced weight and central obesity, as well as in fasting blood glucose, lipid profile and C-reactive protein in treated groups with formulation irrespective of diet(33). Recently a randomized trial in humans was done by Saimaichatree et al stated that CQ augmented UCP1 mRNA in human white adipocytes and reduced waist and hip circumferences in obese humans due to the browning of human white adipocytes (34).

2. For Gastritis and Gastroprotective effect (Antiulcer):

Cissusquadrangularis is an indigenous herb commonly employed as Ayurvedic treatment for gastric ulcers. Many studies stated that the ulcer-protective property of a methanolic extract of *Cissusquadrangularis* was similar to that of the reference drug sucralfate.(35-37). Few studies showed that 500 mg/kg *Cissus* given for 10 days resulted in extensively raising the defensive factors of intestinal mucosa such as glycoproteins, mucosal cell proliferation, lifespan of cells, mucin secretion etc., (38-42).

3. In Inflammation cases (Anti Inflammatory):

Presence of flavonoids, bioflavonoids, several flavones, flavonols, and flavonoids in CQ are responsible for its antiinflammatory activity through the inhibition of lipooxygenase pathway. Both β sitosterol and Luteolin were proved to have antiinflammatory action(43,44). However, the mechanism of CQ is to inhibit both lipoxygenase and cyclooxygenase pathways and stated as a dual inhibitor of arachidonic acid metabolism(14,45,46). There were various preclinical studies that proved its antiinflammatory activity(46-48). Quercetin is another constituent of CQ having antiinflammatory activity by inhibiting PLA2 which modulates the release of inflammatory mediators such as arachidonic acid during inflammation.(49). According to Garcia-Lafuente et al, there were different mechanisms exhibited by high flavonoid content such as modulation of proinflammatory cytokines, modulation of pro-inflammatory gene expression, modulation of inflammatory cells, inhibition of arachidonic acid or nitric oxide synthase(50). Srisook et al concluded that CQ has anti-inflammatory potential due to suppression of NF-kB activation(51).

4. In burns and wound healing (Antibacterial property):

Bahar Mummed et al conducted an in vitro study to investigate the antibacterial potential of methanolic extracts of Nine Ethiopian plants. CQ was one among them. Agar well diffusion and Broth dilution methods were used to assess the antibacterial action of nine plants against four bacterial species such as *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. One among these plants was CQ. The results showed highest inhibitory activity of CQ(18.3 mm) against standard and clinical strains of *S. aureus*(52). This

observation of CQ against *S.aureus* was more prominent than a study conducted by Mengiste et al(53). These studies reveal that CQ can be used as an antibacterial agent. Similar studies showed good antibacterial activity of CQ (54-58).

5. In Cancer (Antioxidant property):

An imbalance between antioxidants and pro-oxidants causes consequences that lead to Oxidative stress, which acts as a key factor in chronic systemic diseases such as hypertension, gastrointestinal, heart, and inflammatory diseases (59).

Numerous photochemical and biological reactions produce highly toxic superoxide radicals. Studies have shown the scavenging effect of C.Q due to its ability to donate hydrogen(60). Mishra et al investigated the antioxidant activity of ethyl acetate fraction of *Cissusquadrangularis* Linn extract at a concentration of 100 ppm by using both the β -carotene linoleic acid model and 1, 1-diphenyl-2-picrylhydrazyl model. Their study results found that CQ showed 64.8% antioxidant activity in the β -carotene linoleic acid model and 61.6% in the 1, 1-diphenyl-2-picrylhydrazyl model(47). Another study using the ethanol extract of CQ and methanol extract of CQ proved that CQ has potent antioxidant properties and also showed prominent anticancer effects against leukemic cells HL-60(61).

According to Chidambaramurthy et al, the presence of β -carotene in C.Q is responsible for scavenging superoxide radicals and suppressing singlet oxygen(62). Whereas Nair et al. has reported that vitamin C plays a major constituent of C.Q that has the capability of inhibiting in vitro lipid peroxidation and scavenging effect on hydroxyl and peroxy radicals(63). The antioxidative composition of C.Q is mainly responsible for potent antioxidant activity and free-radical scavenging activity in both in vitro. and in vivo studies. As CQ extracts proved to be nontoxic and antioxidant, it is often used as potential therapeutic agents (64).

