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A Complete Review On Phytochemical Constituents Obtained From Cissus- Quadrangularis For Joint Pain Management

Kevang Prajapati[1*], Ms. Purvi Ramanuj[2], Dr. Pragnesh Patani[3]

[1*]Student, Khyati College of Pharmacy, Palodia, Ahmedabad.
[2]Associate Professor, Department of Pharmaceutical Chemistry & QA, Khyati College of Pharmacy, Palodia, Ahmedabad.
[3]Principal, Khyati College of Pharmacy, Palodia, Ahmedabad.

***Corresponding Author:** Kevang Prajapati
*Student, Khyati College of Pharmacy, Palodiya, Ahmedabad, Email: k.viramgami03@gmail.com

Abstract
CISSUS QUADRANGULARIS(CQ), is a traditional medicinal plant commonly used in Southeast Asian and African medicine for joint pain management , has garnered attention for its potential therapeutic benefits and commonly known as 'HADJOD' in india. *CISSUS QUADRANGULARIS* to be an important herb in traditional and modern medicine and it is valuable for bone health, inflammatory benefits, fractures, joint pain, low bone mass, anthelmintic, asthma, & many other conditions. Joint pain occurs in many conditions like Arthritis, injury, overuse, infection, bursitis, tendinitis, autoimmune disorders and etc. *CISSUS QYADRANGULARIS*, a well-known Ayurvedic herb, has gained attention for its potential benefits in joint pain management.

Keywords: *CISSUS QUADRANGULARIS*, Vitaceae, Traditional medicinal plant, Joint pain management, Inflammatory benefits, Anthelmintic, Arthritis, intramembranous ossification.

1. Introduction to Joint Pain

Joint pain is a common and often debilitating condition that affects people of all ages, mostly old age people . It can arise from a range of causes, including injuries, infections, inflammation, autoimmune disorders, and age-related wear and tear. Joint pain may present as acute, such as following an injury, or it can become chronic, as seen in conditions like osteoarthritis or rheumatoid arthritis. The impact of joint pain can be significant, affecting mobility, quality of life, and daily functioning. Understanding the underlying causes and mechanisms of joint pain is crucial for developing effective treatment strategies and improving patient outcomes.
Bone and joint pain can arise from a variety of causes, including trauma, infection, inflammation, autoimmune conditions, genetic disorders, age-related changes, and cancer. This pain may present as acute, recurring, or chronic.[3] Osteoarthritis, a common form of chronic musculoskeletal pain, exemplifies the widespread impact of such conditions. The complexity of bone and joint pain, with its diverse origins and manifestations, necessitates a nuanced approach to treatment. Effective pain management often requires addressing multiple underlying factors and may involve strategies tailored to each individual's specific needs.[4] [5]
Joint pain is characterized by a decrease in bone mineral density and changes in bone protein structure, which increase the risk of fractures. *Cissus quadrangularis*, a plant known for its potential health benefits, has shown promise in combating joint pain.[6] It is believed to support metabolic processes and enhance the absorption of essential minerals such as strontium, calcium, and sulfur. Research involving ovariectomized rats-a model commonly used to study osteoporosis—has demonstrated that ethanol extracts of *Cissus quadrangularis*, administered at doses of 500 and 750 milligrams per kilogram, exhibit antiosteoporotic effects, suggesting its potential as a therapeutic agent for bone health.[7]

1.1 Mechanism of Joint Pain

Joint pain is discomfort that affects one or more Joints in your body. A joint is where the ends of two or more of your bones come together. For example, your hip joint is where your thigh bone meets your pelvis.
Nociceptors (sensory fibers that respond to stimuli that are potentially damaging to the organism) play a crucial role in protecting the body by detecting and signaling potential or actual tissue damage. [8] They trigger pain responses that prompt us to withdraw from harmful stimuli, ultimately preventing further injury and allowing for timely medical intervention. This mechanism helps in preserving tissue integrity and overall health.[9]
Studying the various classes of nociceptors is crucial for understanding how different types of pain are processed and experienced. Each class has unique properties, such as varying conduction speeds and stimulus responses, which influence how pain is perceived and managed. This knowledge helps in developing targeted treatments and interventions for different pain conditions, improving patient care and pain relief strategies.[10] Recent RNA sequencing and behavioral studies reveal that nociceptors have distinct molecular profiles and functional roles. These findings confirm that different nociceptor populations are specialized for specific types of sensory

information—such as thermal, chemical, or mechanical stimuli—and for different tissue areas, aligning with the labeled line hypothesis. This understanding is vital for developing targeted pain therapies and accurate by addressing various pain modalities.[11][12]

