WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 18, 239-251. Review Article ISSN 2277– 7105

LITERARY REVIEW OF PHARMACOLOGICAL ACTIVITIES OF CISSUS *QUADRANGULARIS L.* W.S.R. TO *ASTHISANDHANAKAR KARMA* (BONE HEALING PROPERTY)

Dr. Sarita Sunil Bedarkar*[1] and Dr. S. S. Shekokar[2]

[1]PhD Scholar, Dept. of Dravyaguna Vigyan, Government Ayurveda College, Nanded, 431601.

[2]Guide (Prof. & HOD), Dept. of Dravyaguna Vigyan, Government Ayurveda College, Nanded, 431601.

Article Received on
23 August 2023,

Revised on 13 Sept. 2023,
Accepted on 03 October 2023

DOI: 10.20959/wjpr202318-29881

***Corresponding Author**
Dr. Sarita S. Bedarkar
M.D., Ph.D. (Sch.)
Dravyaguna Vigyan,
Assistant Professor - at
SST's Ayurveda College,
Sangamner, 422605.

ABSTRACT

Cissus quadrengularis L. or *Asthishrunkhala* is one of the most important plant in *Ayurveda* specially known for its bone fracture healing property. Since long ago *Vaidyas* have been using it for strengthening the bone. It is a common perennial climber, a succulent plant of family Vitaceae, also known as "Bone Setter" in English, or Hadjod in Hindi because of its ability to join bones and *Asthisamhari, Kandvalli, Vajrangi* in *Sanskrit.* In *Ayurveda* it is mentioned that this plant possesses many properties like *Pachana* (digestive aid), *Sara* (relieves constipation), *Asthiyuk* (strengthening bones), *Vrishya* (Aphrodisiac), *Krumighna* (destroys worms), *Arshoghna* (cures piles), *Balya* (provides strength), *Amaghna, Kushthaghna* (cures skin disorders). *Cissus quadrangularis L.* is fleshy, cactus-like climber widely used as a food item in India & is distributed throughout the tropical and subtropical regions. A variety of chemical constituents have been isolated and identified from *Cissus* extracts, including steroids, flavonoids, stilbenes, iridoids, triterpenes and Gallic acid derivatives. Recent Animal and in vitro studies have proved that it provides support in promoting bone fracture healing and as an anti-osteoporotic agent. The present paper is an attempt to highlight the studies in animals, humans and in vitro systems that have been conducted to determine the efficacy in promoting bone fracture healing and as an Anti-osteoporotic.

KEYWORDS: *Cissus quadrangularis L*, Pharmacological, Phytochemical, *Asthisandhanakar karma*, Bone healing property.

INTRODUCTION

The World Health Organization (WHO)[1] estimates that 20,000 to 35,000 plant species are used by numerous ethnic groups worldwide as pharmaceuticals, cosmetics, nutraceuticals, and treatments. Nearly 80% of people in developing countries use traditional medicines to maintain their health and vitality.[2] The therapeutic properties of various plant species have steered the development of many traditional herbal remedies over time. The world continues to rely on plant-based medicines to treat a variety of illnesses, such as alternative or complementary therapies, primarily to avoid side effects and find relief for ailments for which there is little to no effective allopathic treatment available.

The activity of plants used in traditional medicine across the world is something that many researchers are interested in scientifically validating and explaining. Herbal medications and extracts have recently attracted fresh interest for a number of reasons, including their low cost, lack of adverse effects, potential to treat chronic illnesses and disorders, traditional uses, and preventative measures. Due to this, recently these conventional treatments have gained greater scientific patronage. *Ayurveda* (use of drugs to preserve health, longevity, and energy and also mental and physical wellbeing) have been crucial to the development of this life science.

Cissus quadrangularis L., also known as Edible Stemmed Vine (English), is being studied for its medicinal prospective. It is an annual or perennial plant with whole leaves that are buff in color with a greenish tinge that demands a warm tropical environment and is grown by stem cuttings in June and July.[3] Though this plant has a wide range of medicinal uses, some of the most common are for weight loss, anthelmintic, muscular pains, asthma, repair of broken bones, antiulcer, anti hemorrhoidal, antimicrobial, etc.[4]

In order to heal properly, fractures are typically treated with reduction, retention, and rehabilitation. A fracture typically heals in three weeks, but there are numerous *Ayurvedic* medications that speed up the process and help patients become independent sooner. *Asthishrunkhala*, also known as *Cissus quadrangularis*, is an example of an effective herb that has been tested and shown to be effective through research studies. A literature review of

the scientific studies of this herb has been conducted in order to increase public awareness towards this miraculous herb to corroborate its bone healing and related activities.

