

## Review- Pharmacological Activities Based on Different Extracts of *Cissus quadrangularis*

Subhashri S, Vedha Hari BN, \*Ramya Devi D

Department of Pharmaceutical Technology, School of Chemical and Biotechnology, SASTRA University, Thanjavur-613401. Tamilnadu, India.

### ABSTRACT

Since ancient age nature has been a source of medicinal agents and many of the traditional drugs have been isolated from natural source. Research focus on the natural source has been increased recently due to its minimum side effects. Articles reveal that almost more than 15000 plants have been used by different ethnic communities in India. Many active compounds have been isolated from the plants through various extraction method using different solvents and these are pharmacologically active. The isolated chemical constituents from *Cissus quadrangularis* extract, which plays major role including gallic acid derivatives, steroids, iridoids, flavonoids, stilbenes and triterpenes. This review is concentrated on the different extracts of *Cissus quadrangularis* and its activity against numerous pathophysiological effects. Versatile activity of this plant has revealed it as a valuable medicinal plant.

### Key words:

### 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, Hadbhanga in Oria, Vedhari in Gujrati, 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. <sup>[1, 2]</sup> In Indian traditional medicine CQ is used as a component of a plaster for treating swelling and bone fractures. <sup>[3]</sup> Plant derived medicines have been established on the basis of traditional information.<sup>[4]</sup> 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. <sup>[5]</sup> Nanoparticles against anticancer activity were also studied. <sup>[6]</sup> Screening of aqueous extract against central nervous depressant resulted in increased muscle relaxation. <sup>[7]</sup> An investigation of the petroleum ether and methanol extract against hepatoprotective effect can be attributed to its antioxidant property. <sup>[8]</sup> Various fraction of ethanolic extract of CQ was screened against osteoporotic activity. <sup>[9]</sup> 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. <sup>[10]</sup>

### 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*

*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.<sup>[6]</sup> Herbal scaffold incorporated with CQE extract also shown an improved hMSC (Human Mesenchymal Stem Cells) proliferation and stimulated osteogenic differentiation and biomineralization process. Presence of calcium, phosphorous, potassium and magnesium was also confirmed by the results of XRD and EDAX.<sup>[11]</sup> 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.<sup>[9]</sup> DEXA (Dual-energy X-ray absorptiometry) and histopathology outcomes indicated that a phytoestrogen-rich fraction from aerial parts of *C. quadrangularis* prevented bone loss.<sup>[12]</sup> 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 H<sub>2</sub>O<sub>2</sub> exposure, as compared with control.<sup>[13]</sup>

**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.<sup>[14]</sup>

**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 shown 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.<sup>[15]</sup> Ethanollic extract of CQ regulated the osteoblastic activity by enhanced ALP activity effect which was likely mediated by MAPK (Mitogen-activated protein kinases)-dependent pathway.<sup>[16]</sup>

**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.<sup>[17]</sup> In analgesic test, reduction in the number of writhes was observed in mice (induced with acetic acid) when administered with CQ, also reduction in licking time was seen in the formalin test.<sup>[18]</sup> 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 CCl<sub>4</sub> and CQE-treated animals. Methanol extract of CQ showed high antibacterial activity against the Gram-negative and Gram-positive bacteria when tested *in vitro*.<sup>[19]</sup>

