

# *Asthishṛṅkhalā* (Cissus quadrangularis Linn) A New Emerging Medicine for Osteoarthritis: A Review

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## ABSTRACT

Osteoarthritis (OA) is the most prevalent kind of arthritis in developed and developing worlds. It is a degenerative joint disease affecting mostly the articular cartilage. Aging affects joints that have been repeatedly pressed over time, such as knees, hips, fingers, and the lumbar spine. Osteoarthritis is a major cause of disability and social expenditure among the elderly. Several herbs and their formulations have been mentioned in ancient Ayurvedic texts that play an important role in bone mending process; *Asthishṛṅkhalā* is one of them. Its root, stem, and leaf are most important part used medicinally. *Bhāvaprakāsh* and *Cakradatta* describe *Asthishṛṅkhalā* (Cissus quadrangularis, Linn) as a general tonic, especially for bone fracture or bone loss. According to recent studies, that the stem of *Asthishṛṅkhalā* has showed the presence of many important classes of phytoconstituents like carbohydrates, alkaloids, amino acid, protein, saponin, glycosides, phenolic compound, steroids and tannins. Estimation of carotene, total flavonoid content, steroidal content, Vit C, Vit A, calcium and saponins also have been reported in phytochemical analysis. Probably as a result of these chemical ingredients, it is utilized in clinical practice by Ayurvedic practitioners in variety of diseases including osteoarthritis. In present context, brief account of osteoarthritis has been taken under the influence of indigenous medical plant *Asthishṛṅkhalā*.

**Key Words** Ayurveda, *Asthishṛṅkhalā*, *Cissus quadrangularis*, Medicinal plant, Osteoarthritis, Sandhigatavāta

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## INTRODUCTION

Osteoarthritis is a condition that typically affects the elderly. It is a leading cause of impairment in older persons around the world. According to the World Health Organization (WHO), symptomatic osteoarthritis affects 9.6 % of men and 18 % of women over the age of 60 in the developed and developing worlds. More than eighty percent of

people with osteoarthritis experience mobility restrictions, and twenty-five percent have difficulty doing their primary daily tasks<sup>1</sup>.

Osteoarthritis is the second most prevalent rheumatologic condition and the most common joint illness in India, with a frequency ranging from 22% to 39%. In India, it is the most frequent type of joint illness. Women are more

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likely than males to suffer from osteoarthritis. Women over the age of 65 years who have symptoms of osteoarthritis (OA) are about twice as likely as those over the age of 65 years who have radiological evidence of OA<sup>2</sup>.

The disease osteoarthritis is comparable to the disease *Sandhigataavāta* a kind of *Vātavyādhi* of indigenous system of medicine. The chief presenting symptoms is joint pain in knee OA. Similarly, *Sandhisūla* is the prominent feature of *Sandhigataavāta*. In knee OA swelling due to joint effusion is found which is tested by Patellar tap, fluid displacement test or ballottement test. This is very similar to the *Vātapūrṇadr̥tisparśa* sign of *Sandhigataavāta* which pointed out that the swelling feels as a leather bag filled with air which displaces on applying pressure. In knee OA, pain typically increases with joint use i.e., on standing, walking, flexing or extending the joint. *Ācharya Caraka* mentioned the *ākuñcana-prasāraṇa janya vedanā* which literally means pain during flexion and extension of the joint. Patients of knee OA often describes presence of cracking, grinding sound on climbing stairs, squatting etc. This is clinically known as crepitus which can be audible in both passive and active movements as well as can be palpated on knee joint during examination, which is correlated with the term *Ātopa* of Ayurveda. It is explained as *Guḍaguḍa-śabdaḥ* in a different context but is some sort of friction sound at the time of palpation of affected joints. *Susṛuta* added the term '*sandhi-hanti*' which means the destruction

of the joint. In knee OA it is evident through X-ray or MR imaging that degenerative destruction of bone and cartilages are the main culprit for the production of the disease<sup>3,4</sup>.