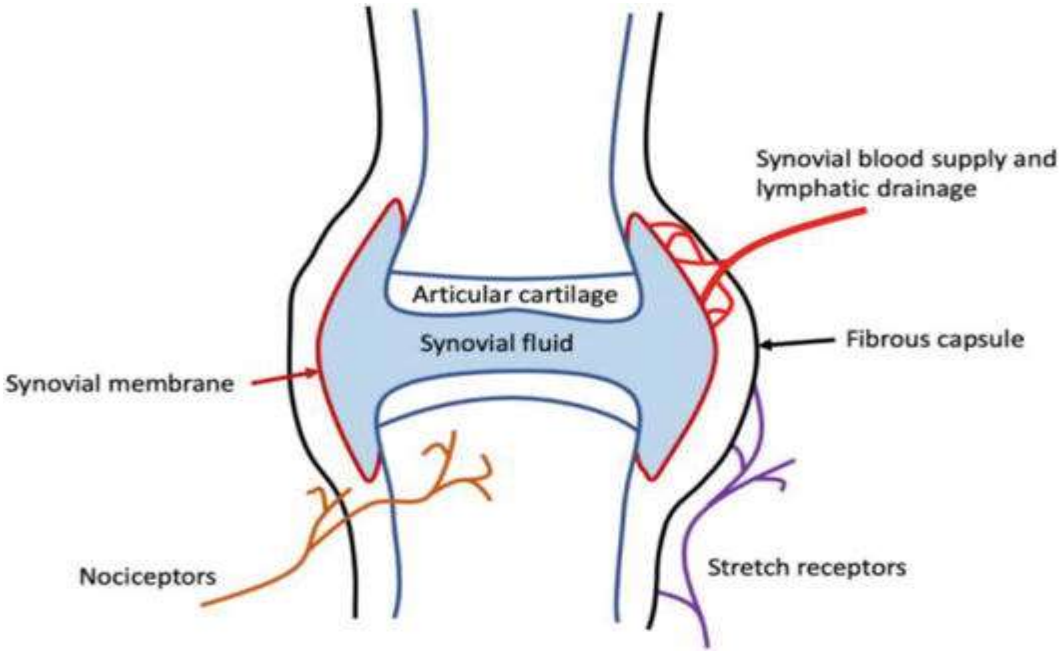

Figure : 1 Structure of Synovial Joint

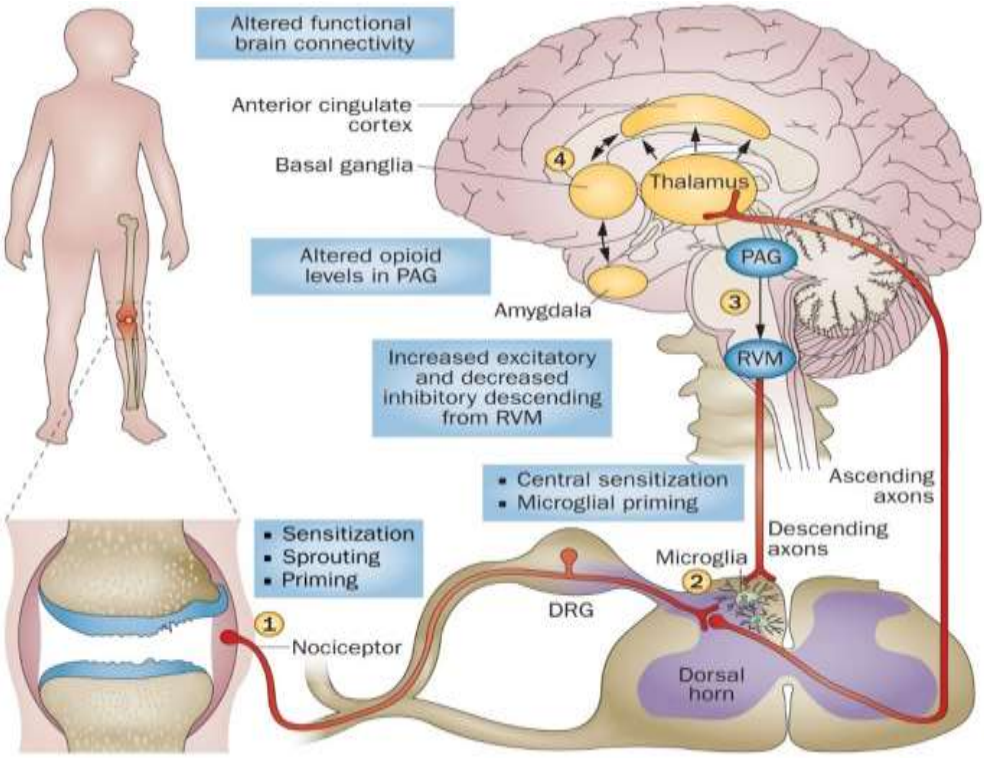

Figure : 2 Mechanism of Joint Pain

2. *Cissus quadrangularis*

Cissus quadrangularis is a succulent, perennial climbing plant commonly found across India, particularly in tropical regions. Known by various names in Indian languages - such as 'Asthisamdhani' in Sanskrit and 'Perandai' in Tamil-it is also referred to as the Edible-stemmed Vine in English. This plant displays different morphological variants, including square-stemmed, round-stemmed, and flat-stemmed types, with the square-stemmed and round-stemmed varieties being the most frequently encountered. [13]

CQ is noted for its rich content of nutrients and bioactive compounds, including ascorbic acid (Vitamin C), carotene (Vitamin A), anabolic steroids, and calcium. The round-stemmed variety is particularly distinguished by its wingless stem, and anatomical studies reveal the presence of needle-shaped calcium oxalate crystals,

raphides, and intrafascicular cambium in the stem. Research on CQ has explored various extracts obtained using solvents like methanol, petroleum ether, ethanol, aqueous solutions, and ethyl acetate. Each part of the plant exhibits different pharmacological activities, with the efficacy of these activities varying depending on the type of extract used. [14]

Cissus quadrangularis holds significant importance in Indian traditional medicine, particularly for its application in treating swelling and bone fractures. Known for its reputed bone-healing properties, CQ has been traditionally used in the form of plasters to aid in the recovery of fractures and to alleviate swelling. [15](CQ) is a versatile medicinal plant with a broad