



PHARMACOLOGICAL ACTIVITIES AND THERAPEUTIC APPLICATIONS OF *CISSUS QUADRANGULARIS* IN HEALTH AND DISEASE: COMPREHENSIVE REVIEW

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ABSTRACT

Background: *Cissus quadrangularis*, a perennial medicinal plant widely known as Veld grape or Hadjod, has been extensively utilized in traditional Ayurvedic medicine for its diverse therapeutic properties. In recent years, it has attracted considerable scientific interest because of its broad spectrum of pharmacological activities and its potential role in managing various health conditions. **Methodology:** We conducted a systematic literature review using electronic databases, including PubMed, Scopus, and Google Scholar. We identified relevant studies on the pharmacological activities of *C. quadrangularis* using appropriate keywords. This review included both preclinical (in vitro and in vivo) and clinical studies. We critically analyzed and synthesized the data to understand the plant's mechanisms of action and therapeutic applications. **Results and Discussion:** The findings reveal that *C. quadrangularis* exhibits multiple pharmacological activities, including bone healing, anti-obesity, anti-ulcerative, anti-diabetic, antioxidant, and gastroprotective effects. These activities are primarily attributed to its rich phytochemical profile comprising flavonoids, triterpenoids, and phytosterols. Experimental and clinical evidence supports its traditional uses, particularly for bone regeneration and metabolic disorders. Despite promising outcomes, variations in study design and a lack of large-scale clinical trials highlight the need for further mechanistic and standardized investigations. **Conclusion:** *Cissus quadrangularis* demonstrates significant therapeutic potential as a multifunctional medicinal plant. Its integration into modern healthcare systems could offer novel and effective strategies for managing various diseases. However, further well-designed clinical studies are essential to validate its efficacy, safety, and optimal therapeutic applications.

INTRODUCTION

Cissus quadrangularis L., a perennial plant belonging to the family Vitaceae, is widely recognized in traditional medicine systems, particularly Ayurveda, for its diverse therapeutic

applications. Commonly referred to as Veld grape or Hadjod, the plant is indigenous to the Indian subcontinent and has traditionally been used to treat bone fractures, inflammation, gastrointestinal disorders, and metabolic conditions [1]. In

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recent years, scientific interest has grown in elucidating the phytochemical composition and pharmacological properties of *C. quadrangularis*. Studies have identified a variety of bioactive constituents, including flavonoids, triterpenoids, and phytosterols, which drive its multiple biological activities [2]. Experimental and clinical investigations have demonstrated its potential in bone regeneration, antioxidant defense, anti-inflammatory activity, and metabolic regulation, thereby supporting many of its traditional claims [3].

The plant is also known by several vernacular names across different regions, such as Hadjod, Asthisamharaka, Harbhanga, Perandai, Pirandai, Nalleru, and Adamant creeper, reflecting its widespread use and cultural significance, as given in Table 1 [4]. Overall, *Cissus quadrangularis* represents a promising medicinal plant with significant pharmacological potential. Continued research is essential to validate its therapeutic efficacy further and support its integration into evidence-based modern healthcare [5].

Table 1: Vernacular Names of *Cissus quadrangularis*

S. No.	Vernacular Name	Language/Region	Country/State
1	Hadjod	Hindi	India
2	Asthisamadhani	Sanskrit	India
3	Harjor	Bengali	India (West Bengal)
4	Nalleru	Telugu	India (Andhra Pradesh, Telangana)
5	Perandai	Tamil	India (Tamil Nadu)
6	Vajravalli	Kannada	India (Karnataka)
7	Changalam Paranda	Malayalam	India (Kerala)
8	Kandavalli	Marathi	India (Maharashtra)
9	Vedhari	Gujarati	India (Gujarat)
10	Bone Setter Plant	English	Global
11	Devil's Backbone	English	Global
12	Adamant Creeper	English	Global
13	Pirandai	Tamil (alternate)	India
14	Mangaravalli	Kannada (alternate)	India
15	Veldt Grape	English	Africa/Global
16	Edible Stemmed Vine	Common Name	Global
17	Asthisamharaka	Sanskrit (alternate)	India

METHODOLOGY

We conducted a systematic search of PubMed, Scopus, and Google Scholar for studies published between 2015 and 2026. We specifically targeted literature addressing the pharmacological activities and therapeutic applications of *Cissus quadrangularis* in health and disease. Using predefined inclusion criteria, we selected relevant studies and synthesized data on therapeutic potential, delivery strategies, and emerging trends (Figure 1).

2. History of medicinal use of *Cissus quadrangularis*

The historical use of *Cissus quadrangularis* spans centuries and is deeply rooted in the traditional medicinal practices of cultures across the Indian subcontinent and beyond. Known by various vernacular names such as Hadjod, Veld grape, and Asthisamharaka, this resilient plant has garnered a rich tapestry of uses and lore over time. In traditional Ayurvedic medicine, *C. quadrangularis* occupies a revered position, valued for its diverse therapeutic properties [6]. It has been extensively employed to treat a wide array of ailments, earning it the

moniker "Asthisamharaka," which translates to "bone setter" in Sanskrit. One of its most renowned applications is managing bone fractures and joint disorders. The plant's ability to accelerate bone healing and promote bone density has made it a staple remedy for fractures and osteoporosis. Beyond its orthopedic applications, *C. quadrangularis* has been utilized to address a spectrum of health concerns. It is revered for its anti-inflammatory properties, making it beneficial for alleviating conditions such as arthritis and rheumatism. Additionally, its antioxidant activity makes it valuable for combating oxidative stress and supporting overall health [7].