Plant profile

Fig. No. 1: Stem & Leaf.

Fig. No. 2: Stem & Fruit.

AIMS AND OBJECTIVES

Aim- To study the pharmacological activities of *Cissus quadrangularis L.* w.s.r. to *Asthisandhanakar karma* (Bone healing property) through a literary review.

Objectives

1. To review *Asthishrunkhala* & its *Asthisanshanakar karma* according to Classical texts.
2. To review Bone healing property of *Asthishrunkhala* according to Modern Science.

MATERIALS AND METHODS

Data for literature review has been collected from classical texts- *Bruhatrayi, Laghutrayi* & *Nighantus,* Modern text & related websites.

Drug Review

According to Ancient Literature

निरुक्ति- Synonyms & Their Nirukti Etymology[5]

१. अस्थिसंहारी (भा.) - अस्थि भग्नं संहारयति योजयतीति ।

It helps to reunion of the fracture bones.

२. अस्थिश्रृंखला (भा.) - लता अस्नां श्रृंखलेव प्रतिभाति |

It looks like chain structure

३. अस्थिसंयोजकः (प्रि) - भग्नमस्थि संयोजयतीति ।

It promotes union of Fracture

४. ग्रन्थिमान (भा.) - काण्डे ग्रन्थियुक्तः |

It has nodular stem.

५. चतुः सिरः (श.) - चतस्रः सिराः काण्डेऽस्य ।

It having quadrangular stem.

६. वज्रवल्लरी (कै.) - वज्रमस्थि, तस्य लतेव ।

Asthisamhari is a weak plant.

ECOLOGY/HABITAT

This herb can be found in hotter regions like India, Malaysia, Pakistan, Bangladesh, Sri Lanka, and Pakistan. It is grown in plains, coastal regions, jungles, and wastelands up to 500 meters above sea level. Cuttings are used to propagate the plant.[6]

TAXONOMY

Kingdom Plantae – Plants

Sub kingdom - Tracheobionta - Vascular plants

Super division - Spermatophyta - Seed plants

Division - Magnoliophyta- Flowering plants

Class - Magnoliopsida - Dicotyledons

Subclass - Rosidae

Order - Rhamnales[7]

Morphology

Family Vitaceae, or the grape family Virginia creeper, which typically has lianas with alternate, frequently palmately lobed or compound, occasionally pinnate, leaves. A tendril, or modified inflorescence that forms from a displaced bud, opposes the leaf and attaches to the support by twining or by forming adhesive discs, with swollen nodes in most cases. The fruits are berries, the flowers are 4 or 5 merous, and the seeds have a prominent cordlike raphe that extends to a chalazas knot. The petals form a cap that falls off when the flower opens.[8]

Genus *Cissus L.* – Simple, entire leaf trees are known as treebines. Acutely angled or winged stems and branches are present. Small, polygamous flowers are arranged in terminal panicles. Calyx is deciduous, short, and entire. Four to five imbricate petals. There are exactly as many stamens as petals, but only one of them is functional. Filiform style and unilocular ovary with a single ovule. Fruit is a juicy drupe.[9]

Species - *Cissus quadrangularis L*.