**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.<sup>[20]</sup> Dose of 1000 mg/Kg methanol extract of CQ

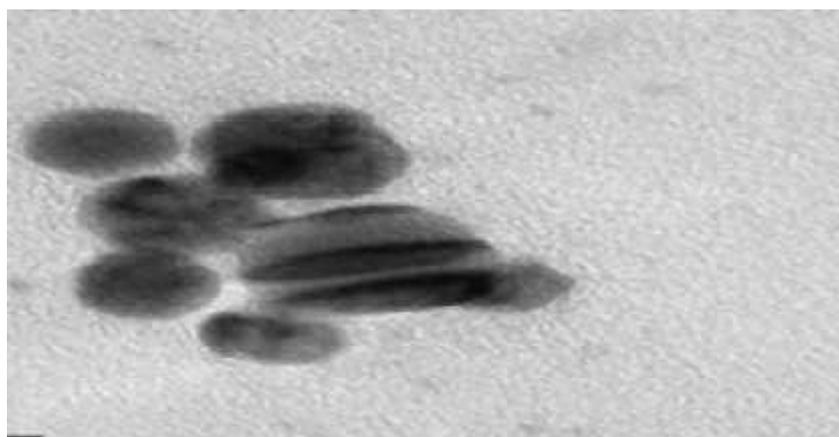


Fig 2: Tem images of silver chloride nano particles

Table 1: Compiled data of the activities carried out for different extracts

Ethanol Extract	Osteoblastic activity, Antiosteoporotic activity, Effect on insulin growth factor of osteoblast cells,
Methanol Extract	Antimicrobial and anti-oxidant activity, Antiulcer activity, Osteoblastic activity
Ethyl Acetate	Antioxidant and Antimicrobial Activity, Effect on gene expression
Aqueous Extract	Antimicrobial activity, Anti-Parasitic activity, Central Nervous Depressant Activity, Antiepileptic Activity
Active Acetone Fraction	Anti-inflammatory Activity
Petroleum Ether Extract	Antiosteoporotic activity
Chloroform Extract	Anti-bacterial Activity

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. [21] Rats treated with CQ showed a significant decrease in lipid peroxidation (LPO) and improvement in the antioxidant activity was observed. [22] 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. [23]

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. [24]

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 µg/mL) minimal inhibitory concentration. [25] 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. [26] 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<sup>-1</sup> of extract changed to 1617cm<sup>-1</sup> after synthesis confirming the reduction of silver ions to silver nanoparticles. [27]

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 micropluss 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. [28]

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. [29]

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. [30]

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  $\alpha$ -carotene linoleic acid system and 1, 1-diphenyl-2-picrylhydrazyl system respectively. A test against gram- positive bacteria showed a better activity. [31]

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. [32]

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. [33] 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. [34]

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  $\mu$ 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. [35] Growth of osteopenia 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 (Overactomized) 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. [36]

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 [37]

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  $\mu$ g/ml,

0.4  $\mu$ g/ml, and 20  $\mu$ 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 TNF . [38]

## 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.

## ACKNOWLEDGEMENT

The authors are thankful to the management of SASTRA University, Thanjavur for providing the infrastructure and facilities to complete this article.

## REFERENCES

1. Jainu M, Devi CSS. In Vitro and In Vivo evaluation of free-radical scavenging potential of *Cissus quadrangularis*. *Pharmaceutical Biology* 2005; 43(9): 773-779.
2. Gopinath V, Priyadarshini S, MeeraPriyadharsshini N, Pandian K, Velusamy P. Biogenic synthesis of antibacterial silver chloride nanoparticles using leaf extracts of *Cissus quadrangularis* Linn. *Materials Letters* 2013; 91: 224-227.
3. Annie Shirwaikar, Saleemulla Khan, Malinib S. Antiosteoporotic effects of ethanol extracts of *Cissus quadrangularis* Linn. on ovariectomized rat. *Journal of Ethnopharmacology* 2003; 89(2-3): 245-250.
4. Yadav P, Ganeshpurkar A, Rai G. In vitro H(+) - K(+) ATPase inhibitory potential of methanolic extract of *Cissus quadrangularis* Linn. *Pharmacognosy* 2012; 4(2): 123-126.
5. Mallika Jainu, Vijai Mohan K, Shyamala Devi CS. Protective effect of *Cissus quadrangularis* on neutrophil mediated tissue injury induced by aspirin in rats. *Journal of Ethnopharmacology* 2006; 104(3): 302-305.
6. Manmeet Kumara, Preeti Rawat, Preeti Dixit, Devendra Mishraa, Abnish K. Gautamb, Rashmi Pandey, Divya Singh, Naibedya Chattopadhyay, Rakesh Maurya. Anti-osteoporotic constituents from Indian medicinal plants. *Phytomedicine* 2010; 17: 993-999.
7. Balasubramaniana P, Jayalakshmi K, Vidhyab N, Prasada R, Khaleefathullah Sheriff A, Kathiravana G, Rajagopala K, Sripathi, Sureban M. Antiviral activity of ancient system of ayurvedic medicinal plant *Cissusquadrangularis* L. (Vitaceae). *Journal of Basic and Clinical Pharmacy* 2010; 001(001): 37-40.
8. Unnati M. Shah, Patel SM, Patel PH, Hingorani L, Jadhav RB. Development and Validation of a Simple Isocratic HPLC Method for Simultaneous Estimation of Phytosterols in *Cissus quadrangularis*. *Indian J Pharm Sci* 2010; 72(6): 753-758.
9. Gabriel Fernandes, Jameela Banu. Medicinal properties of plants from the genus *Cissus*: A review.