6. In diabetes(Antidiabetic activity):

Cissusquadrangularis exhibits significant anti diabetic activity which was revealed in a study by Srivastava et al where ethyl acetate and hydro alcoholic extracts of *Cissusquadrangularis* were tested by inducing diabetes in wistar albino rats through administration of alloxan and their reduction of blood glucose level was comparable to glibenclamide treated group (65). Similar studies proved its antidiabetic activity in artificially induced diabetes in rats (66). Lekshmi et al has reported similar antidiabetic activity of ethyl acetate fraction of CQ and suggested its mechanism of action through regulation of carbohydrate metabolic enzymes such as Hexokinase, Glucokinase, pyruvate kinase and Glucose 6-phosphatase etc.(67). Similar results obtained from the study conducted in diabetic rats using ethanolic extract of CQ compared with glyburide(68).

7. In healing fractures (Osteogenic property) and osteoblastic differentiation:

CQ has been traditionally used as Bone aid for healing of bone fractures and joint pain, generally named as “Bonesetter” , also called as “Hadjod” in Hindi and “Asthisamdhani” in Sanskrit as it is able to join bones. Fractures are generally treated with casting, Open or closed reduction, fixation and rehabilitation for proper union and it requires approximately a month for complete healing. Traditional systems of medicine like siddha and ayurveda has suggested list of herbs which aid in fastening this healing process, CQ is one among them(). Studies have revealed that CQ is responsible for early callus formation, and calcification because of its ability to increase the rate of formation of collagen fibers(69).

According to Mishra et al , Presence of an anabolic steroid in C.Q functions as estrogenic receptors of bone which lead to early ossification and increased absorption of strontium, sulfur, Calcium by osteoblasts. Presence of vitamins and steroids in C.Q causes early connective tissue regeneration and enhanced mineralization of callus(14).

According to Parisuthiman et al , C.Q enhanced biomineralization of osteoblasts due to its mechanism of action on up regulation of MAPK dependent alkaline phosphatase pathway(70). CQ has the tendency to increase DNA synthesis and matrix mineralization of human osteoblast like SaOS-2 cell through its anabolic action by enhanced protein and mRNA expression of Runx2 which is participated in bone matrix regulatory proteins(71). Systemic administration of CQ reduces the bone healing period of about 2 weeks(72).

8. In osteoporosis (Anti osteoporotic):

Ethanol extract of the CQ exhibited a prominent antiosteoporotic effect in an animal study where osteoporosis induced rat models were ovariectomized and CQ were given at two different dose levels of 500 and 750mg/kg per day to one group ,its antiosteoporotic effect was compared with raloxifen (5.4mg/kg) given to another group(73). Aswar et al stated that phytoestrogen-rich fraction derived from CQ showed good antiosteoporotic activity due to its ability of increasing serum estrogen, vitamin D3, blood calcium, bone mineral content and bone mineral density in ovariectomized rats(74).

Another study by Potu et al in which ovariectomizedwistar rat model of osteoporosis and suggested that mechanism of petroleum ether extract of CQ suppressed bone reabsorption caused by deficiency in estrogen(75). Another study evaluated the identification of active phytochemical constituents in CQ responsible for its antiosteoporotic effect. In this study freeze-dried CQ juice and sequential extracts such as dichloromethane, hexane, water and ethanol were assessed to find their effects on bone mechanism in an ovariectomizedosteoporotic mice model and finally concluded that The hexane extract showed antiosteoporotic activity with protective effect against bone loss induced in osteoporotic induced mice model without any toxic effects throughout the entire experiment(76).

9. Ant arthriticactivity:

Numerous preclinical studies revealed the antiarthritic potential of CQ in Adjuvant induced Arthritis(77) and collagen induced arthritis (78). Samarasinghe et al reported that the nanoformulation of LakshadiGuggul (CQ with other contents) in novel alginate-enclosed chitosan calcium phosphate decreasing joint swelling by declining paw scores in mice and histopathological evaluation showed an improved regeneration of cartilage(78).

10. In Painful conditions(Anti analgesic and antipyretic):

Panthong et al conducted the study to investigate the analgesic and anti-inflammatory activities and also the venotonic effect of the methanol extract of CQ in comparison with drugs as a reference in mice. Regarding analgesic activity, CQ showed the peripheral and central analgesic activity due to its ability to reduce the number of writhes significantly in acetic acid-induced writhing response. In formalin test, CQ also caused the significant reduction of licking time in both phases of the test(46).