Vernacular Names

Botanical Name- *Cissus quadrangularis Linn.*

English name: Edible stemmed vine

Sanskrit Name: *Asthisamdhani, Asthisamhari, Vajravalli, Asthishrinkhala, Asthisamhara, Kandavalli, Vajrangi, Asthisamyojaka*

Hindi name: Hadjod, Harjora, *Asthisanhari*

Bengali name: Harjora

Gujarati name: Hadasankala Vedhari

Kannad name: Mangroli

Malyalam name: Cannalam Paranta, Piranta

Marathi name: Hadsandhi, Kandvel

Punjabi Name: Haddjor

Tamil Name: Perandai, Pirantai

Telugu Name: Nalleru

Oria: Hadbhanga

Common Name: Hadjora[10]

Phytoconstituents

Studies on the phytochemistry of Cissus quadrangularis have revealed that it contains a wide range of useful components, including flavonoids, triterpenoids, Vitamin C, stilbene derivatives of iridoids, sterols, triterpenes, alkaloids, fatty acids, and methyl esters. Two asymmetrical tetracyclic triterpenoids, ascorbic acid, triterpene, -sitosterol, ketosteroid, and calcium were found to be the main components of this plant. A significant amount of calcium ions and phosphorus, both of which are necessary for bone growth, are present in the stem extract.[11]

PARTS USED- Whole plant, root, stem, leaf.

TRADITIONAL AND FOLKLORE USES

The traditional best parts of the plant for healing bone fractures are the roots and stems. The plant has been used to treat osteoarthritis, rheumatoid arthritis, and osteoporosis according to *Ayurveda*. The plant's stem juice is used to treat epistaxis, otorrhoea, scurvy, and menstrual disorders. Cattle are fed the herb to encourage milk production. The thick, fleshy, quadrangular stem has traditionally been used to treat anemia, gastritis, constipation, eye conditions, and piles.[12]

Asthisandhanakar karma* according to *Ayurveda

***Ayurvedic* properties**

Rasa- *Madhura*

Guna- *Laghu, Ruksha, Sara*

Veerya- *Ushna*

Vipaka - *Madhura*

Doshaghnata- *Kaphavatashamaka, Pittavardhaka.*[13]

References for its bone healing activities from some *Ayurvedic* lexicons

भावप्रकाश:-

१. वायुप्रशमने-

काण्डं त्वग्विरहितमस्थिश्रृङखलाया माषार्धं द्विदलमकुञ्चकं तदर्धम् ।

सम्पिष्टं तदनु ततस्तिलस्य तैले संपक्वं वटकमतीव वातहारि ॥[14]

चक्रदत्त:-

२. भग्नरोगे - सघृतेनास्थिसंहारम् ...।

सन्धियुक्तेऽस्थिभग्ने च पिवेत् क्षीरेण मानवः ॥[15]

शोढल:-

३.ऊरुस्तम्भे – सार्धं मांसैरस्थिश्रृङ्गाटिकाया भुड़े यद्वा व्यंजनेनापरेण ।

क्षिप्रं शाम्यत्यस्थिभङ्गोऽस्य नूनं वातव्याधिः चातितीव्रोऽपि यः स्यात् ॥[16]

वैद्यमनोरमा -

४. पुत्रकामार्थम् - वज्रवल्लीरसे तुल्यं तैलं तत्कल्कमिश्रितम् ।

ऋतुस्नाता वधूः पिण्डं भक्षयेत् पुत्रकांक्षिणी ॥[17]

कैय्यदेव-

५. अस्थिसन्धानजननी- वज्रवल्ली सरा रूक्षा कृमिदुर्नामनाशिनी ||

दीपन्युष्णा विपाके च स्याद्वी वृष्या बलप्रदा |

अस्थिसन्धानजननी वातश्लेष्महरा गुरुः ||[18]

Author	***Rasa***	***Vipak***	***Virya Karma*/Pharmacological actions**
Bhavprakash	***Madhur***	***Madhur***	***Ushna Asthiyuk***
Kaiyyadev	***Madhur***	***Amla***	***Ushna Asthisandhanajanani***
Chakradatta	**-**	**-**	***- Sandhi yukteasthibhagne***

Asthishrinkhala is *Madhura* in *rasa, Madhura vipaki,* and *Ushna viryatmak*[19], and it possesses *Laghu, Ruksha & Sara guna.* It is a *Vichitra pratyarabdha dravya*. Though it possesses *Laghu, Ruksha guna,* which helps in *Rakta stambhan* and *Kleda shoshan* and also *Madhur rasa* causes *Sarva dhatu bruhan* and consequently *Asthi bruhan and Sandhana*. In *Asthi bhagna*, there is loss of normal integrity of bone. For the fracture healing, *Sandhana karma* is needed.

