INTRODUCTION

Cissus quadrangularis (CQ) which is succulent perennial climber (Fig 1), scattered all over India particularly in tropical regions, usually called as ‘Asthisamdhani’ in Sanskrit, Vajravalli in Sanskrit, Kandvel in Marathi, Haddjor in Punjabi, Haddbhanga in Oriya, Vedhari in Gujarati, Perandai in Tamil, Nalleru in Telugu and Veldgrap in Indian languages and in English it is called as Edible-stemmed Vine. Based on morphological characters three different variants have been identified, they are square - stemmed, round-stemmed and flat-stemmed. Frequently available varieties are square-stemmed and round-stemmed. These are rich in source of ascorbic acid, carotene A, anabolic steroid substance and calcium. The round-stemmed variety is characterised by the presence of wingless stem. Anatomical section of the stem shows a deposit of characteristic acicular or needle shaped calcium oxalate crystals, raphides and intrafascicular cambium. Many research on the different extracts of Cissus quadrangularis has been carried out, some solvents which are used predominantly to extract the crude compounds includes methanol, petroleum ether, ethanol, aqueous, ethyl acetate. The whole plant is considered to be edible while each part of the plant pharmacologically contributes to some activity. The efficacy against different activities varies for different extract. [1, 2] In Indian traditional medicine CQ is used as a component of a plaster for treating swelling and bone fractures. [3] Plant derived medicines have been established on the basis of traditional information. [4] It also act against many activities which mainly includes analgesic, antimicrobial, antiviral, antioxidant, antiosteoporotic, for irregular menstruation, asthma, piles, tumor, bone fracture, wounds, scurvy. Biosynthesis of nanoparticles using the aqueous CQ leaf and stem extract was depicted against bacterial effect. [5] Nanoparticles against anticancer activity were also studied. [6] Screening of aqueous extract against central nervous depressant resulted in increased muscle relaxation. [7] An investigation of the petroleum ether and methanol extract against hepatoprotective effect can be attributed to its antioxidant property. [8] Various fraction of ethanolic extract of CQ was screened against osteoporotic activity. [9] This review has been compiled to focus on various strategies adapted for CQ extraction and establishment of its diverse pharmacological activities. The study decorum is classified based on the solvent (menstrum) used for extraction of active components from the leaf and stem of the plant.

Ethanol extract: Anti-ulcer activity: Ulcer is generally defined as a disruption in the biological membrane that obstructs the organ functionality to which that membrane belongs to. One of the most prominent ulcer to which CQE has a greatest activity is Peptic ulcer. So many works have been carried out against ulcer with the extract of Cissus quadrangularis (CQE) carried out using ethanol, those results revealed that when an ulcerated rats were given a 500 mg/kg of dose, extract had an greater effect against ulcer activity of 71.2%. This was compared with a standard ulcer drugs which exhibited 71.9% ulcer activity when administered with 30 mg/kg. It is noticeable that rats pre-treated CQE shows an enhanced effect of ulcer activity. [10]

ANTI-OSTEOPOROTIC ACTIVITY:
Reduction in the bone mineral density leads to osteoporosis. It causes fracture and alteration in the protein present in the bone. Traditionally Cissus
**Fig 1: Stems and leaves of cissus quadrangularis**

*Cissus quadrangularis* is used as a bone setter. Various works have been carried out to study the activity against osteoporotic effect. Datas revealed that some of the compounds present in CQE had a capability to increase the alkaline phosphatase (ALP), which is a marker of osteoblast differentiation. [6] Herbal scaffold incorporated with CQE extract also showed an improved hMSC (Human Mesenchymal Stem Cells) proliferation and stimulated osteogenic differentiation and bio-mineralization process. Presence of calcium, phosphorous, potassium and magnesium was also confirmed by the results of XRD and EDAX. [11] A significant increase in thickness of the cortical bone and individual trabecula were observed when 750 mg/kg dose of CQE were administered orally from 9th day of gestation till delivery. [9] DEXA (Dual-energy X-ray absorptiometry) and histopathology outcomes indicated that a phytoestrogen-rich fraction from aerial parts of *C. quadrangularis* prevented bone loss. [12] Improvement in the protein expression of superoxide dismutase (Cu/Zn-SOD, Mn-SOD), glutathione peroxidase (GPx) and endothelial nitric oxide synthase (eNOS) in the cells treated with CQE prior to H2O2 exposure, as compared with control. [13]

**Effect on Insulin Growth Factor of Osteoblast Cells:** A proliferation in the mRNA expression of IGF-I, IGF-II, IGF-IR was observed when cells were treated with *Cissus quadrangularis* in RT-PCR (Reverse Transcription and Polymerase Chain Reaction Analysis) analysis. Western blotting and Immuno radiometric analysis showed increased levels of IGF-I, IGF-II and IGFBP-3 and protein levels of IGF-IR. These results conclude that *Cissus quadrangularis* have an efficient effect on the IGF system components of human osteoblast like SaOS-2 cells. [14]