The plant's adaptability to arid, rocky terrain has made it an invaluable resource for communities living in harsh environments. Its prevalence in regions such as Maharashtra, Tamil Nadu, and Rajasthan underscores its integral role in traditional healing practices across diverse landscapes. Furthermore, *C. quadrangularis* holds significance in folklore and cultural traditions. In some regions, it is believed to have mystical properties that ward off evil spirits and bring good

fortune to those who cultivate it. Its association with bone health has also led to its symbolic representation of strength and resilience. In summary, the historical use of *Cissus quadrangularis* attests to its enduring legacy as a botanical marvel [8]. From ancient Ayurvedic texts to contemporary herbal medicine, its multifaceted benefits continue to be revered and explored, ensuring its continued prominence in traditional healing practices and modern pharmacology alike [9].

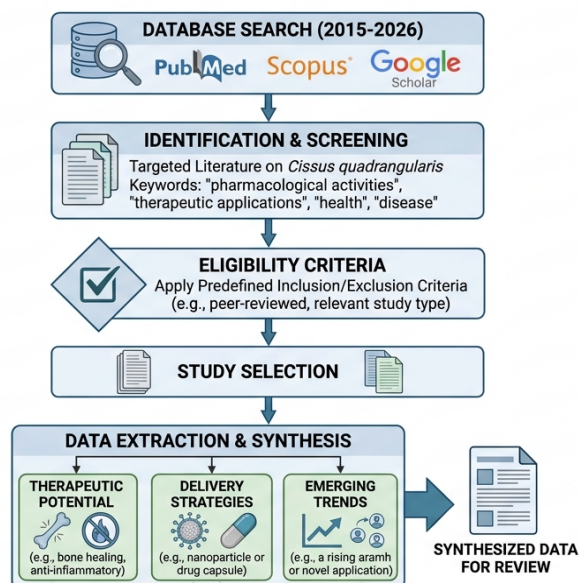


Figure 1: Methodology for systematic literature review on *Cissus quadrangularis*

3. Botanical/Taxonomical Details

Cissus quadrangularis is characterized by its distinctive square-shaped stems, which give rise to its species epithet "quadrangularis." The plant has succulent, climbing or creeping stems with tendrils and often forms dense mats or spreads across various surfaces. The leaves are simple, opposite, and fleshy, with serrated margins. The roots are fibrous and can penetrate deep into the soil [10]. *C. quadrangularis* typically produces small, greenish-white flowers in clusters, followed by red or black berries containing seeds (Table 2).

4. Geographical Distribution of *Cissus quadrangularis* in India

Cissus quadrangularis is native to the Indian subcontinent and is widely distributed across various regions. It thrives in tropical and subtropical climates and is commonly found in dry, rocky, and sandy areas. In India, the plant is especially prevalent in states such as Maharashtra, Tamil Nadu, Andhra Pradesh, Karnataka, Rajasthan & Gujarat. *C. quadrangularis*, commonly known as Veld grape or Hadjod, is indigenous to the Indian

subcontinent, where it enjoys a widespread distribution across diverse ecological niches. Its natural habitat spans the subcontinent, encompassing regions with tropical and subtropical climates. Within India, this botanical gem thrives in a range of environments, from arid, rocky terrain to sandy expanses. Its adaptability to these varied conditions makes it resilient, allowing it to flourish even in the harshest landscapes [11]. In India, *C. quadrangularis* is particularly prominent in several states. The plant is notably prevalent in Maharashtra, Tamil Nadu, Andhra Pradesh, Karnataka, Rajasthan, and Gujarat, where it often forms dense thickets or sprawls across the terrain [12]. Its presence in these regions is not merely incidental; it is deeply intertwined with the cultural fabric and traditional healing practices of these areas. Beyond its native range, *C. quadrangularis* has also garnered global attention. Its reputation as a medicinal powerhouse has transcended geographical boundaries, propelling it into the spotlight of international botanical research [13]. While its primary stronghold remains in the Indian subcontinent, it has also been introduced and cultivated in various other tropical and subtropical regions worldwide. In essence, the geographical distribution of *Cissus quadrangularis* underscores its significance both locally and globally. Its prevalence across the Indian subcontinent reflects its deep-rooted connection with the land and its people. At the same time, its global reach highlights its universal appeal as a botanical marvel with profound medicinal potential [14].

Table 2: Taxonomic Details of *Cissus quadrangularis*

Taxonomic Rank	Classification
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Vitales
Family	Vitaceae
Genus	Cissus
Species	<i>quadrangularis</i>
Binomial Name	<i>Cissus quadrangularis</i>

5. Phytochemical Screening and Phytoconstituents

Extensive phytochemical investigations have revealed various bioactive compounds in different parts of *Cissus quadrangularis*. Phytochemical screening has identified alkaloids, flavonoids, tannins, steroids, terpenoids, saponins, and phenolic compounds among its constituents [11-20]. Table 3 lists notable phytoconstituents.