spectrum of therapeutic activities. It is traditionally used for its analgesic, antimicrobial, antiviral, and antioxidant properties, making it effective in treating pain, infections, and oxidative stress. Additionally, CQ has been found to have antiosteoporotic effects, aiding in bone health and fracture recovery. It also supports menstrual regulation, asthma management, and digestive health issues such as piles. Its potential extends to tumor management, wound healing, and preventing scurvy due to its rich nutritional content. Recent advancements have explored the biosynthesis of nanoparticles using aqueous extracts of CQ leaves and stems. These nanoparticles exhibit notable antibacterial effects, merging traditional medicinal benefits with cutting-edge nanotechnology.[16] Various fraction of ethanolic extract of CQ was screened against osteoporotic activity.[17]

2.1 Pharmacognosy of *Cissus quadrangularis*

Synonyms & Common Names [18-19]

Cissus succulent, *Cissus tetragona*, *Vitis quadrangularis*, *Vitissucculenta*, Hadjod, Hadjora, Asthisamharaka.

Biological Source: Plant Parts Used: whole plant used specially leaves, roots and stem.

Family : *Vitaceae*

Taxonomy of *Cissus quadrangularis*

- Kingdom *Plantae* – Plants
- Subkingdom *Tracheobionta* – Vascular plants
- Class *Magnoliopsida* – Dicotyledons
- Order *Rhamnales*
- Family *Vitaceae* – Grape family
- Genus *Cissus* L. – Treebine
- Species *Cissus quadrangularis* L.

Figure : 3 *Cissus quadrangularis*

Types of *Cissus quadrangularis*

- Cissus bifida Schumach. & Thonn.
- Cissus edulis Dalzell.
- Cissus fischeri Gilg.
- Cissus quadrangula L.
- Cissus quadrangula Salisb.
- Cissus succulenta (Galpin) Burtt-Davy.
- Cissus tetragona Harv.

- Cissus tetraptera Hook. f.