Asthisanharaka is *Madhur rasatmak* and *Madhur vipaki*, the *Madhur rasa* is composed of *Jala* and *Prithvi mahabhuta. Jala mahabhuta* causes *Dhatu poshan* and *Bruhan* due to its *Snigdha guna,* and *Prithvi mahabhuta* having the *gurutva*[20] it helps to produce mass i.e. *Asthi dhatu.*

Bruhan and *Vardhan* which in *Ayurvedic* terms is known as *Sandhanakara* property (bone healing property). Thus *Asthisanharaka* helps in healing of *Asthi bhagna* due to all its properties like *Madhura rasa and, Madhur vipaka (Dhatu bruhan).* According to *Bhavaprakasha, Asthisanharaka* is *Vrishya.*[21] Hence this property of *Asthisanharaka* also helps in healing of *Bhagna.*

Common uses

In *Asthi bhagna*, according to *Aacharya Chakradatta* if stem of *Asthisanharaka* is fried in ghee and administered with milk is beneficial for the treatment of fractures and osteoarthritis.[22]

FORMULATION AND PREPARATIONS

The plant is incorporated in various formulations along with different herbs. These include *Laksadi Guggulu, Asthisamharadi Churna, Asthisamhara Taila, Dasyadi Kwatha, Darvi Kwatha* etc.[23]

Physiology of bone fracture healing

There are three major phases of fracture healing,[24] two of which can be further sub-divided to make a total of five phases

1. Reactive phase

i. Fracture and inflammatory phase

ii. Granulation tissue formation

2. Reparative phase

iii. Cartilage callus formation

iv. Lamellar bone deposition

3. Remodeling phase

v. Remodeling to original bone contour

Pharmacological activities

- **Bone healing activity**

Animal experiment

In a study on albino rats, a paste made of the plant's alcoholic extract speeds up the healing of fractures when administered intramuscularly and locally.[25] Ethanol extract (95%) has been

shown to influence early regeneration and quick mineralization of bone fracture healing process and enhances the development of cortical bone and trabeculae in fetal femur. This effect may be related to the high content of calcium, phosphorus, and phytoestrogen steroids in the extract.[26] An ovariectomized rat model of osteoporosis exhibits anti-osteoporotic activity in response to two different dose levels of 500 and 750 mg per kg per weight in ethanol extract (95%) of the whole plant.[27]

Animal experiment

In a study to assess the effect of Cissus extracts on the healing process of a dog's experimentally fractured radius ulna, the treated group's fracture healed completely in 21 days while the control group's fracture remained incomplete.[28] In addition, the treated group showed osteoblastic cells replacing cartilaginous cells and the union of fractured gaps in various places with the development of new bony trabeculae, whereas bony trabeculae were not present in the control group.[29]

- **Analgesic activity**

When tested using the Heffner's clip and Eddy's hot plate methods, Cissus demonstrated noticeably greater analgesic activity than Aspirin. Its wide margin of safety for the treatment of pain can be seen by the fact that the optimal effective dose for analgesic effect fell between 1/20th and 1/10th of its LD50. Cissus' analgesic effects could be very helpful in easing the pain brought on by bone fractures.[30]

Toxicological study

When given orally to mice, rats, and guinea pigs for ten days, the Cissus quadrangularis extract does not have any toxic effects. However, after receiving the medication intravenously, the animals began to convulse and died in five minutes. In guinea pigs, the MLD came out to be 15.5 mg/Kg.[31] The drug is safe even at higher doses for a longer duration of treatment, according to toxicological analysis of the plant. Numerous studies have demonstrated that the Cissus quadrangularis extract has no known toxic effects.[32]

Human trial

A clinical study on patients treated with external applications of the paste made from Cissus for various types of fractures revealed that earlier collagen fiber formation led to earlier calcification and callus formation.[33] In addition to neutralizing cortisone's anti-anabolic effect on fracture healing, this also promotes the callus's mineralization.[34]

In another clinical study group experienced a significant early increase in tensile strength. Cissus therefore improves the chemical makeup of the fractured bone, including its mucopolysaccharides, collagen, calcium, phosphorus, and other elements as well as its functional effectiveness.[35]

DISCUSSION

According to *Ayurveda Asthisanharaka* helps in healing of *Asthi bhagna* due to all its properties like *Madhura rasa and, Madhur vipaka (Dhatu bruhan). Madhur rasa* causes *Sarva Dhatu Bruhan* and consequently *Asthi bruhan and Sandhana*. The *Madhur rasa* is composed of *Jala* and *Prithvi mahabhuta. Jala mahabhuta* causes *Dhatu poshan* and *Bruhan* due to its *Snigdha guna,* and *Prithvi mahabhuta* having the *Gurutva,* it helps to produce mass i.e. *Asthi dhatu*.