Table 3: Notable phytoconstituents of *Cissus quadrangularis*

Phytochemical Test	Method	Constituents Determined	Inference
Alkaloids	Dragendorff's reagent or Mayer's reagent	Alkaloids	Presence indicates potential pharmacological activity [11]
Flavonoids	Shinoda test or AlCl ₃ test	Flavonoids	Presence suggests antioxidant and anti-inflammatory properties [12]
Tannins	Ferric chloride test	Tannins	Presence indicates astringent and antioxidant properties [13]
Steroids and Terpenoids	Salkowski's test or Liebermann-Burchard test	Steroids and terpenoids	Presence suggests potential anti-inflammatory & antimicrobial activities [14]
Saponins	Froth test or Hemolysis test	Saponins	Presence indicates potential cholesterol-lowering and anticancer effects [15]
Phenolic Compounds	Folin-Ciocalteu assay or Ferric chloride test	Phenolic compounds	Presence suggests antioxidant and anti-inflammatory properties [16]
Glycosides	Keller-Kiliani test or Legal's test	Glycosides	Presence indicates potential cardioprotective and anti-inflammatory effects [17]
Carbohydrates	Molisch's test or Benedict's test	Carbohydrates	Presence provides an energy source and structural support for the plant [18]
Proteins and Amino Acids	Biuret test or Ninhydrin test	Proteins and amino acids	Presence indicates nutritive value and potential wound healing properties [19]
Lipids	Sudan III test or Vanillin-Sulfuric Acid test	Lipids	Presence suggests energy storage & structural components of cell membranes [20]

5.1 *Cissus quadrangularis* bioactive phytoconstituents

Cissus quadrangularis is a rich source of diverse bioactive phytoconstituents that contribute to its wide range of pharmacological activities. Major classes of compounds identified in different parts of the plant include ketosteroids, flavonoids, triterpenoids, phenolics, stilbenes, iridoids, and essential minerals (Figure 2) [21].

Ketosteroids and Phytosterols: The plant contains significant levels of ketosteroids, particularly β -sitosterol and its glycosides, which are associated with bone regeneration and anti-inflammatory activities. Reported concentrations of β -sitosterol range from approximately 5–20 mg/g of dried plant material, depending on extraction method and plant part.

Flavonoids: Key flavonoids such as quercetin, kaempferol, and rutin are well documented in *C. quadrangularis*. These compounds are responsible for antioxidant & anti-inflammatory effects. Quantitative studies indicate that quercetin content typically ranges from 0.05–2.5 mg/g, while rutin and kaempferol are present at comparable or slightly lower concentrations. Triterpenoids, including oleanolic acid, α -amyirin, β -amyirin, and friedelin, have been identified and contribute to hepatoprotective, anti-diabetic, and anti-inflammatory activities. α - and β -amyirin are generally reported in the range of 0.1–3.0 mg/g, whereas friedelin is present at lower levels, typically 0.01–1.5 mg/g [22].

Phenolic Compounds: Phenolic constituents such as gallic acid, catechin, and ellagic acid contribute significantly to antioxidant and anticancer potential. These compounds are usually found in concentrations ranging from 0.1–5 mg/g, depending on extraction conditions and plant source.

Stilbenes and Derivatives: Stilbene derivatives, including resveratrol, piceatannol, quadrangularin-A, and pallidol, are important bioactive molecules with antioxidant and cardioprotective properties. Resveratrol content is generally reported in the range of 0.01–0.5 mg/g, while other stilbenes occur in comparable or slightly lower concentrations.

Iridoids and Other Constituents: Iridoid glycosides such as catalpol derivatives (e.g., 6-O-meta-methoxy-benzoyl catalpol) and picroside contribute to anti-inflammatory and immunomodulatory activities. The plant also contains vitamins (notably vitamin C), carotenoids, and tannins [24].

Mineral Composition: The root and stem parts are rich in essential minerals. Reported values (per 100 g of plant material) include potassium (~67.5 mg), calcium (~39.5 mg), iron (~7.5 mg), zinc (~3.0 mg), sodium (~22.5 mg), magnesium (~1.15 mg), and trace levels of copper and other elements.

Variability and Analytical Considerations: Phytoconstituent concentrations in *C. quadrangularis* vary significantly with

plant age, geographical origin, environmental conditions, and extraction techniques. Advanced analytical methods such as High-Performance Liquid Chromatography (HPLC), Gas

Chromatography–Mass Spectrometry (GC–MS), and spectrophotometric assays are routinely used to quantify and characterize these compounds accurately.

