PLAUSIBLE ROLE OF CISSUS QUADRANGULARIS IN OSTEOGENESIS OF BONE

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Abstract
Cissus quadrangularis is a widely known herb in India and south India in particular.It is widely mentioned in ancient Indian medical texts.The bone healing ability of CQ is outlined in Ayurvedhicmedicine.However ,research on effect of CQ in humans are few and far.This review tries to give a clear picture on the available literature that describes the osteogenetic role of CQ in general and mandibular bone in particular.CQ is suggested as a plant herb in treatment of bone fractures and bone loss as it is safe or usage and side effects are not identified so far.

Keywords: Bone, Cissusqua drangularis, mandibularbone, pirandai, osteoblast.

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1. Introduction

Cissus quadrangularis (CQ) also known as Veldt grape is a climbing tendril with fleshy quadrangular stems with the leaf portion constitutes only 5% - 8% of the aerial plant parts the fleshy, green stem constitutes the major portion of CQ.

The plant is widely distributed throughout tropical and subtropical regions of the world such as India, Sri Lanka, South Africa, Thailand, Java and Philippines. It grows well in otter climate.
The plant is known as Harishankar or Hadjod in Hindi and Asthisanghata, Kandavalli, Vajrangi, etc., in Sanskrit. Hadjod means 'that which joins the bones'.CQ is known as 'pirandai' in Tamil. Due to its bone ligation properties, the plant is referred to as 'Asthisamharaka' in Sanskrit.

The entire parts (root, stem, and leaves) of the plant have been cited in both Ayurvedic and Unani systems for its medicinal values. CQ belonging to Vitaceae family is one of the most widely used for the treatment of piles, anorexia, indigestion, chronic ulcers, asthma, otorrhoea, wounds and in augmenting fracture healing process.
The stout quadrangular stem is traditionally used for treatment of bone fracture, piles, chronic ulcers, asthma, scurvy, irregular menstruation, constipation and blindness. There are also many folklore literature that discusses the medicinal role of CQ in bone formation and fracture healing [1-4].

This plant is studied for its phytochemical constitution, pharmacological activities and toxicological evaluation. It is used for bone healing. It has been proved safe and effective according to Grades of Recommendations Assessment Development and Evaluation (GRADE) in the treatment of bone fractures, hemorrhoids and body weight reduction [5].

Bioactive Components of CQ.
The major constituents found CQ are ascorbic acid, carotene A, ketosteroid, triterpenoids, unsymmetric tetracyclic triterpenoids along with β-sitosterol, β-amyrin, and β-amyrone. In addition, it also contains flavonoids, phytosterols, resveratrol, piceatannol, pallidol, parthenocissine, quadragularins and water-soluble glycosides .The unique chemical constituents of CQ are -novel flavonoids and indanes, as well as phytosterols and keto-steroids–have shown promise as powerful and efficient antioxidants.
Root powder often provides a steady source of mineral resources including potassium calcium, zinc , sodium , Iron, lead , cadmium , copper and magnesium[6,7].