- Journal of Medicinal Plants Research 2012; 6(16): 3080-3086.
10. Ayyanar M, Ignacimuthu S. Pharmacological actions of *Cassia auriculata* L. and *Cissus quadrangularis* wall: A short review. *Journal of Pharmacology and Toxicology* 2008; 3(3): 213-221.
  11. Kumar R, Sharma AK, Saraf SA, Gupta R. CNS activity of aqueous extract of root of *Cissus quadrangularis* Linn. (Vitaceae). *Journal of Dietary Supplements* 2010; 7(1): 1-8.
  12. Rao MS, Bhagath Kumar P, Narayana Swamy VB, Gopalan Kutty N. *Cissus quadrangularis* plant extract enhances the development of cortical bone and trabeculae in the fetal femur. *Pharmacologyonline* 2007; 3: 190-202.
  13. Tarat Sapsrithonga, Weeraya Kaewprema, Sarunya Tongumpaia, Punnee Nusuetrong, Duangdeun Meksuriyena. *Cissus quadrangularis* ethanol extracts upregulates superoxide dismutase, glutathione peroxidase and endothelial nitric oxide synthase expression in hydrogen peroxide-injured human ECV304 cells. *Journal of Ethnopharmacology* 2012; 143(2): 664-672.
  14. Sridhar Muthusami, Ilangovan Ramachandran, Senthilkumar Krishnamoorthy, Ramajayam Govindan, Srinivasan Narasimhan. *Cissus quadrangularis* augments IGF system components in human osteoblast like SaOS-2 cells. *Growth Hormone & IGF Research* 2011; 21(6): 343-348.
  15. Garima Mishra, Saurabh Srivastava, Nagori BP. Pharmacological and Therapeutic Activity of *Cissus quadrangularis*: An Overview. *International Journal of PharmTech Research* 2010; 2(2): 1298-1310.
  16. Parisuthiman D, Singhatanadgit W, Dechatiwongse T, Koontongkaew S. *Cissus quadrangularis* extract enhances biomineralization through up-regulation of MAPK-dependent alkaline phosphatase activity in osteoblasts. In *Vitro Cellular and Developmental Biology – Animal* 2008; 1-7.
  17. Sathish Kumar T, Anandan A, Jegadeesan M. Identification of chemical compounds in *Cissus quadrangularis* L. Variant-I of different sample using GC-MS analysis. *Archives of Applied Science Research* 2012; 4 (4): 1782-1787.
  18. Sathyaprabha G, Kumaravel S, Ruffina D, Praveenkumar P. A Comparative study on Antioxidant, Proximate analysis, Antimicrobial activity and phytochemical analysis of *Aloe vera* and *Cissus quadrangularis* by GC-MS. *Journal of Pharmacy Research* 2010; 3(12): 2970-2973.
  19. Ampai Panthonga, Wanicha Supraditaporna, Duangta Kanjanapothia, Tawat Taesotikula, Vichai Reutrakulb. Analgesic, anti-inflammatory and venotonic effects of *Cissus quadrangularis* Linn. *Journal of Ethnopharmacology* 2007; 110(2): 264-270.
  20. Kashikar N, George I. Antibacterial activity of *Cissus quadrangularis* Linn. *Indian Journal of Pharmaceutical Sciences* 2006; 68(2): 245-247.
  21. Mallika Jainu, Kunju Vijai Mohan. Protective role of ascorbic acid isolated from *Cissus quadrangularis* on NSAID induced toxicity through immuno modulating response and growth factors expression. *International Immunopharmacology* 2008; 8(13-14): 1721-1727.
  22. Shanthi G, Vijay kanth G, Hitesh L, Ganesan M. Antiulcerogenic activities of the methanolic extract of *Cissus quadrangularis* in wistar. *International Journal of Toxicology* 2010; 7(2).
  23. Viswanatha Swamy AHM, Rucha V Kulkarni, Thippeswamy AHM, Koti BC, Aparna Gore. Evaluations of hepatoprotective activity of *Cissus quadrangularis* stem extract against isoniazid-induced liver damage in rats. *Indian J Pharma* 2010; 42(6); 397-400.