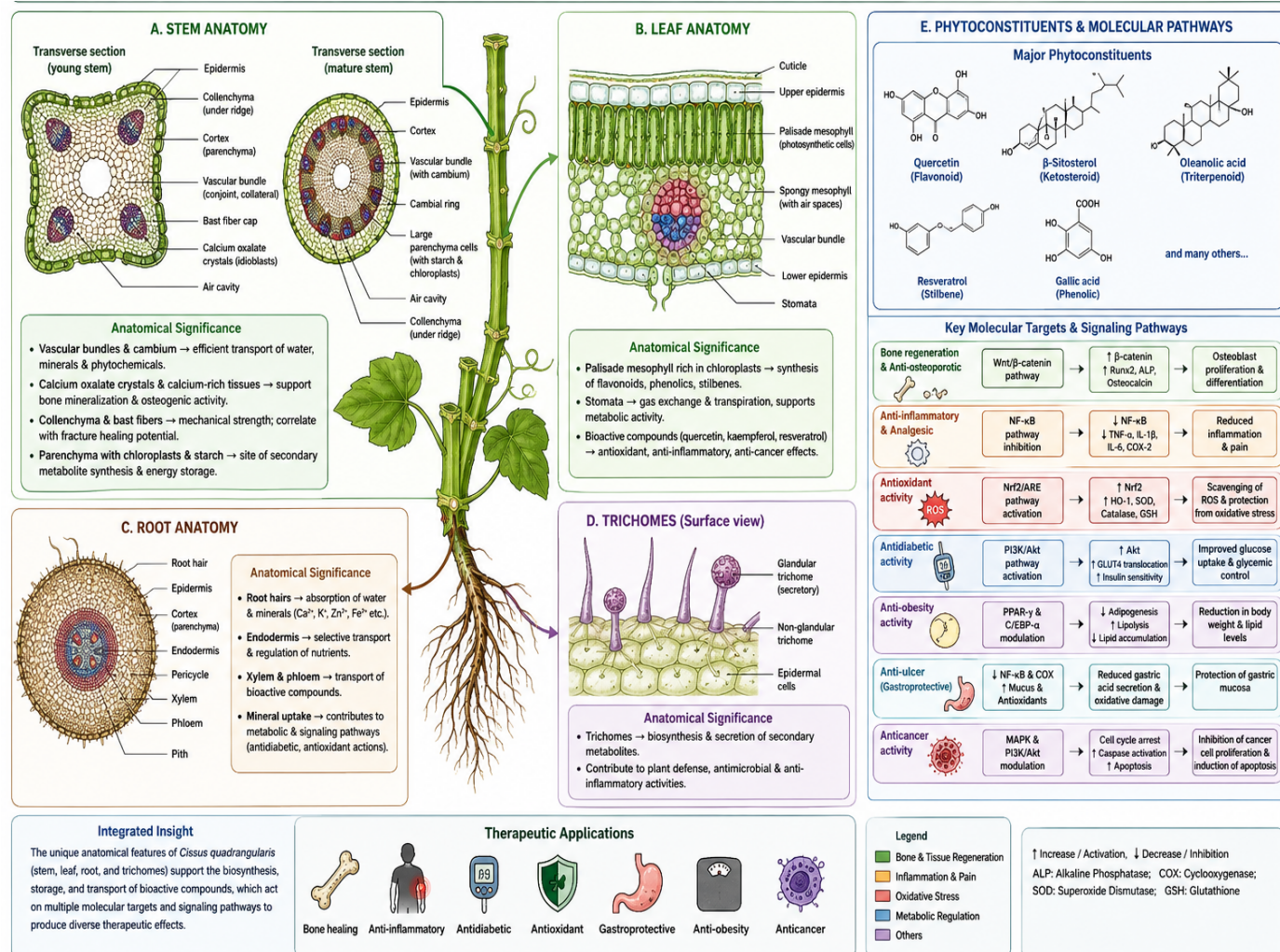


Figure 2: Stem–leaf–root anatomy linked with molecular pathways and chemical structure of bioactive compounds of *C. quadrangularis*

5.2 Mechanistic Basis of Pharmacological Activities of *Cissus quadrangularis*

The therapeutic potential of *Cissus quadrangularis* (CQL) extends beyond traditional claims and is increasingly supported by mechanistic evidence at molecular and cellular levels. While earlier reports largely describe its pharmacological effects, recent studies highlight that these activities are mediated through modulation of key signaling pathways, transcription factors, and biochemical targets [25]. Bone regenerative and anti-osteoporotic activity is one of CQL's most prominent effects. Mechanistically, CQL stimulates osteoblast proliferation and differentiation by activating the Wnt/β-catenin signaling pathway, increasing expression of osteogenic markers such as

Runx2, alkaline phosphatase (ALP), and osteocalcin. Concurrently, it suppresses osteoclastogenesis by modulating the RANK/RANKL/OPG axis, thereby inhibiting bone resorption. Calcium, phytosterols (e.g., β-sitosterol), and anabolic compounds further support mineralization and extracellular matrix formation [27].

The anti-inflammatory and analgesic effects are mediated through inhibition of pro-inflammatory signaling cascades. Bioactive flavonoids such as quercetin inhibit activation of the NF-κB pathway, downregulating cytokines including TNF-α, IL-1β, and IL-6. Additionally, suppression of cyclooxygenase (COX-2) and lipoxygenase (LOX) pathways reduces

prostaglandin synthesis, thereby alleviating inflammation and pain at the cellular level [28].

CQL exhibits potent antioxidant activity, primarily through phenolic and flavonoid constituents. These compounds activate the Nrf2/ARE signaling pathway, which enhances transcription of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase. This mechanism is critical in mitigating oxidative stress, a key contributor to chronic diseases including diabetes, cancer, and cardiovascular disorders [29].

