Long-term tooth loss in periodontally treated patients and cissus quadrangularis

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The goal of periodontal therapy remains to provide a dentition that functions in health and comfort for the life of the patient. Studies determining long-term tooth loss in periodontally treated patients demonstrate that, for the majority of periodontal patients, this goal is a reality.

Periodontal therapy involves two primary components. First elimination of the periodontal infection, by eliminating the pathogenic periodontal microflora, which induces substantial favorable clinical changes in the periodontium. However, the anatomic defect resulting from active periodontitis still persists and is represented clinically by loss of clinical attachment, increased probing depths, and radiographic bone loss. The substantial efforts made to alter this defect represent the second component of periodontal therapy.

Regenerative treatment has as its goal elimination of periodontal defects by regenerating the lost periodontium including bone, cementum, and periodontal ligament. A number of therapies such as implantation of autografts, allografts and alloplastic materials, chemical root conditioning, growth factors, guided tissue regeneration, platelet rich plasma and combination of these have been used in clinical practice to reconstruct the periodontal tissues. Also, traditional herbal products like those derived from plants have been used and evaluated for being used in modern medicine. 8

Medicinal plant is any plant which in one or more of its organ contains substance that can be used for therapeutic purpose or which is a precursor for synthesis of useful drugs (According to WHO). Medicines are prepared from variety of plant materials like leaves, stems, root, barks and so on. They

mainly contain biologically active ingredients and are used primarily for treating mild or chronic ailments.

Herbs can be prepared at homes in many ways using either fresh or dried ingredient example : roots, bark or other plant parts can be boiled into strong solutions called “ Decoctions” then honey and sugar can be added to infusions and decoctions to make syrups. Now herbal medicines can also prepared in the form of pills, capsules or powders or in more concentrated liquid form called extracts and tinctures, they can also be applied topically in creams or ointments or applied directly to the skin as poultices. 8

Cissus quadrangularis, a perennial climber widely used in traditional medicinal systems of India has been reported to possess bone fracture healing, antibacterial, antifungal, antioxidant, anthelmintic, antihemorrhoidal and analgesic activities. It has been recognized as a rich source of carotenoids, triterpenoids and ascorbic acid and is proved to have potential for medical effects. 3

Phytochemical studies of Cissus quadrangularis have shown the presence of various versatile constituents such as flavanoids, triterpenoids, Vitamin C, stilbene derivatives and many others, e. g. resveratrol, piceatannol, pallidol perthenocissin and phytosterols. Out of which ascorbic acid, triterpene, β-sitosterol, ketosteroid, two asymmetrical tetracyclic triterpenoids and calcium were identified as major constituents of this plant. 3

Studies on cissus quadrangularis

Deka et al in 1994 performed a preliminary study on effect of Cissus quadrangularis in accelerating healing process of experimentally fractured radius-ulna of dog and concluded that there was faster initiation of healing process than the control animals on radiological and histopathological examinations as well as the healing was almost complete on 21st day of fracture in the treated animals and remained incomplete in the control animals.

Murthy et al in 2003 performed a study where Antioxidant and Antimicrobial Activity of Cissus quadrangularis L were assessed and the prepared extract showed presence of sterols, vitamin C, and tannins as phytoconstituents. The ethyl acetate extract showed maximum antioxidant effect and antimicrobial activity against Gram-positive bacteria, including Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, and Streptococcus species.

Jainu et al in 2005 performed a study which demonstrates the healing effect of Cissus quadrangularis extract (CQE) through inhibitory action on generation of lipid peroxidation, pro-inflammatory cytokines and neutrophil infiltration. Administration of CQE attenuated the gastric lesions induced by aspirin and this was accompanied by the rise in uric acid, antioxidative enzymes, SH groups, and a significant decrease in lipid peroxidase, TNF-α, MPO and XO activities suggesting significant gastroprotective activity could be mediated by the antioxidant activity as well as by the attenuation of oxidative mechanism and proinflammatory cytokines.