According to *Ashraya Ashrayi bhava* described by *Vagbhata Shamana* of *Vata Dosha* leads to *Asthi Vriddhi*. *Madhura vipaka* and *Ushna virya* of *Asthishrunkhala* leads to *Shamana* (alleviation) of *Vata dosha*. *Madhura rasa, Madhura vipaka*, *Sara guna* and *Raktashodhana* property of *Asthishrunkhala* may have any effect on local circulation with increasing cellularity and vascularity thus the promoting process of healing of fracture faster and bone union.

The previous animal and clinical studies also have suggested in the pharmacological activities that that *Asthishrunkhala* enhances the development of cortical bone and trabeculae in fetal femur, which may be due to its calcium, phosphorous and phytoestrogen steroids contents and also shown to influence early regeneration and quick mineralization of bone fracture healing process. It also showed early gain in the tensile strength of bones. It possess greater analgesic activity than Aspirin and can be used at higher doses for prolonged duration without any toxic effect.

The above all explained animal and clinical studies proves that *Cissus quadrangularis* shows more efficacy in Bone healing activity as compared to conventional treatment regimen thus reducing the duration of healing and pain. This proves the *Asthisandhanakar karma* i.e. Bone healing property of the valuable magical drug – *Asthishrunkhala* i.e. Cissus *quadrangularis L.*

Conclusion and further scope

- Above scientific preclinical and clinical studies proved that - *Asthishrunkhala* (*Cissus quadrangularis*) acts as potent anti-inflammatory and analgesic drug, which reduces the requisite for analgesics and promotes early healing and mobility.
- The drug is readily available, affordable, and effective, causing no toxicity even in higher doses in prolonged use so can act as the best medication for fracture patients.
- It influences early regeneration of bones so causes speedy recovery of fractured bone thereby reducing time and pains of the subjects.
- The drug efficiently acts as a potent analgesic causing relief from the pain brought on by bone fractures.
- All the pharmacological activities and its chemical constituents suggests that - the drug *Asthishrunkhala (Cissus quadrangularis L.)* proves to be an effective treatment and accessible regimen for achieving normal tensile strength in shorter duration for bone healing.

REFERENCES

1. WHO launches the first global strategy on traditional and alternative medicine, 16 May 2002.
2. Trivedi, PC. Herbal medicine: traditional practices (Ed). Aavishkar Publishers, Jaipur, 2006; pp 322.
3. Anonymous (1992) Indian Medicinal Plants, Vol 2, Orient Longman Ltd, p. 112.
4. Anonymous (1992) Indian Medicinal Plants. Vol 2, Orient Longman Ltd, p. 112.
5. Sharma P.V., "Namarupajnanam" (Characterization of Medicinal Plants), Chaukhambha Viswabharati Oriental Publishers and Distributors, Varanasi, Reprint 2011.
6. Anonymous (1992) Indian Medicinal Plants. Vol 2, Orient Longman Ltd, p. 112.
7. Rastogi RP, Mehrotra BN, Compendium of Indian Medicinal Plants, Part I, Publication and information directorate 1995; p.104.
8. Rastogi RP, Mehrotra BN, Compendium of Indian Medicinal Plants, Part I, Publication and information directorate 1995; p.104.
9. Rastogi RP, Mehrotra BN, Compendium of Indian Medicinal Plants, Part I, Publication and information directorate 1995; p.104.
10. Sharma P.V, "DRAVYAGUNA VIJNANA" text book, Vol- 2, Chaukhambha Bharti Academy, Varanasi, page-827.