The antidiabetic activity of CQL involves multiple molecular targets. It enhances insulin sensitivity by activating the PI3K/Akt signaling pathway, facilitating glucose uptake via GLUT4 translocation. Additionally, inhibition of carbohydrate-digesting enzymes such as α -amylase and α -glucosidase reduces postprandial hyperglycemia. These antioxidant and anti-inflammatory effects further improve pancreatic β -cell function and reduce insulin resistance [12].

In the context of anti-obesity activity, CQL modulates adipogenesis by downregulating transcription factors such as PPAR- γ and C/EBP- α , thereby inhibiting adipocyte differentiation and lipid accumulation. It also promotes lipolysis and improves lipid metabolism, although detailed pathway-level evidence remains limited and warrants further investigation [15]. The gastroprotective effects are associated with enhanced mucosal defense mechanisms, increased mucus secretion, and reduced gastric acid output. At the molecular level, these effects are linked to reduced oxidative stress and suppressed NF- κ B-mediated inflammatory responses, along with upregulation of cytoprotective factors [7].

Emerging evidence suggests anticancer potential, with bioactive stilbenes such as resveratrol inducing apoptosis by activating caspase-dependent pathways, promoting cell cycle arrest, and inhibiting proliferation by modulating MAPK and PI3K/Akt signaling pathways. However, these findings are predominantly derived from in vitro and in vivo studies and require clinical validation [8].

Despite these advancements, significant research gaps remain. Most studies rely on crude extracts, with limited emphasis on isolating bioactive compounds, validating targets, and profiling

pharmacokinetics. Furthermore, integration of omics-based approaches (genomics, proteomics, metabolomics) is lacking, which could provide deeper insights into system-level mechanisms. Well-designed clinical trials are also needed to correlate mechanistic findings with therapeutic outcomes [9].

Cissus quadrangularis exerts its pharmacological effects through a complex network of molecular pathways involving Wnt/ β -catenin (bone regeneration), NF- κ B (inflammation), Nrf2/ARE (oxidative stress), PI3K/Akt (metabolic regulation), and MAPK signaling (cell survival and apoptosis). Incorporation of pathway-based illustrations and mechanistic models in future studies will significantly enhance the scientific rigor and translational relevance of this medicinal plant [21].

6. Various Methods of Plant Propagation

Cissus quadrangularis, commonly known as Hadjod or Veld grape, can be propagated through various methods to support commercial cultivation. These methods support efficient, sustainable production of this valuable medicinal plant.

6.1 Seed Propagation

Although less common because of its slow growth and variable seed viability, *C. quadrangularis* can be propagated from seeds. Seeds should be collected from mature berries and sown in well-drained soil with adequate moisture and sunlight. Germination may take several weeks, and seedlings require careful nurturing until they reach transplanting size [25].

6.2 Stem Cutting

Stem cuttings are a popular method for propagating *C. quadrangularis* because they produce rapid, reliable results. Healthy stem cuttings, typically taken from mature plants, are planted in well-draining soil or rooting medium. Regular misting and humidity control can enhance rooting success. Once roots develop, transplant cuttings into larger containers or directly into the field.

6.3 Layering

Layering involves encouraging stem nodes to root while still attached to the parent plant. This method can be particularly effective for *C. quadrangularis* because it can produce adventitious roots at stem nodes. A portion of the stem is wounded and buried in soil while still attached to the parent plant. Once roots develop, the new plant can be separated and transplanted [26].

6.4 Tissue Culture

In commercial cultivation, tissue culture techniques may be employed to rapidly propagate large numbers of uniform plants from small plant tissues. This method offers advantages such as disease-free plantlets and year-round propagation, though it requires a higher initial investment.

By using these propagation methods, growers can establish and maintain large-scale *Cissus quadrangularis* plantations to meet demand for its medicinal properties in industries such as pharmaceuticals, herbal supplements, and traditional medicine. Careful attention to planting techniques, environmental conditions, and pest management ensures successful cultivation and sustainable harvesting of this valuable botanical resource [27].

7. Microscopic characters of the plant

The transverse section of a young stem of *Cissus quadrangularis* presents a rectangular outline, characterized by intermittent rings of vascular bundles. These bundles are oriented parallel to the lower surface of the epidermis, with 3 to 4 bundles beneath the wings, showing more pronounced development than those along the flat sides. This vascular arrangement is conjoint and collateral, with a prominent cap of bast fibers surrounded by idioblasts containing clusters of calcium oxalate crystals. Numerous air cavities are dispersed throughout the section, enhancing tissue aeration [28]. In older stems, a complete ring of vascular strands with a well-developed cambium ring encircles the stem, except for the flat broad sides. Actinocytic stomata are distributed uniformly across the epidermis, forming a distinctive girdle-like sheath when viewed from the surface. The epidermal cells have thick walls and appear rectangular to pentangular in surface view. Within the cortex, thin-walled parenchymatous cells predominate, housing chloroplasts, starch grains, and raphides of calcium oxalate. Additionally, a collenchymatous arc is observed outside the vascular bundles in the cortex beneath each of the four angles [29].