Sanyal et al in 2005 studied Calcite growth in Cissus quadrangularis plant extract, as traditional Indian bone-healing aid and found that the the plant contains a high percentage of calcium probably due to its thick cell wall, which makes it suitable for growth of mineral crystals and the presence of phosphorous in the plant can also be exploited for synthesizing hydroxyapatite.

Oben et al in 2006 studied the use of a Cissus quadrangularis formulation in the management of weight loss and metabolic syndrome and all participants received two daily doses of the formulation or placebo and remained on a normal or calorie-controlled diet for 8 weeks. It was concluded that there was statistically significant reductions was observed in weight and central obesity, as well as in fasting blood glucose, total cholesterol, LDL-cholesterol, triglycerides, and C-reactive protein in participants who received the formulation, irrespective of diet.

Panthong et al in 2006 studied Analgesic, anti-inflammatory and venotonic effects of Cissus quadrangularis and found that CQ provoked a significant reduction of the number of writhes in acetic acid-induced writhing response in mice and significantly reduced the licking time in both phases of the formalin test suggesting the peripheral and central analgesic activity of CQ . CQ when added into the tissue bath also produced contraction of human umbilical vein. An explanation for this result would be the fact that CQ possesses venotonic effect.

Rao et al in 2007 showed Cissus quadrangularis plant extract enhances the development of cortical bone and trabeculae in the fetal femur in wistar rats. In the study, pregnant rats were administered with Ethanol extract of Cissus quadrangularis (CQ), orally, with dosage of 750 mg/kg body weight from 9th day of gestation till delivery and femur bone of the newborn pups were collected, decalcified and processed for paraffin sectioning. Results showed a significantly increase in thickness of the cortical bone at mid shaft level compared to control rats. 3

Mishra et al in 2009 studied antibacterial and antifungal activity of n-hexane, chloroform, ethyl acetate, methanol and aqueous extracts of Cissus quadrangularis Linn where the methanolic and aqueous extracts showed remarkable inhibitory activity against various gram-positive and gram-negative bacteria as compared to moderate inhibitory effect against test fungal strains using disc diffusion method where antibiotic Norfloxacin (5 µg/ml) was used as standard for bacterial culture and Ketoconazole (5 µg/ml) for fungal culture.

Potu et al in 2009 conducted a study to evaluate the effects of the petroleum ether extract of CQ on the proliferation rate of bone marrow mesenchymal stem cells, the differentiation of marrow mesenchymal stem cells into osteoblasts (osteoblastogenesis) and extracellular matrix calcification. He concluded that cells grown in osteogenic media containing 100, 200 or 300 µg/mL petroleum ether extract of CQ enhanced the differentiation of marrow mesenchymal stem cells into ALP-positive osteoblasts and increased extracellular matrix calcification.

Potu et al in 2009 evaluated the effect of petroleum-ether extract of CQ in osteoporotic wistar rat developed by ovariectomy. The findings were assessed on the basis of animal weight, morphology of femur, and histochemical localization of alkaline phosphatase (ALP) (an osteoblastic marker) and tartrate-resistant acid phosphatase (TRAP) (an osteoclastic marker) in upper end of femur. it was concluded that the petroleum-ether extract of CQ reduced bone loss, as evidenced by the weight gain in femur, and also reduced the osteoclastic activity thereby facilitating bone formation which was assessed by ALP staining in the femur sections.

Parisuthiman et al in 2009 evaluated the ethanol extract of CQ-E on osteoblast differentiation and function were analyzed using murine osteoblastic cells. The results suggested that CQ-E may regulate osteoblastic activity by enhancing ALP activity by MAPK dependent pathway which lead to an initiation and a further increase in the extent of mineralized nodule formation in vitro, thus suggesting the osteogenic effect of CQ-E in enhancing bone healing in vivo.

Muthusami et al in 2011 studied the effects of ethanolic extract of CQ on the proliferation, differentiation and matrix mineralization of human osteoblast like SaOS-2 cells. T hymidine incorporation assay showed that CQ treatment has increased the DNA synthesis of human osteoblastic SaOS-2 cells indicating increased proliferation of these cells and the data on alizarin red and ALP staining revealed increased matrix mineralization of human osteoblast like SaOS-2 cells.