Similar results were found by Priyankavijay et al in a study conducted in albino rats using ethanolic extract of CQ revealed that CQ caused a significant reduction in the edema induced by carrageenan within duration of 1 to 5 hrs(47).

11. In neurological diseases(Antiepileptic activity):

In an animal study, Aqueous extract of *Cissusquadrangularis* exhibited the anxiolytic and antiepileptic effects in mice as CQ significantly raised the latency to clonic and generalized tonic-clonic seizures and reduced the frequency and duration of seizures in a dose-dependent manner(79). Another study showed similar results in isonicotinichydrazide acid induced Swiss mice model that CQ prolonged the onset time of seizures and significantly delayed the paw licking time. Also The extract exhibited a significant smooth muscle relaxant activity(80).

12. In fertility issues(Hormonal balance):

Santhoshkumar et al investigated the fertility effects of Ethanolic extract of CQ has resulted in prominent restoration of abnormalities induced by lead acetate in rat models. A few studies suggested that CQ contains numerous phytochemicals such as terpenoids, alkaloids, flavonoids, phenolics and steroidal saponins are responsible for its restorative activity of antioxidant enzymes which in turn inhibit pregnancy abortion and abortion induction(81).

13. Anthelmintic and antiplasmodial activity:

Zenebe et al found that methanol extract of CQ at different doses (1.25, 2.5, 5 and 10 mg/ml) showed prominent ($p < 0.05$) activity in an adult motility assay in a dose dependant manner, similar significant activity observed in egg hatch inhibition assay against *Haemonchus contortus*. The mechanism action of CQ may be its ability to block ATP synthesis by interrupting with oxidative phosphorylation in worms and its anthelmintic effect may be due to presence of phytochemical constituents such as flavonoids, phenols, tannins and alkaloids(82). Few studies also suggested that CQ can be used as an antihelminthic (83-85).

14. Antihemorrhoidal activity:

Pirshahid et al suggested that CQ exhibited venoconstrictive effect on the denuded vein and intact endothelium of rat inferior vena cava with EC50 values of 0.03 and 0.01 μ g/ml respectively. It has been said that Oral administration of 200 mg of CQ twice a day for a week significantly declined the hemorrhoidal symptoms in hemorrhoidal patients when compared to commercial drugs(86). Some studies revealed that Flavonoids may be one of the major phytochemicals to treat haemorrhoidal diseases by reducing localized bleeding, pain and itching (87). There could be a possible mechanism of improving capillary resistance and tonicity of veins with decreasing capillary permeability. (88-90).

Safety and their efficacy:

A systematic review was done by Sawangjit et al on clinical efficacy and safety of C.Q. They searched 12 electronic databases that included a total of 9 studies(1108 patients). They suggested that Clinical effects of CQ combination products on low density lipoprotein, triglyceride, body weight reduction, total cholesterol and fasting blood sugar were significantly higher than placebo. Clinical effects of CQ in treating bone fractures significantly reduces bone pain compared to placebo. Regarding safety, most of the included studies (6 of 9) indicated that *Cissus* was safe when used for a short period of time around 1 to 10 weeks. Though some adverse effects from C.Q were reported in the literature, most of them were mild and similar to placebo or pharmacotherapy. But there was less data on long-term safety in all studies that were included for review. So for long-term safety, studies should be investigated in a longer term(91).

Another review by Stohs et al concluded that all studies such as in vitro, in animals, in humans that have been determined the safety and efficacy of various *Cissus* extracts, CQ seems to be extremely safe and without any adverse effects at the commonly used doses(92).

Dental applications (A herbal for Osseointegration):

1. Dental caries (Antibacterial):

Literature revealed that CQ has antibacterial potential against various pathogens such as *Bacillus subtilis*, *Bacillus cereus*, *Staphylococcus aureus*, and *Streptococcus* species(62). MuthuSakthivel et al conducted the study to determine the antibacterial potential of antibacterial cysteine protease(Cp) which was extracted from CQ against *Bacillus cereus* and *Bacillus megaterium* and concluded that its antibacterial potential from the higher zone of inhibition. Also, it has been found that there was degradation of the peptidoglycan layer of bacteria by Cp in TEM images(93).