Traditional systems of medicine including Ayurveda continue to be extensively practised for the management of ailments since centuries. Due to rising population, insufficient supply of trademarked medications and rising drug resistance against diseases, plant-based medicines are gaining momentum for its utilization worldwide. Ayurveda recommends single or mixed herbal, mineral, and animal medicines. Single herbal medications are important in Ayurvedic therapies due to their ease of administration since centuries. *Sandhigataavāta* is treated with several herbal medicines, some of which have been researched scientifically in clinical and pre-clinical investigations. Many unpublished investigations have recently been conducted by numerous institutes. Due to its effectiveness and safety for human usage, *C. quadrangularis* has gained great interest in recent years. It has long been used as a folk remedy for pain and diseases like menstruation problems and bone damage. A propensity for healing fractured bones has earned it the moniker "Bone Setter". *C. quadrangularis* is now broadly utilized in sporting circles to maintain joint health during strenuous activity.

## METHODOLOGY

The Ayurvedic traditional texts and electronic databases PubMed, Scopus, ScienceDirect, Web

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of Science, and Google Scholar were searched for works containing the following keywords: *Cissus quadrangularis*, antimicrobial, anti-obesity, anti-inflammatory, bone resorption, and antioxidant. The inclusion of *C. quadrangularis* was based on previously published publications on the pharmacological actions of the plant, which are explored in depth. All of the information was retrieved and discussed in detail under the appropriate subheadings.

### *Cissus quadrangularis*

According to the World Health Organization, around 80% of the world's population is dependent on traditional systems of medicine. There are several herbal preparations listed in ancient Ayurvedic texts that are useful in the process of bone mending. There are several synonyms have been given for this plant in classical texts of *Āyurveda*, because of its therapeutic properties; *Haḍajoda* (*C. quadrangularis*) is one of them, and its literally means as "connecting the bone or fracture healing process."

**Table -1 Ayurvedic Pharmacodynamics<sup>7</sup>**

<b>Botanical Name</b>	<b><i>Cissus Quadrangularis</i></b>	<b>Family</b>	<b>Vitaceae</b>
<b>Hindi:</b>	<i>Haḍajoda</i>	<b>English</b>	<i>Edible Stemmed Vine</i>
<b>Synonym</b>	<i>Vajra, Valli, Asthisamharaka</i>	<b>Gaṇa</b>	<i>Caraka: Balya, Brimhaṇiya, Madhuraskandha</i>
<b>Rasa-</b>	<i>Madhura</i>	<b>Doṣa Karma</b>	<i>Kapha- Vātahara, Vṛśhya, Pācana, Cakshusya</i>
<b>Guṇa-</b>	<i>Laghu, Rūksha</i>	<b>Rogahntā</b>	<i>Asthibhagna, Netra Rog, Arśa</i>
<b>Virya-</b>	<i>Ūshṇa</i>	<b>Dosage</b>	Paste 5-10gm, Fresh Juice 10-20ml
<b>Vipāka-</b>	<i>Katu</i>	<b>Part Used</b>	Stem, leaves and root

### Phytochemistry:

The plant's pharmacological action is beneficial owing to the existence of their chemical constituents as per modern pharmacopeia. *C.*

*quadrangularis* is a fleshy plant of the Vitaceae family. It is a medicinal plant native to India and Africa. It has been referenced in ancient Ayurvedic texts such as *Asthisṛmkhalā*, *Asthisamhāraka* by *Bhāvaprakāsha*<sup>5</sup>, and *Cakradatta*<sup>6</sup> as a general tonic, notably for the treatment of fractures and bone loss. There are a variety of internal and external applications of this plant that have been explored and proven to be useful. Ayurvedic pharmacodynamics of *Asthisamhāraka* mentioned in Table -1.



**Figure 1** *Asthisṛmkhalā* (*C. quadrangularis*) Plant

*quadrangularis* contains a variety of bioactive components, including alkaloids, resveratrol, piceatannol, pallidol, parthenocissin, *quadrangularins*, ascorbic acid, carotene,

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phytosterol substance, calcium flavinoids, vitamins, enzymes, nicotinic acid, and tyrosin. *Cissus quadrangularis* includes a number of different terpenoid constituents, including balsam ketone, amyirin, onecer-7ene-3-21 diol, taraxerol, and friedelin ketone. Tetracyclic triterpenoid, onecer-7ene-3-21 diol, and two steroidal principles I and II, -sitosterol and - amyirin, are the primary chemical components. Two asymmetrical tetracyclic triterpenoids and two steroidal principles are included in the stem<sup>8</sup>.