This intricate microscopic anatomy of the stem of *Cissus quadrangularis* reflects adaptations that support vascular transport, mechanical strength, and physiological processes such as gas exchange and mineral storage. Understanding these characteristics enhances our comprehension of the plant's morphology and its ecological and pharmacological significance. The microscopic examination of *Cissus quadrangularis* reveals distinctive anatomical features that

contribute to its unique identity and medicinal properties. Here is a detailed description of its microscopic characters:

7.1 Stem

The stem of *C. quadrangularis* exhibits characteristic features when observed under a microscope. It has four distinct ridges or wings, giving it a square shape in cross-section. The outermost layer, or epidermis, consists of rectangular cells with a thin cuticle layer. Beneath the epidermis lies the cortex, composed of parenchyma cells interspersed with vascular bundles. The vascular bundles contain xylem and phloem tissues that transport water and nutrients throughout the plant [30].

7.2 Leaf

Microscopic examination of *C. quadrangularis* leaves reveals a dorsiventral structure typical of dicotyledonous plants. The upper epidermis is covered with a thin cuticle layer and contains stomata, specialized pores that regulate gas exchange and transpiration. Beneath the upper epidermis lies the palisade mesophyll, composed of elongated cells arranged parallel to the leaf surface, optimized for photosynthesis. The spongy mesophyll, located below the palisade layer, contains irregularly shaped cells with air spaces for gas exchange and water vapor diffusion [23].

7.3 Root

The microscopic examination of *C. quadrangularis* roots showcases its primary functions in anchorage, absorption, and storage. The outermost root layer, the epidermis, is covered with root hairs that increase surface area for water and mineral absorption. Beneath the epidermis lies the cortex, composed of parenchyma cells and endodermis, which regulates the passage of water and nutrients into the vascular cylinder. The vascular cylinder, or stele, contains xylem and phloem tissues arranged in a central axis, facilitating the transport of water and nutrients throughout the plant.

7.4 Trichomes

Trichomes, or hair-like structures, may be present on the stems, leaves, and other parts of *C. quadrangularis*. These trichomes can vary in shape, size, and density, and their presence may contribute to the plant's defense mechanisms, water retention, or secretion of secondary metabolites [26]. In summary, the microscopic examination of *Cissus quadrangularis* reveals a complex array of anatomical structures adapted to its ecological

niche and medicinal properties. Understanding these microscopic characters enhances our appreciation of the plant's morphology, physiology, and potential pharmacological applications.

8. Powder characteristics of the plant

The powdered form of *Cissus quadrangularis* exhibits distinct characteristics under microscopic examination, providing valuable insights into its composition and quality. Here are some key features of the powder characteristics of the plant:

8.1 Color: The powder of *C. quadrangularis* typically presents a range of colors depending on the plant parts used and the processing method employed. It may vary from pale green to brownish-green, reflecting the presence of chlorophyll and other pigments in the plant tissues.

8.2 Texture: The texture of the powder can vary from fine and powdery to slightly gritty, depending on factors such as particle size and the presence of fibrous or crystalline materials.

8.3 Odor: *C. quadrangularis* powder may have a characteristic herbal or earthy odor, which can vary in intensity depending on factors such as the age of the plant material and the processing method [17].

8.4 Particle Size: The particle size of the powder can vary depending on the grinding method used. It may range from fine particles to coarser fragments, with a distribution that affects the powder's flow properties and suitability for various applications.

8.5 Microscopic Features: Microscopic examination of the powder may reveal the presence of various plant tissues and cellular structures, such as trichomes, stomata, parenchyma cells, vascular bundles, and calcium oxalate crystals. These features provide information about the plant's identity, purity, and quality [6].

8.6 Moisture Content: The powder's moisture content is an important parameter that influences its stability and shelf life. Proper drying and storage conditions are essential to maintain the powder's quality and prevent microbial contamination.

8.7 Chemical Constituents: Chemical analysis of the powder may reveal the presence of phytochemicals such as alkaloids,

flavonoids, tannins, steroids, terpenoids, and phenolic compounds. These bioactive constituents contribute to the plant's pharmacological properties and therapeutic potential. Overall, the powder character of *Cissus quadrangularis* is influenced by various factors, including its botanical composition, processing method, and storage conditions. Understanding these characteristics is essential for assessing the powder's quality, authenticity, and suitability for use in pharmaceuticals, herbal supplements, and traditional medicine [9].

9. Pharmacological Activities of Bioactive Constituents

The bioactive constituents in *Cissus quadrangularis* exert a wide range of pharmacological effects that have been extensively studied and documented. Some of the notable pharmacological activities include:

9.1 Anti-inflammatory Activity

Compounds such as quercetin and kaempferol exhibit potent anti-inflammatory effects by inhibiting pro-inflammatory mediators and pathways, making *C. quadrangularis* beneficial in managing inflammatory conditions such as arthritis and osteoporosis [7].

9.2 Bone Healing and Fracture Repair

C. quadrangularis is renowned for its ability to enhance bone regeneration and accelerate fracture healing. Ketosteroids and flavonoids present in the plant stimulate osteoblast proliferation and differentiation, promoting bone formation and mineralization. The anabolic steroid derived from *Cissus quadrangularis* has shown a notable impact on accelerating fracture healing by promoting early connective tissue formation. This effect is attributed to vitamins and steroids in *C. quadrangularis*, which exert specific effects on bone regeneration processes [8].