  24. Jainu M, Devi CS. Effect of *Cissus quadrangularis* on gastric mucosal defensive factors in experimentally induced gastric ulcer-a comparative study with sucralfate. *J Med Food* 2004; 7(3): 372-376.
  25. Deka DK, Lahon J, Saikia, Mukit. Effect of *Cissus quadrangularis* in accelerating healing Process of experimentally fractured radius-ulna of dog: A preliminary study. *Indian Journal of Pharmacology* 1994; 26: 44 – 45.
  26. Sivakama Valli J, Vaseeharan B. Biosynthesis of silver nanoparticles by *Cissus quadrangularis* extracts. *Materials Letters* 2012; 82: 171-173.
  27. Renugadevi K, Inbakandan D, Bavanilatha M, Poornima V, *Cissus quadrangularis* assisted biosynthesis of silver Nanoparticles with antimicrobial and anticancer potentials. *Int J Pharm Bio Sci* 2012; 3(3): 437 – 445.
  28. Mundada SJ, Agrawal M, Dewade R. Central nervous system depressant activity of aqueous extract of *Cissus quadrangularis*. *International Journal of Biomedical Research* 2011; 1(3): 141-146.
  29. Sivakama Valli J, Vaseeharan B. Biosynthesis of silver nanoparticles by *Cissus quadrangularis* extracts. *Materials Letters* 2012; 82: 171-173.
  30. Klaokwan Srisooka, Mullika Palachota, Nadtaya Mongkola, Ekaruth Srisook, Songklod Sarapusita. Anti-inflammatory effect of ethyl acetate extract from *Cissus quadrangularis* Linn may be involved with induction of heme oxygenase-1 and suppression of NF- B activation. *J.Jep* 2010; 11: 029.
  31. Chidambara Murthy KN, Vanitha A, Swamy. MM, Ravishankar GA. Antioxidant and antimicrobial activity of *Cissus quadrangularis* L. *Journal of Medicinal Food* 2003; 6(2): 99-105.
  32. Potu BK, Rao MS, Nampurath GK, Chamallamudi MR, Prasad K, Nayak SR, Dharmavarapu PK, Kedage V, Bhat KMR. Evidence-based assessments of antiosteoporotic activity of petroleum-ether extract of *Cissus quadrangularis* on ovariectomy-induced osteoporosis. *Upsala Journal of Medical Sciences* 2009; 114(3): 140-148.
  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.
34. Potu BK, Nampurath GK, Rao MS, Bhat KM. Effect of *Cissus quadrangularis* Linn on the development of osteopenia induced by ovariectomy in rats. *Clin Ter*, 2011; 162(4); 307-312.
35. Arti M. Bhujadea, Suhas Talmalea, Naresh Kumarb, Geetika Guptab, Reddanna P, Samar K. Dasc, Patila MB. Evaluation of *Cissus quadrangularis* extracts as an inhibitor of COX, 5-LOX, and proinflammatory mediators. *Journal of Ethnopharmacology* 2012; 141(3): 989-996.
36. Austin A, Jegadeesan M, Gowrishankar R. In vitro helico bactericidal activity of *Cissus quadrangularis* L. variant II. *Indian Journal of Microbiology* 2004; 44(1): 67-68.
37. Soumya S, Sajesh KM, Jayakumar R, Nair SV, Chennazhi KP. Development of a phytochemical scaffold for bone tissue engineering using *Cissus quadrangularis* extract. *Carbohydrate Polymers* 2012; 87(2): 1787-1795.
38. Muthusami S, Senthilkumar k, Vignesh, Ilangovan R, Stanley J, Selvamurugan N, Srinivasan N. Effects of *Cissus quadrangularis* on the proliferation, differentiation and matrix mineralization of human osteoblast like SaOS-2 cells. *Journal of Cellular Biochemistry* 2011; 112(4): 1035-1045.