Srivastava et al in 2011 evaluated Anti-diabetic property of Cissus quadrangularis extracts (CQE) in alloxan induced diabetic rats. The CQE exhibited similar mechanism of action as Glibenclamide i. e. by stimulation of surviving ß-cell to release more insulin. Thereby, suggesting favorable Anti-diabetic effect of Cissus quadrangulari.

Lal et al in 2012 clinically evaluated the osteogenic potential of hydroxyapatite (HA), Cissus quadrangularis (CQ), and oxidized cellulose membrane (OCM) and compared with normal bone healing and concluded that high contents of vitamins A and C, calcium oxalate, and some unknown anabolic steroids may be responsible for better osseous fill in CQ sites as compared with control sites. 5

Merinal et al in 2012 performed invitro screening of antimicrobial potentials of ethanol, diethyl ether and aqueous leaf extracts of Cissus quadrangularis L. The ethanol extract showed maximum inhibition against Escherichia coli (10 mm) followed by Staphylococcus aureus (8 mm) and Klebsiella pneumoniae (7mm). Diethyl ether and distilled water extract exhibited minimum to moderate inhibition against tested pathogens.

Singh et al in 2013 studied the osteogenic potential of Cissus quadrangularis (CQ), which was assessed by osteopontin expression. The samples of CQ group examined for osteopontin expression using western blot analysis and flow cytometry showed significant levels of expression of osteopontin protein and CD4+ T cells expressing osteopontin leading to conclusion that CQ

accelerates fracture healing and also causes early remodeling of fracture callus.

Chaudhari et al in 2013 evaluated the anti-hyperglyceamic activity of ethanolic extract of Cissus quadrangularis (EtCQ) against alloxan induced diabetic rats. EtCQ significantly enhanced glucose utilization in oral glucose tolerance test (OGTT) in both non-diabetic and diabetic rats. It was concluded from the data obtained from OGTT, it concluded that administration of EtCQ effectively prevented the increase in serum glucose level without causing a hypoglycaemic state.

Basker et al in 2013 evaluated Antibacterial efficacy of Cissus quadrangularis from different provinces. The conclusion is that CQ showed maximum action against E. coli then Pseudomonas putida then Staphylococcus aureus and least activity against β-hemolytic staphylococcus and most antibacterial effect is shown by CQ from Tamil Nadu.

Enechi et al in 2013 studied antiulcer activities of the ethanol extract of CQ roots on indomethacin and ethanol-induced gastric ulcers. The results obtained showed that the ulceration in gastric linings of the stomach of rats pre-treated with the CQ extract before induction with ethanol and indomethacin decreased significantly suggesting antiulcer activities of CQ.

Suganya et al in 2013 evaluted synergistic effect of CQ and Hydroxyapatite with Polycaprolactone (PCL) by fabricating PCL-CQ-HA nanofibrous scaffolds by electro-spinning and compared with PCL-CQ and PCL (control) nanofibrous scaffolds. The response of human foetal osteoblast cells on these scaffolds

were evaluated using MTS assay, alkaline phosphatase activity, alizarin red staining, and osteocalcin expression for bone tissue regeneration. The cellular response to both groups of scaffolds was better than for the control PCL and most favourable with PCL-CQ-HA nanofibrous scaffolds. Results showed that PCL-CQ-HA nanofibrous scaffolds had appropriate surface roughness for the osteoblast adhesion, proliferation and mineralization comparing with other scaffolds.

Sirasanagandla et al in 2013 evaluated preventive role of emblica offcinalis (EO) and cissus quadrangularis (CQ) on bone loss in osteoporosis. Treatment with EO and CQ significantly increased the serum ALP levels, while the serum TRAP and hydroxyproline levels were significantly restored towards normal level. Loss of bone mass and strength due to osteoporosis was significantly reduced with EO and CQ treatments.

Sirasanagandla et al in 2014 evaluated Protective effect of petroleum ether extract of Cissus quadranularis (PECQ) on diabetes induced delayed fetal skeletal ossification. Fewer ossification centers and decreased extent of ossification of forelimb and hindlimb bones were observed in the neonatal pups of diabetic control group. PECQ pretreatment significantly restored the ossification centers and improved the extent of ossification of forelimb and hindlimb bones suggesting its protective effect.