9.3 Anti-Obesity Activity

A study of a *Cissus quadrangularis* formulation named Cylaris used a double-masked, placebo-controlled design. The findings showed reduced waist circumference and body mass index among test subjects, along with decreased serum lipid levels. **Analgesic and Antinociceptive Properties:** The plant extracts demonstrate analgesic effects by modulating pain perception pathways and reducing nociceptive responses. These properties make *C. quadrangularis* a potential adjunct therapy for pain management [9].

9.4. Antioxidant Activity and Free Radical Scavenging Activity

The presence of flavonoids, phenolic compounds, and other antioxidants in *C. quadrangularis* confers potent antioxidant properties, scavenging free radicals and protecting cells from oxidative damage. This activity helps combat oxidative stress-related disorders. The methanol extract of *Cissus quadrangularis* has demonstrated robust antioxidant and free

radical scavenging activity both in vitro and in vivo. This activity is primarily attributed to β -carotene in the plant [11,12].

9.5 Anti-diabetic Effects

Triterpenoids like oleanolic acid exhibit hypoglycemic & insulin sensitizing effects, contributing to the management of diabetes mellitus by regulating blood glucose levels and improving insulin sensitivity [16-17].

Table 4: A. Summary of Preclinical Studies (In Vitro and Animal Studies) and B. Summary of Human Clinical Trials

A. Section- Summary of Preclinical Studies (In Vitro and Animal Studies)				
Research Title	Scientific Name	Methodology	Pharmacological Activity	Application
Evaluation of <i>Cissus quadrangularis</i> extracts	<i>Cissus quadrangularis</i>	In vivo study on rabbits with bone defects	Bone regeneration enhancement	Orthopedic medicine for bone fracture healing [12]
Antioxidant and anti-inflammatory activity	<i>Cissus quadrangularis</i>	In vitro assays	Antioxidant and anti-inflammatory effects	Treatment of oxidative stress and inflammatory conditions [13]
Evaluation of analgesic activity of <i>Cissus</i>	<i>Cissus quadrangularis</i>	In vivo animal models	Analgesic effects	Pain management [18]
Effect of <i>Cissus quadrangularis</i> extract	<i>Cissus quadrangularis</i>	Animal study	Gastroprotective and anti-inflammatory effects	Treatment of gastric ulcers and inflammation [19]
Immunomodulatory activity of <i>Cissus</i>	<i>Cissus quadrangularis</i>	In vivo animal models	Immunomodulatory effects	Enhancement of immune response [20]
Antimicrobial activity of <i>Cissus</i>	<i>Cissus quadrangularis</i>	In vitro study	Antimicrobial effects	Treatment of microbial infections [22]
Evaluation of hepatoprotective activity	<i>Cissus quadrangularis</i>	Animal study	Hepatoprotective effects	Liver protection and management of hepatic disorders [24]
B. Section - Summary of Human Clinical Trials				
Research Title	Scientific Name	Methodology	Pharmacological Activity	Application
<i>Cissus quadrangularis</i> in the treatment of metabolic disorders	<i>Cissus quadrangularis</i>	Randomized controlled trial	Anti-obesity and metabolic syndrome management	Management of obesity & metabolic disorders [14]
Evaluation of the effect of <i>C. quadrangularis</i>	<i>Cissus quadrangularis</i>	Clinical trial	Acceleration of fracture healing	Orthopedic treatment of bone fractures [15]
Evaluation of the effect of <i>C. quadrangularis</i> in postmenopausal women	<i>Cissus quadrangularis</i>	Clinical trial	Relief of postmenopausal symptoms	Management of menopausal symptoms [21]

9.6 Anti-Ulcerative Activity

The anti-ulcerative properties of *Cissus quadrangularis* extract were observed through its inhibition of the enzyme H⁺K⁺-ATPase, responsible for gastric acid secretion in the stomach [22-23].

9.7 Hepatoprotective Activity

Certain phytoconstituents, including oleanolic acid, possess hepatoprotective properties by preventing liver damage, enhancing liver function, and reducing oxidative stress. *C.*

quadrangularis extracts have shown promise in mitigating liver disorders such as hepatitis and hepatic fibrosis [28].

9.8 Gastroprotective Activity

Cissus quadrangularis, rich in carotenoids, triterpenoids, and ascorbic acid, has been traditionally used for gastrointestinal ailments. Its extract, known as *Cissus quadrangularis* extract (CQE), has exhibited gastroprotective effects in various studies, including protection against aspirin-induced gastric mucosal damage [1]. *Cissus quadrangularis* is a versatile plant with a rich

phytochemical profile and diverse pharmacological activities. Scientific evidence supports its traditional uses in Ayurvedic medicine, highlighting its potential as a valuable therapeutic agent for various health conditions. Further research is warranted to elucidate the underlying mechanisms of action and optimize its clinical applications. Nonetheless, *C. quadrangularis* holds promise as a natural remedy with wide-ranging health benefits and deserves continued attention and exploration in pharmacognosy and herbal medicine (Table 4, Sections A and B) [22-32].