Recent novel research was done by SurachaiRattanasuk et al, in which seven human bacterial pathogens were isolated from clinical samples of patients at Roi Et hospital to find the anti-human pathogenic bacterial activity of *Cissusquadrangularis* against antibiotic-resistant bacteria where CQ extracts with different solvents were involved. This study revealed that ethanol extract of CQ showed the highest inhibition zone at 15 mm against *E.faecalis* and *P.aeruginosa*, which leads to the development of new antibiotic drugs for antibiotic-resistant bacterial diseases(94).

2. Periodontal regeneration:

CQ was proved to have the capacity to help in bone regeneration and is traditionally used as bone aid. A clinical trial was done by Anurag Jain et al, in which 20 patients with single intrabony defects were involved. This study compared the bovine-derived HA with CQ(composite graft) and bovine-derived HA alone in periodontal regeneration of intrabony defects, the observed results showed better performance in tested groups(Composite graft) than that of HA alone(95). Another recent clinical trial by NandLal et al compared the osteogenic property of oxidized cellulose membrane (OCM), CQ, and HA with that of normal healing bone in 20 patients with periodontal bony defects and found that Osseous healing with CQ was better than that of the control group(96).

3. Dental implants (Osteogenic property):

As discussed earlier, *Cissusquadrangularis* has a lot of osteogenic capacity, so it can be implemented not only in bone fracture healing but also in implant dentistry. Hamed Al-Sultan et al conducted an animal study involving a total of 25 mature male rabbits, divided into 5 groups (4-trial and 1 control). Two implants were placed in each rabbit's tibia so a total of 15 orthodontic implants were used. Apart from CQ (1000 mg/kg), the other natural products used in this study were Virgin coconut oil (2 mL / Kg), *Nigella Sativa* oil (0.5 mL / Kg), and Curcumin (15 mg/ Kg). The results concluded that a significant difference was found in both primary and secondary stability of the implant, So these natural products could be used as an additive(97).

Recent research interests in hydrophilic surfaces of implants in promoting osseointegration. Praneeth Raj Pachimallaa et al conducted a preliminary study in rabbits in which a new hydrophilic hydrogel was prepared with a combination of *Cissusquadrangularis* (CQ) and Chitosan . A total of twenty implants and ten rabbits were used in this study. These twenty implants were divided into two groups namely the treated and the control group. This gel was applied on the surface of the implant and placed in treated groups and control groups without hydrogel. After a healing period of 12 weeks, animals were euthanized and implants were subjected for torque removal tests and samples were undergone for histologic evaluation. The results ended with higher torque removal and bone formation in the treated group than the control group and confirmed that hydrogel with CQ and chitosan has osteogenic properties promoting the osseointegration of implants(98).

Anil Mangutti et al conducted a pilot clinical study where a total of 6 patients were randomized into the control and study groups. Each patient of both groups got either multiple or single implants. The Control group was given only routine antibiotics and analgesics while CQ alone was provided to the study group without other medications. The results ended with there was minimal pain and swelling in the study group than that in the control group. The osteogenic capacity of CQ was revealed from raised serum alkaline phosphatase levels which lead to enhanced bone healing(99).

4. Healing of oral and maxillofacial bone fractures :

A Randomized controlled clinical trial with 60 (patients having simple mandibular fracture was done by NimishaSingh et al. This study compared the osteogenic potential with osteopontinexpression between CQ treated group and control group without CQ intervention and concluded that CQ enhanced bone remodeling than control group(100). Similar to this study, a pilot study in mandibular fractures was done by Nayak et al and found a significant raise in the alkaline phosphatase levels in the CQ treated group than control group. However the other parameters such as clinical, radiographic, and biochemical findings showed no significant statistical difference between treated and control group(101).

Another pilot study was done by Brahmakshatriya et al in patients with maxillofacial fractures ,divided into two groups, one group of patients were given orally 500 mcg of CQ capsules thrice daily for duration of 6 weeks, another group without any treatment. These study results ended with formation of early callus and bone completion in a treated group with CQ than control group and suggested as an aid to reduce the healing period of bone fractures(102). While Altaweel et al conducted a study in which alveolar ridge distraction was done in twenty patients with atrophic ridge . These patients were divided into two groups, Group I patients were given CA capsules and Group II patients were provided placebo drugs, after a consolidation period of 3 months, removal of distractors was done, followed by placement of implants. Clinical parameters such as implant stability, wound healing were checked. Histological analysis and radiographic assessment were done. The study results revealed that CQ enhanced bone density in the distracted area and around the implant than in the control group(103).