Brahmkshatriya et al in 2015 clinically evaluated Cissus quadrangularis as osteogenic agent in maxillofacial fracture where the patients in experimental group received CQ capsule in the dose of 500 mg thrice a day for 6 weeks

and control group received no supplement. After 15 days, the mobility was completely absent in Cissus group, whereas slight mobility persisted in the control group. There was early periosteum reaction and bridging between the fractures ends at the site of mandibular fracture on the 21st day and complete deposition of bone fragment on 45th day in CQ group.

Managutti in 2015 evaluated clinical efficacy of cissus quadrangularis in pain management and bone healing after implant placement. Use of cissus quadrangularis after implant placement showed significant effect on pain and swelling management. Also rising level of serum alkaline phosphatase and good bone density when compared to control group indicated new bone formation thus helps in osteointegration.

Sultan et al in 2015 conducted a study to estimate any possible effect of the natural products extract on the stability of orthodontic implant. Four different natural products extract were used in this study include; Curcumin 15mg/kg, Nigella Sativa oil 0. 5 ml/kg, Cissus Quadrangularis 1000mg/kg and Virgin coconut oil 2 ml/kg. Results showed a significant differences between primary and secondary stability, with improvement in stability for implants in Curcumin, Cissus Quadrangularis and virgin coconut oil. Concluding that natural products mentioned above could be used possibly for increasing the bone implant integration expressed by implant stability.

Kanwar et al in 2015 evaluated anti-inflammatory responses on chondrocytes by CQ. It was found that Exposure of chondrocytes to IL-1β induced significant toxicity and cell death whereas treatment with CQ

alleviated IL-1β induced cell toxicity and upregulated cell growth and proliferation. CQ inhibited gene expression of cytokines and matrix metalloproteinases, known to aggravate cartilage and bone destruction, and augmented expression of survivin by inhibiting p38 MAPK suggesting its anti-inflammatory action.

Selvamaleeswaran et al in 2016 studied Antimicrobial Activity of CQ against some pathogenic bacteria. Disc diffusion method with aqueous extract showed maximum antibacterial and antifungal activity against Pseudomonas aeruginosa and Mucor species and the ethyl acetate extract and methanol extract of both fresh and dry stems further exhibited antimicrobial activity against Gram-positive bacteria, including Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, and Streptococcus species.

Giri et al in 2017 evaluated fracture healing property of ethanolic extract of CQ using 3-point bending model in rats. CQ orally 500mg/kg body weight once a day was fed for 30 days to the rats. Skiagram showed evidence of union in CQ treated group with extensive bony deposition indicative of definite action of CQ on the rate of healing of fractures.

Shadmani et al in 2017 studied potential analgesic effect of Cissus quadrangularis L And Lepedium sativum L. along with their combination extracts. The extracts were analyzed at doses of 50, 100 and 200 mg/kg. Analgesic activity at dose of 100mg/kg and 200mg/kg for all extracts were found with significant analgesic activity. The results suggest that the

methnolic root extracts of CQ and LS contains some active principles, which possess analgesic activity.

Latha et al in 2018 studied protective effect of ethanolic extract of Cissus `quadrangularis (EECQ) in streptozotocin (STZ) induced type-2 diabetes rat model and on SHSY5Y neuronal cells. Oral administration of EECQ (100, 200, & 400 mg/kg) significantly reverted the effects of STZ and restored the changes induced by STZ to normal. Also EECQ treated cells showed protective effect against STZ induced cytotoxicity and reduced the ROS generated by hyperglycemia suggesting that the ethanolic extract of Cissus quadrangularis possess hypoglycemic and neuroprotective activity.

Rajagopalan et al in 2018 studied effect of Cissus quadrangularis on bone healing in 80yrs aged woman. The patient was prescribed 750 mg/day of CQ along with calcium supplements. 15th and 30th day of follow up and the X-ray revealed bone healing. The patient presented a remarkable increase in the rate of healing in the bone fracture with a decrease in pain and swelling with an oral dosage of dry powder for 30 days