Table 5: Ayurvedic formulation of *Cissus quadrangularis*

Ayurvedic Preparation	Composition	Application
Asthisamharaka Taila	<i>Cissus quadrangularis</i> extract, sesame oil	External application for massage to relieve joint pain
Asthisamharaka Ghrita	<i>Cissus quadrangularis</i> extract, ghee	Oral consumption for strengthening bones and joints[12]
Hadjodadi Yoga	<i>Cissus quadrangularis</i> extract, other herbs	Oral consumption as a tonic for bone health and healing[15]
Asthisanhari Leham	<i>Cissus quadrangularis</i> extract, jaggery, ghee	Oral consumption for bone health and fracture healing
Hadjodadi Churna	<i>Cissus quadrangularis</i> powder, other herbal powders	Oral consumption for bone strength and joint health[30]
Asthisamharaka Kwatha	<i>Cissus quadrangularis</i> decoction	Oral consumption for bone health and fracture healing
Akshadi Guggul	Laksha (Lacciferlacca), Asthisamharaka (<i>Cissus quadrangularis</i>), Guggulu (<i>Commiphora mukul</i>), and other herbs	Widely used in Ayurvedic treatment for bone-related diseases and fracture healing[15]
Zeotone Soft Gel Capsule	Contains <i>Cissus quadrangularis</i> extract and other ingredients	Beneficial for bone health and fracture healing. Convenient oral consumption in soft gel capsule form[16]
Panchajeeraka Gudam	Panchajeeraka (a combination of five cumin seeds), Guda (jaggery), and other herbs	An effective Ayurvedic medicine for post-natal care that aids digestive and respiratory health. Available in herbal jam form[18]

CONCLUSION

Exploring natural products for their therapeutic potential is an ongoing endeavor driven by the need to mitigate the side effects associated with conventional medicine. *Cissus quadrangularis* (CQL), commonly known as Hadjod or Asthisamadhani in India, has traditionally been used to manage various ailments. This climbing herb is indigenous to the hottest regions of India and is adaptable to cultivation in coastal plains, jungles, and wastelands up to 500 meters elevation. Traditional medicine has used its stem, root, and leaves for conditions such as piles, tumors, muscle pain, and bone fractures. Primarily recognized for its anti-osteoporotic activity, CQL exhibits extensive therapeutic potential across a spectrum of ailments. Numerous studies have investigated extracts from different parts of the plant, revealing a diverse range of pharmacological actions. Animal studies have

10. Ayurvedic medicine with *Cissus* as an ingredient

These Ayurvedic preparations use *Cissus quadrangularis* and other herbs to enhance its therapeutic effects. They are used for various purposes such as improving bone density, relieving joint pain, promoting fracture healing & strengthening musculoskeletal health (Table 5) [5-18]. Depending on the specific formulation and individual health needs, these preparations may be consumed orally or applied externally through massage. Consult a qualified Ayurvedic practitioner for proper dosage and usage guidelines.

demonstrated CQL's efficacy against severe and chronic conditions, supporting claims of anti-cancer, analgesic, and anti-inflammatory effects. Moreover, researchers have identified over 46 compounds, including flavonoids, alkaloids, terpenes, and steroids, in various parts of CQL. Key constituents such as quercetin, kaempferol, and β -sitosterol are believed to underlie its therapeutic properties, including analgesic, antidiabetic, antiulcer, anticancer, anti-inflammatory, and estrogenic activities. Despite extensive research, gaps exist in past studies of CQL. Future investigations should consider extracts beyond ethanolic and methanolic, and prioritize bio-guided isolation and pharmacokinetic studies. Furthermore, elucidating the molecular mechanisms of CQL's pharmacological actions using modern scientific tools will provide a more comprehensive understanding of its therapeutic potential, thereby rationalizing

its use in clinical practice. In this review, most pharmacological studies have focused on the therapeutic potential of *Cissus quadrangularis* stem, leaves, and roots, with limited investigation of its fruits and flowers. Future research should prioritize these neglected plant parts to further expand our understanding of its medicinal properties. Additionally, while preclinical studies have shown promising anti-obesity activity in *Cissus quadrangularis*, clinical data supporting its efficacy in humans remain limited. Similarly, despite its widespread use in marketed formulations for bone disorders, comprehensive clinical data are lacking. Future studies should aim to validate dosage regimens and therapeutic outcomes in clinical settings. Furthermore, while many traditional claims of *Cissus quadrangularis* have been supported by in vitro and in vivo studies, others, such as its efficacy in treating piles, blindness, and skin diseases, require validation through modern scientific approaches. This review provides a foundation for future research endeavors, serving as a roadmap for investigating the therapeutic potential of *Cissus quadrangularis* in greater depth.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Leena Daunday: Conceptualization, literature search and data collection, analysis of published literature, and manuscript drafting. Kriti Naurange: Literature search, collection and organization of relevant information, critical analysis, and manuscript preparation. Komal Sahu: Literature review, critical revision of the manuscript, and preparation of tables/figures. Monika Bhairam: Conceptualization, supervision, critical evaluation of the literature, scientific guidance, manuscript review and editing, and final approval of the manuscript.

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