Conclusion:

Recent research interests towards natural sources and their derived products especially from plants as it has a lot of potential medicinal properties. Among those, *Cissusquadrangularis* is an excellent traditional herb used for treatment of various purposes. This review emphasis on its background, morphological characteristics, pharmacological activities and listed out its all medicinal and dental applications. Because of its ability to enhance bone formation and its

osteogenic potential, it can be implemented in research areas of bone tissue regeneration. Its applications in various areas of dentistry such as apexogenesis procedures, as anticariogenic agent, Dentin-pulp complex regeneration, bone regeneration in dental implants require more preclinical and clinical studies to be investigated further for future purposes. Its administration as a hydrogel in surface of dental implants make a new path to the research areas of implant dentistry. It can be concluded that *Cissusquadrangularis*, a bone setter will definitely be a trend setter in all research areas of dentistry especially in bone tissue regeneration.

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Figure no.1



Figure no.2 Schematic representation of medical uses of CQ

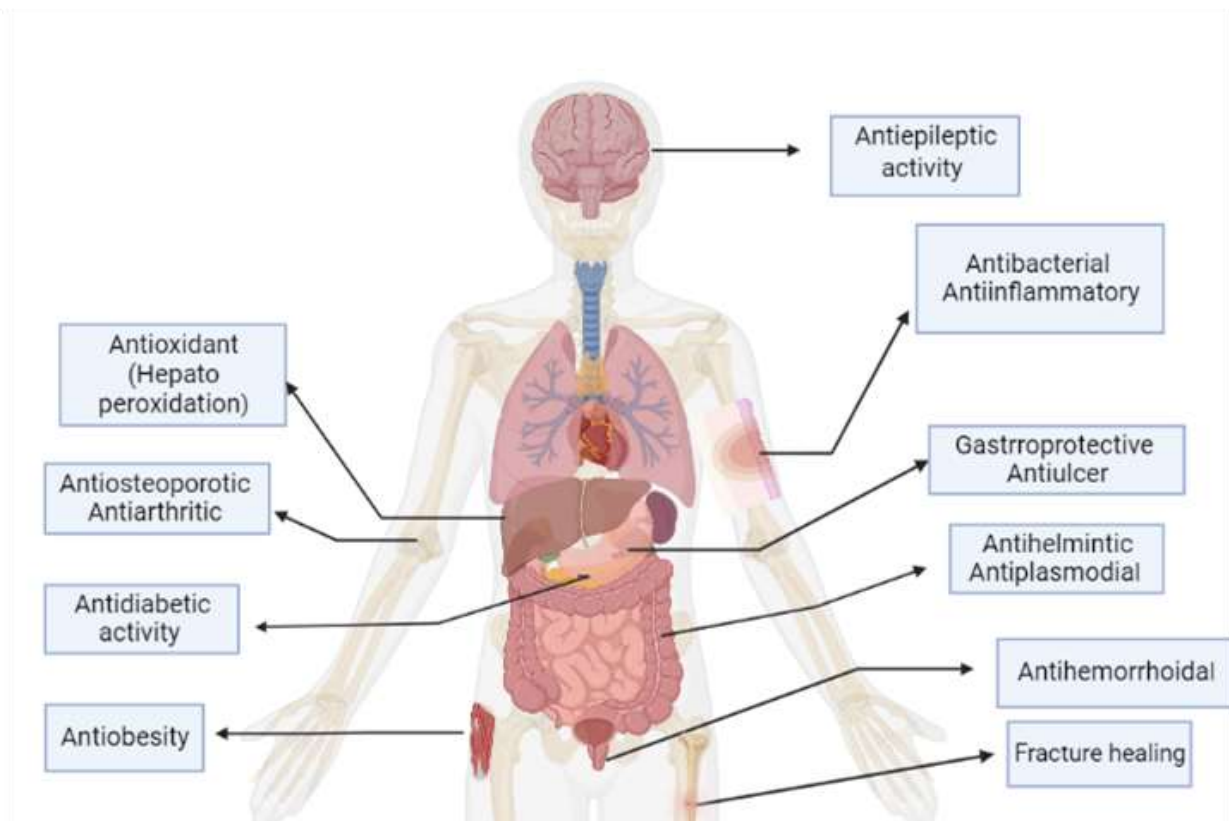


Figure no.2 Schematic representation of dental applications of CQ