### Toxicity:

Bioactive chemicals generated from plants are continually in demand and are the major focus of study. Despite rising market demand for herbal medicines, medicinal plant safety remains an issue. *Cissus quadrangularis* L. extracts were studied by Teka Feyera et al.<sup>9</sup> for phytochemical and biosafety purposes (aerial parts). Acute (2000mg/kg single dose) and sub-acute (200 and 400mg/kg repeated doses) oral toxicity were examined in Swiss albino mice. To assess the toxicity of the crude extracts, body weight, PCV, Hb level, and mortality were measured. There were various secondary metabolites found in the plant. The plant's methanol and chloroform extracts at 2000 mg/kg did not cause death or weight loss in the acute toxicity trial. However, in sub-acute toxicity studies, *C. quadrangularis* extract showed minimal mortality and a little rise in haematological markers.

### Toxicological studies:

There have been a few toxicological investigations conducted on the genus *Cissus*. *C. quadrangularis* has an LD50 of 681 mg/kg (Dhawan et al., 1977)<sup>10</sup>. In another work on *C. quadrangularis*, the LD50 was determined to be 1000 mg/kg through ip route (Swamy et al., 2006)<sup>11</sup>. On vegetative samples, the LD50 was high (853.09mg/kg). Parameters of hematology and biochemistry were within normal limits. Histopathological examinations indicated modest alterations in the liver hepatocytes, nonspecific hazy enlargement of the glomeruli, and normal function of other essential organs. The LD50 for variation II was shown to be 797.3 mg/kg (Austin and Jegadeesan, 2002)<sup>12</sup>. Seasonal variation across samples resulted in a little variance in the fatal dosage. Bioactive principles are observed to be more abundant in samples obtained prior to blooming. Another 14-day acute oral toxicity trial in rats with ethanol extract at a dose of 5000 mg/kg revealed no symptoms of intoxication, gross pathological lesions, or mortality.

Sub chronic toxicity studies at dosages of up to 5000mg/kg revealed no treatment-related changes in clinical observations or biological markers (Verma, 2018)<sup>13</sup>.

### Clinical studies of *Asthisṛṃkhalā* on bone repair, fracture healing and pain reduction:

**Reduces fracture healing time:** Clinical study has revealed that *C. quadrangularis* significantly reduces the time required for fractures to heal due to its osteogenic action, based on radiological and clinical findings<sup>14</sup>. *C. quadrangularis* strengthens

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the skeletal system of shattered bone using mucopolysaccharides, collagen, phosphorus, and calcium. Mucopolysaccharides are used as basic ingredients in the repair process. Rapid usage of these basic materials early in the healing phase will result in the completion of the healing process. *C. quadrangularis* not only increases mucopolysaccharide accumulation, but also causes an earlier removal of mucopolysaccharides from the fractured region, which is related with faster calcification and hard callus development.<sup>15</sup>

In fracture healing, *C. quadrangularis* stimulates metabolism and increases calcium, sulphur, and strontium absorption by osteoblasts. Amino acids like lysine aid in calcium absorption. *Cissus* includes Vitamin A and C, which help to create collagen<sup>16-18</sup>.

### **Reduction in pain and swelling**

The administration of *C. quadrangularis* resulted in an early reduction in pain and oedema, as well as a decrease in mobility at the fracture site, which might be related to higher blood calcium and phosphorus levels<sup>15</sup>. One research revealed that callus development occurred early in the course of the trial and clinical discomfort, soreness, and swelling were absent in the *Cissus* group, according to the radiological findings<sup>17</sup>.