Role of CQ in osteogenesis
Osteogenic modulators play a key role in osteogenesis.[8].The role of CQ in preventing loss of bone and enabling thickening of trabecular and corticular bone in ovarectomised rats is reported by Jameela et al.[9].
In the presence of CQ bone mineralisation happens much faster [10].CQ also increases the deposition of mucopolysaccharides which preludes bone formation[11]. CQ plays a significant role in mineralization of corticular bone .In a study by Jameela et al in ovarectomized rats it was found that CQ induced leptin secretion increases apoptosis of osteoclasts. The same study has also reported the ability of CQ in converting procollagen to collagen.[8] A study done by Potuet al supplementing 500mg/kg of CQ powder on ovarectomized female rats is found to increase the thickness of corticular bone[12]. One of the phyto constituents, 6O trans cinnamoyl in CQ is found to have anti osteoporotic activity[13]. A study involving ethanolic extract of CQ has shown increased osteoblastic activity enabled through MAPkinase pathway[14]. The phytoestrogen component of CQ was shown to increase bone density in ovarectomized rats Radiographically as well as histologically[15] Human studies with respect bone mineralisation and healing of fractures by CQ are far and few. A study carried out by Mishra et al,2010 has shown a 53% reduction in fracture healing on external application of CQ paste [16]. A study by Singh et al using a formulation called osteoseal, that contains CQ, Asparagus and Moringa in the ratio 4:1:2, is shown to hasten the rate of mandibular fracture healing [17]. C. quadrangularis builds up the skeletal of the fractured bone, namely its mucopolysaccharides, collagen, phosphorus, calcium, and others. Mucopolysaccharides supplies raw materials for repair. CQ not only causes the greater accumulation of mucopolysaccharides but also an early disappearance of mucopolysaccharides from the fractured area, associated with the earlier calcification and firm callus formation.[18] The extracts from stem of this plant have been used widely for the early repair of fractures, gout, back pain, and irregular menstruation since ancient time. The steroidal substances from C. quadrangularis have shown marked influence on the rate of fracture-healing and quicker mineralization of the callus.
In addition to the phyto components C. quadrangularis also contains high amount of Vitamin C, Vitamin A, anabolic steroidal substances, and calcium. The steroidal substances from CQ showed marked influence on early regeneration of all connective tissue of mesenchymal origin, and thereby, improve the bone healing [19].

The 3 ketosteroid present in CQ is osteogenic in nature and acts on estrogen receptor o the bone cell [20].Also ,the ketosreroid has anatagonistic property of glucocorticoid receptor and helps in maintaining bone health[21].

Furthermore, Phytosteroids found in CQ are found to be precursor of vitamin D3. Along with this the saponins present in CQ have been reported to affect the permeability of the small intestinal mucosal cells due to its strong surface-active properties and thus have an effect on active nutrient transport [22], which includes easy absorption of dietary calcium through the enterocytes.

In dentistry, experiments are done to test the ability of CQ to heal Maxillofacial fractures.The maxillofacial fractures take at least 12–16 weeks to heal.

C. quadrangularis contains high amount of Vitamin C, Vitamin A, anabolic steroidal substances, and calcium. The steroidal substances from the C. quadrangularis showed marked influence on early regeneration of all connective tissue of mesenchymal origin, and thereby, improve the bone healing. This will stimulate the cells of mesenchymal origin, namely the fibroblasts, the chondroblasts, and the osteoblasts by C. quadrangularis. These cells have greater impact on osteoblastic proliferation than other cellular responses[24].

Active constituents of Cissus quadrangularis may stimulate the proliferation and differentiation of mesenchymal cells (MSCs) and promote new bone formation through the WntLRP5-B-Creatnin signalling pathway of pre-osteoblast formation. It can be used to treat various bone disorders and can also be used as a preventive measure for disorders that lead to decreased bone mineral density.[25]

Cissus quadrangularis is rich in vitamin C and beta-carotene. a study in 9 people observed that taking 500 mg of Cissus quadrangularis 3 times per day for 6 weeks helped speed the healing of fractured jaw bones. It also appeared to reduce pain and swelling

With the available evidence CQ is considered as a potent component to treat mandibular fractures. The role of CQ in PDL regeneration of intra bony periodontal defects has been evaluated in association with hydroxyapatite bone filler [22]. The same author has also mentioned the use of CQ as a biomaterial in dentistry.

Still deeper research is the needed to elucidate the use of CQ in dentistry and to understand the potential role of CQ in oral health.

2. Conclusion

Bone formation requires nutrients such as vitamin C,minerals, mucopolysaccharides in addition to Calcium, phosphorus ,protein and Vitamin D3.CQ is complete in this aspect and its bone healing property due to phyto sterols and flavonoids are enhanced by the presence of minerals and other nutraceutical substances in its bioactive components. Further research in human subjects would enable much larger and significant application of CQ in bone healing in general and alveolar bone in particular.

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