**Osteoblastic activity:** Osteoblast is a mononucleate cells which is responsible for the formation of the bone. These cells are specialized fibroblasts cells which express bone sialoprotein and osteocalcin. Many researches on this activity have been carried out. Those results showed that the alizarin red ALP (Alkaline Phosphatase) staining showed an increase in mineral deposition on human osteoblast cells like SaOS-2, and the anabolic actions were facilitated through improved mRNA and protein expression of Runx2, a key transcription factor of bone matrix proteins. [15] Ethanolic extract of CQ regulated the osteoblastic activity by enhanced ALP activity effect which was likely mediated by MAPK (Mitogen-activated protein kinases)-dependent pathway. [16] Methanol extract: Anti-microbial and anti-oxidant activity: Antioxidants are those compounds which defense against free radical damage. These compounds help in maintaining an optimum health of an individual. Agents that have an activity against microorganisms are anti-microbial agents. Some of the microbes include bacteria, fungi. To confirm the presence of anti-microbial and anti-oxidant activity by *Cissus quadrangularis* many research have been carried out. Phytochemical screening revealed the presence of general steroids and Terpinoids were authenticated. Purified compound of methanol extract showed statistically significant effect (p<0.01) against antiviral activity of HSV 1 and 2 at a level of 1: 400 dilution. In 100% concentration of extraction, zone of inhibition was very high which confirmed the presence of antimicrobial activity against human pathogens by *Cissus quadrangularis*. The Proximate analysis indicated the nutrients efficacy. [17] In algogenic test, reduction in the number of writhes was observed in mice (induced with acetic acid) when administered with CQE, also reduction in licking time was seen in the formalin test. [18] CQ extract (CQE) showed anti-lipid peroxidative, free-radical scavenging property and enhanced the liver damage by an increase in anti-oxidant enzymes activities. The activities of liver marker enzymes and antioxidant defense enzymes in rat liver homogenate were assessed in CCl4 and CQE-treated animals. Methanol extract of CQ showed high antibacterial activity against the Gram-negative and Gram-positive bacteria when tested *in vitro*. [19] Anti-ulcer activity: Many researches on the methanol extract against ulcer activity were carried out, which showed an isolated ascorbic acid compound from methanol extract of *Cissus quadrangularis* evaluated for gastric ulcer possessed greater activity when compared with standard anti-ulcer drug of Omeprazole treatment, wherein the dose of the extract was optimized as 50 mg/kg. [20] Dose of 1000 mg/Kg methanol extract of CQ
Compounds of Cissus quadrangularis were extracted using methanol to study the in-vitro H (+) –K (+) ATPase inhibitory potential. Quantification of phenolic and flavonoid contents from extract was carried out at different concentrations of standard and extract H(+)-K(+) ATPase inhibition assay was carried out. Pathway action of CQ for improved osteoblastic activity was studied using methanolic extract, from anterior pituitary it is followed by adrenal, testes and liver and thyroid gland which leads to the release of calcitonin by parafollicular cells and thereby a decrease in serum calcium since calcitonin increases the osteoblastic activity. 

Aqueous extract: Anti-microbial activity: The silver chloride nanoparticles (AgCl-NPs) using aqueous extract of Cissus quadrangularis (Fig 2) was tested for antibacterial activity by evaluating against bacterial pathogens of MDR (Multi Drug Resistant) strains by MIC (Minimum Inhibitory Concentration) test. The biosynthesized silver nanoparticles having surface plasmon resonance (SPR) at 450 nm in UV showed antibacterial activity which significantly controlled the growth of gram positive and gram negative bacteria at (10 g/mL) minimal inhibitory concentration. Synthesis of silver nanoparticle by microwave irradiation studied for anticancer activity and cytotoxicity study for synthesized silver nanoparticles showed a IC 50 value as 643g and 903g for the Hep2 and Vero cell line respectively. Silver nanoparticles studied for antimicrobial activity had maximum zone of inhibition to be 12mm for Staphylococcus aureus and minimum of 7mm for Bacillus cereus. Absorption spectra of Ag nanoparticles found in the reaction media at 10 min has absorbance peak at 421nm. The FTIR peak at 1615 cm

**Fig 2: Tem images of silver chloride nano particles**

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<th>Table 1: Compiled data of the activities carried out for different extracts</th>
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administered orally to aspirin induced gastric ulcer wistar rats promoted ulcer protection at a faster phase when compared with ranitidine (RTD) (30mg/Kg) as standard drug. Rats treated with CQ showed a significant decrease in lipid peroxidation (LPO) and improvement in the antioxidant activity was observed. When 500 mg/kg of CQE was administered for treating peptic ulcer, it showed an increase in the resistance of mucosa against ulcerogens and induced the cellular proliferation for healing of ulcer.