Phytochemical Constituents

The aerial parts of Cissus quadrangularis have been found to possess a diverse range of phytochemical compounds, both primary and secondary metabolites, which are of considerable interest for their potential therapeutic applications. Primary Metabolites of *Cissus quadrangularis.*[18] [19]

- **Lipids:** These include both cyclic and acyclic forms, which are essential for various biological functions.
- **Fatty Acids:** Important for cellular membrane structure and function.
- **Methyl Esters:** These compounds have various roles in plant metabolism.
- **Proteins:** Fundamental for numerous physiological processes.
- **Amino Acids:** The building blocks of proteins, crucial for growth and repair.
- **Iridoids:** These are a type of secondary metabolite but are included here due to their varied roles in plant defense and human health.
- **Gums and Mucilage:** These polysaccharides contribute to the plant's structural integrity and have potential uses in food and pharmaceutical industries.

Secondary Metabolites: [20]

- **Alkaloids:** Known for their diverse pharmacological effects, including analgesic, anti-inflammatory, and antimicrobial properties. Their presence suggests potential therapeutic applications in pain management and infection control.
- **Saponins:** These compounds are recognized for their ability to enhance immune responses and exhibit antimicrobial and anti-inflammatory effects. Their inclusion highlights the plant's potential in immunomodulatory and anti-pathogenic therapies.
- **Tannins:** With their astringent properties, tannins are useful in treating gastrointestinal issues and possess antimicrobial and antioxidant qualities. This suggests that the underground parts of the plant could be beneficial in digestive health and wound healing.
- **Flavonoids:** These are well-known for their antioxidant properties, which can protect cells from oxidative damage and contribute to overall health. The presence of flavonoids supports the plant's potential as a source of natural antioxidants.
- **Glycosides:** These compounds have various biological activities, including effects on cardiovascular health and metabolic processes. Their presence in the extracts suggests potential applications in heart health and other therapeutic areas.
- **Phytosterols:** These compounds can help reduce cholesterol levels and have anti-inflammatory effects.
- **Steroids:** Plant steroids can influence various physiological processes and have potential medicinal applications.
- **Stilbenes:** Known for their antioxidant and anti-cancer properties.
- **Triterpenoids:** These are involved in plant defense and have been associated with anti-inflammatory and anti-cancer activities.
- **Carotene:** A precursor to vitamin A with antioxidant properties.
- **Vitamin C:** An essential vitamin with antioxidant properties and immune-boosting effects.

Botanical Description

The plant is a perennial herbaceous climber comprising a thick quadrangular stem along with other aerial components such as tendrils, leaves, inflorescence, flowers, fruits and other parts of plant. [21]

Figure;4 Fruit

Figure:5 Flower

Figure: Leaves

Stem
The plant has a moist, thick, and fleshy stem that is deep green, smooth, and four-angled with wing-like projections and slight fuzz. When young, it features angular branches and long tendrils but becomes nearly leafless as it ages.

Fruit
The plant produces globose, red berries that are succulent and highly acidic, ranging from 6 to 10 mm in diameter. Each berry contains a single obovoid seed, which is smooth and measures 4 to 8 mm across. The plant flowers and fruits primarily during June and July.

Flower
The flower on the stem is 2 mm long, with pink to white petals. The hypanthium is green, cup-like, and 2 mm wide, with a truncate or obscurely lobed shape. The flower features four distinct petals that are ovate-oblong, acute, and hooded at the apex, each measuring 1.5 mm in length. It has a disc-shaped form, longer than the glabrous ovary, which includes a slender style and a small stigma.

Leaves
The plant's leaves are simple, ovate or reniform, and range from entire to cordate, with serrulate, dentate, or crenate-serrate margins. They are 3–7 lobed, with a terminal lobe that is triangular or sub-spathulate, and are membranous and glabrous on both sides, measuring 3–5 by 5–3 cm. The stipules are ovate or cuneate, obtuse, and deciduous.