### **The other beneficial effects of *Asthisrnkhala*:**

a. **Anti-obesity activity:** A study was carried out with the help of a *Cissus quadrangularis* formulation known as *cylaris*. The trial was conducted in a double-blind, placebo-controlled

fashion. The results revealed that the test participant had a decrease waist circumference and a lower body mass index, decreased lipid levels in the serum<sup>19</sup>.

b. **Anti-diabetic activity:** *Cissus quadrangularis* has been shown to have anti-diabetic properties in a trial in which dry powder obtained from ethyl acetate extraction was given<sup>20,21</sup>.

c. **Antioxidant and free radical scavenging activity:** The presence of carotene in the methanol extract of *C. quadrangularis* results in significant antioxidant and free radical scavenging activity in both *vitro* and *in vivo* systems, which is primarily responsible for this activity<sup>22,23</sup>.

d. **Gastro protective Activity:** *Cissus quadrangularis* contains a high concentration of carotenoids, triterpenoids, and ascorbic acid and has an ancient legacy of usage in traditional medicine for the diagnosis of gastrointestinal illnesses. It has also earned substantial recognition for its influence on human nutrition. Numerous investigations explored and established the effect of *Cissus quadrangularis* extract (CQE) on gastrointestinal toxicity and gastroprotective action, as well as the use of CQE in therapeutic intervention for aspirin-induced stomach mucosal injury<sup>24</sup>.

e. **Central nervous system activity:** The root extract has been shown to have stimulant CNS effects, as seen by the decrease in exploratory activities. Methanol root extract contains



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saponins, which have a strong calming effect on mice and also have the ability to reduce spontaneous motor activity<sup>25,26</sup>.

f. **Analgesic, Anti-Inflammatory and Stimulatory Activity:** Methanol extract has analgesic, anti-inflammatory, and venotonic effects in haemorrhoids, the anti-inflammatory action being attributed to flavonoids, namely -sitosterol. The methanol extract of -sitosterolin does have the capacity to inhibit MPO enzymes, indicating a considerable decrease in neutrophil infiltration into the inflamed region. In rats, ethanol extract exerts a protective impact on neutrophils activated by aspirin-induced tissue injury<sup>27</sup>.

g. **Anxiolytic and Antiepileptic Properties** A study report established the effects of aqueous extract of *Cissus quadrangularis* (AECQ) on pre- and post-SE seizures, anxiety problems, and oxidative activity in epileptogenesis mice. AECQ enhanced pre- and post-SE delay and lowered the frequency and duration of tonic-clonic seizures considerably. The EACQ boosted both the number of entries and the duration of time spent in the EPM's open arm. In AECQ-treated mice, decreases in GSH and GABA levels were compensated by increases in MDA and GABA-T levels. AECQ has been established in animal models of epilepsy to be an anticonvulsant extract with anxiolytic properties<sup>28</sup>.

h. **Antibacterial:** Cysteine proteases (Cp) shown a high level of antimicrobial action against pathogenic microorganisms. A Cp was isolated

from the stem of *Cissus quadrangularis* with 5.39 times increase in specific activity and an 8.67 percent recovery. Antibacterial activity of Cp from *C. quadrangularis* was determined against *Bacillus cereus* and *Bacillus megaterium*. Transmission electron microscopy examination indicated that Cp from *C. quadrangularis* destroyed the peptidoglycan layer of bacteria<sup>29</sup>.

### Conclusion:

It is known by the plant called *Asthisṛṃkhalā* (*C. quadrangularis*) which is an Ayurvedic herb used to cure a number of diseases such as bone fractures and osteoarthritis. The presence of a wide range of phytochemical substances in *C. quadrangularis*, including glycosides, alkaloids, flavonoids, tannin, saponin, vitamin C, steroid content, and calcium, suggests that the plant has substantial promise as a therapeutic agent. Taking into consideration the information presented in the preceding sections of ancient and modern knowledge, it can be concluded that *Asthisṛṃkhalā* has the ability to impart osteogenic activity and is therefore beneficial in the treatment of fractured or lost bone, osteoarthritic joint pain, and bony discomfort. The present review contributes to the existing body of knowledge on *C. quadrangularis* Linn. and will be immensely valuable to people who are suffering from bone and joint difficulties as a result of their condition.

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