Osteoblastic activity: Compounds of Cissus quadrangularis were extracted using methanol to study the in-vitro H (+) –K (+) ATPase inhibitory potential. Quantification of phenolic and flavonoid contents from extract was carried out at different concentrations of standard and extract H(+)-K(+) ATPase inhibition assay was carried out. Pathway action of CQ for improved osteoblastic activity was studied using methanolic extract, from anterior pituitary it is followed by adrenal, testes and liver and thyroid gland which leads to the release of calcitonin by parafollicular cells and thereby a decrease in serum calcium since calcitonin increases the osteoblastic activity.

Anti-parasitic activity: Any organism that may possibly lead to the parasitic activity without relying upon any host for completing its life cycle is a parasite. Potential of synthesized silver nanoparticles against parasitic activity was validated using contact toxicity process. The maximum efficacy was against the larvae of microplus with LC50 values of 50.00, 21.72 and 7.61 mg/L; LC90 values of 205.12, 82.99 and 22.68 mg/L. Central Nervous System (CNS) depressant activity: Study of CNS depressant activity was studied using aqueous CQE which showed GABAA- benzodiazepine receptor binding activity. The study reflected that aqueous extract of the stem (150 mg/kg) reduced locomotor activity, produced muscle relaxation and showed anti-anxiety and anti-aggressive activity.

Anti-epileptic activity: Epilepsy is a neurological disorder characterised by seizure. In-vivo study of aqueous extract of Cissus quadrangularis to evaluate antiepileptic activity was carried out using the maximal electroshock. When
250 mg/kg and 500 mg/kg of CQE administered to adult male Swiss mice, they were protected against maximal electroshock seizure, and also delay in the onset time of seizures in isonicotinic hydrazide acid induced mice was observed. The paw licking time was delayed and showed a noticeable smooth muscle relaxant activity. The results put forward that the aqueous extract of Cissus quadrangularis possess smooth muscle relaxant properties. Ethyl acetate extract: Anti-oxidant and anti-microbial activity: Ethyl acetate extract tested for antioxidant and antibacterial activity showed 64.8% and 61.6% antioxidant activity in the β-carotene linoleic acid system and 1, 1-diphenyl-2-picrylhydrazyl system respectively. A test against gram- positive bacteria showed a better activity. Effect on gene expression: Production of nitric oxide in macrophage cells by inducing lipopolysaccharide was inhibited by cqe. Study revealed that at time and dose-dependent manner cqe itself induced hemeoxygenase-1 at protein and mRNA level.

Petroleum ether extract: Anti-osteoporotic activity: Petroleum ether extract of CQ was evaluated for osteoporosis activity on ovariectomy-induced rats. Thickness of trabecular and cortical bone were increased when rats administered with CQ and also strength of the femur bone was increased. The CQ was found to be effective on TRAP and ALP enzymes based on colour intensity and it acted as a possible agent for treating postmenopausal osteoporosis. When treated it showed a decrease in bone loss, as noticed by the weight gain in femur, and also a decreased osteoclastic activity.

Compounds of Cissus quadrangularis extracted using petroleum were evaluated for the proliferation rate of bone marrow mesenchymal stem cells and extracellular matrix calcification. When extract was administered at a concentration of 100, 200 or 300 g/ml, formation of ALP-positive osteoblasts cells from mesenchymal stem cells by differentiation and matrix calcification in extracellular area were improved. CQ stimulates osteoblastogenesis and so it can be used for osteoporosis.

Growth of osteoepinia in ovariectomy induced wistar rats were studied with Raloxifene (RAL) as standard drug to depict CQ showing strong anti-osteoporotic activity. Estimation of serum ALP, Calcium, TRAP and hydroxyproline revealed that OVX (Ovarectomized) group animals showed a substantial rise in their serum levels compared to SHAM (Control) group. ALP and TRAP levels showed an increase in the thickness of cortical and trabecular bone when CQ was administered to rats.

Chloroform extract: anti-bacterial activity: chloroform extract was observed to recover the bioactive principles from the plant, whose extract was screened for its bactericidal activity against helicobacter pylori. Active acetone fraction: Active acetone fractions of Cissus quadrangularis were evaluated against enzyme activity to validate for the inhibition of cyclooxygenase (COX-1), cyclooxygenase (COX-2), and 5-lipoxygenase (5-LOX). This extract showed IC50 values of 7 g/ml, 0.4 g/ml, and 20 g/ml for COX-1, COX-2 and 5-LOX respectively. It showed anti-inflammatory activity along with inhibition of pro-inflammatory mediators like iNOS and TNFα.

CONCLUSION
In present scenario, utilization of the herbal plants for physical and mental ailments is in an uphill movement. Each part of the plant has its unique therapeutic efficacy against different disorders. Isolated compounds from Cissus quadrangularis by different extraction method have shown diverse activity against different disorders.

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REFERENCES
33. Potu BK, Bhat KMR, Rao MS, Nampurath GK,
Chamallamudi MR, Nayak SR, Muttigi MS, Petroleum ether extract of cissus quadrangularis (linn.) enhances bone marrow mesenchymal stem cell proliferation and facilitates osteoblastogenesis. Clinics 2009; 64(10): 993-998.