3. Traditional Uses
A comprehensive review of traditional literature from India and other countries reveals that *Cissus quadrangularis* has been widely used for managing various health issues in both humans and animals. This plant's therapeutic applications are well-documented globally, showcasing its historical significance and broad utility across different cultures. Its uses range from bone health and digestive problems to inflammatory conditions, reflecting its diverse medicinal properties. The extensive traditional knowledge provides a solid foundation for further scientific research into its potential benefits and effectiveness. [22]
In the Indian traditional systems of Siddha and Ayurveda, *Cissus quadrangularis* has been widely used for managing bone-related issues, including fractures, pain, inflammation, osteoporosis, rheumatoid arthritis, and osteoarthritis. Its application in these systems underscores its significance in bone health and joint care. [23]
Traditional literature from the Indian subcontinent, including Pakistan, Bangladesh, and Sri Lanka, as well as other regions worldwide, highlights the use of *Cissus quadrangularis* for a variety of conditions. These include swelling, hemorrhage, digestive issues, chronic ulcers, skin diseases, and helminthiasis, reflecting the plant's broad therapeutic applications.[24]

4. *CISSUS QUDRANGULARIS* in Joint Pain
The phytochemical and pharmacological properties of *Cissus quadrangularis*, emphasizing its traditional and modern therapeutic applications. Traditionally, the plant is well-regarded for its effectiveness in healing fractures and its antibacterial, antifungal, antioxidant, anthelmintic, anti-hemorrhoidal, and analgesic properties. Additionally, *Cissus quadrangularis* demonstrates potential in gastroprotection, acts as a nonsteroidal anti-inflammatory drug (NSAID), and contributes antioxidants that support lipid metabolism and combat oxidative stress. These diverse therapeutic effects underscore the plant's significant value as a medicinal herb with a wide range of applications in health care. [25]
Cissus quadrangularis has demonstrated notable bone healing activity, attributed to its anabolic steroid content, which accelerates fracture healing by promoting early connective tissue formation. Additionally, the plant's vitamins and steroids contribute specifically to enhancing bone repair processes. [26]
Cissus quadrangularis is a well-recognized herb for managing bone-related issues, supported by studies in animal models and human subjects. The plant is effective in treating bone fractures, osteoporosis, and maintaining bone density. Research suggests that *Cissus quadrangularis* contains unidentified anabolic steroids that interact with estrogen receptors in bones. This interaction promotes early ossification and bone remodeling, enhancing mineral metabolism and uptake by osteoblasts, particularly calcium, sulfur, and strontium. [26]

Anti-Inflammatory Activity of *Cissus quadrangularis*
The plant was tested for analgesic and anti-inflammatory activity using the extract that was prepared using a different solvent. The important summaries of all observations are as follows.
The methanolic extract of *Cissus quadrangularis* exhibited significant analgesic and anti-inflammatory effects in studies. The extract demonstrated effective anti-inflammatory properties by inhibiting edema formation induced by ethyl phenylpropionate, carrageenin, and arachidonic acid. [27]
It also showed analgesic activity in the formalin test, suggesting both central and peripheral mechanisms of action. Additionally, the plant's extract was evaluated for its ability to inhibit the cyclooxygenase-I (COX-1)

enzyme, a key player in pain and inflammation. [34] The extract of *Cissus quadrangularis* was evaluated for its ability to inhibit cyclooxygenase-1 (COX-1) using a COX-1 assay, with inhibition percentages reported. Additionally, different extracts of the plant were found to inhibit not only COX-1 but also COX-2 and 5-lipoxygenase (5-LOX) enzyme activities. The inhibition was determined using spectroscopic and polarographic methods.

Anti Obesity Activity

A double-blind, placebo-controlled study of Cylaris found that it may help reduce waist circumference, body mass index, and improve serum lipid levels. [28]

Anti-Diabetic Activity

Cissus quadrangularis stem extract, particularly its ethyl acetate fraction rich in quercetin, demonstrates anti-diabetic potential by boosting antioxidant defenses and reducing inflammation, which may aid in managing diabetic complications. [29]

5. Conclusion

Cissus quadrangularis is a versatile medicinal plant native to Africa and parts of Asia, including India, and is widely used in traditional medicine systems like Ayurveda and African herbal practices. The plant's comprehensive phytochemical profile includes a variety of important compounds such as lipids, fatty acids, proteins, amino acids, alkaloids, flavonoids, saponins, and vitamins, notably vitamin C. Traditional and scientific literature supports its efficacy in treating a range of conditions, including osteoporosis, fractures, ligament damage, pain, and inflammation. Research has validated its pharmacological benefits, including antimicrobial, anti-diabetic, anti-inflammatory, anti-obesity, antioxidant, and hepatoprotective activities. Clinical studies further highlight its effectiveness in wound and fracture healing, as well as its potential in weight management and glucose and lipid regulation. Overall, *Cissus quadrangularis* demonstrates significant therapeutic value and warrants continued use and study for its diverse health benefits.

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