11. Enechi OC, Odonwodo I. An assessment of the phytochemical and nutrient composition of the pulverized root of *Cissus quadrangularis*. Journal of Biomedical Research 1. 2003; p. 63-68.
12. Dr .Sastry J.L.N, DRAVYAGUNA VIJNANA'Text book, Vol-2, Chaukhambha Orientalia, Varanasi, page 676.
13. Bhavprakash Nighantu. Guduchyadi varga, shloka- 226, 227, 228. Chunekar, Pandey, Chaukhamba publication. 2006; Page no. 418.
14. Bhavprakash Nighantu. Guduchyadi varga, shloka- 226, 227, 228. Chunekar, Pandey, Chaukhamba publication. 2006; Page no. 418.
15. Chakradatta Samhita. Bhagna chikitsa –Shloka-10. Tripathi, Dvivedi. Chaukhamba publication .2012; Page 276.
16. Shodhal Nighantu. Lakshmanadi varga, Shloka 668. P V Sharma. Oriental Institute. 1978; P. 76.
17. Vaidyamanorama. Bhagna chikitsa. Sharma. Chaukhamba Orientallia. 2012.
18. Kaiyadev Nighantu. Aaushadhi varg. Sharma. Chaukhamba Orientallia. 2013.
19. Bhavprakash Nighantu- Guduchyadi varga, shloka- 226, 227, 228. Chunekar, Pandey, Chaukhamba publication 2006; Page no. 418.
20. Charaka Samhita,-Su. 26, Aatreybhdrakapyiya Shloka 42, Tripathi, Pandey Chaukhamba publication. 2006.
21. Bhavprakash Nighantu- Guduchyadi varga, shloka- 226, 227, 228 Chunekar, Pandey, Chaukhamba publication 2006; Page no. 418.
22. Chakradatta Samhita- Bhagna chikitsa –Shloka-10, Tripathi, Dvivedi Chaukhamba publication -2012; Page 276.
23. Anonymous (2000) the Ayurveda Pharmacopoeia of India. Part-I, Vol 1, 1st edi. Government of India, Ministry of Health and Family Welfare p. 21, 22, 390.
24. Iain H. Kalfas, MD (2001). *"Principles of Bone Healing"*.
25. Udupa KN, Prasad GC. (1963)The effect of *Cissus quadrangularis* on healing of cortisone treated fracture. Indian Journal of Medical Research, 51: 667.
26. Rao MS, Bhagath KP, NarayanaSwamy VB, Gopalan KN. (2007) *Cissusquadrangular* is plant extract enhances the development of cortical bone and trabeculae in the fetal femur. Pharmacology Online, 3: 190-202.
27. Shirwaikar A, Khan S, Malini S. (2003) Antiosteoporotic effect of ethanol extracts of *Cissus quadrangularis* Linn on ovariectomized rat. Journal of Ethnophramacology, 89: 245-50.

28. K N Udupa Gurucharan. Biochemical & Calcium 45 studies on the effect of Cissus quadrangularis in fracture repair. Ind. Jour. Med. Res, June 1964; 52(5).
29. D K Deka, L.C. Lahon. 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.
30. S P Singh, N Mishra. An experimental study of analgesic activity of Cissus quadrangularis. Indian Journal of Pharmacology (7984) 162.
31. Research Guidelines for evaluating the safety and efficacy of herbal medicines, WHO Regional Office, Western Pacific, Manila, 1994.
32. Prasad GC, Udupa KN., Effect of *Cissus quadrangularis* on the healing of cortisone treated fracture. Indian J Med Res, 1963; 51: 667.
33. K N Udupa. Cissus quadrangularis in healing of fractures, a clinical study; J. Indian Medical Association, June, 1962; 38(11).
34. K N Udupa Gurucharan. Effect of Cissus quadrangularis in healing of cortisone treated fractures, Ind. Jour. Med. Res., June 1963; 51(4).
35. Brahmkshatriya, H. R., Shah, K. A., Ananthkumar, G. B., & Brahmkshatriya, M. H. (2015). Clinical evaluation of Cissus quadrangularis as osteogenic agent in maxillofacial fracture: A pilot study. *Ayu*, 36(2): 169-173. https://doi.org/10.4103/0974-8520.175542.