

REDISCOVERING THE THERAPEUTIC POTENTIAL OF *CISSUS* SPECIES - A Review

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ABSTRACT

The genus Cissus, often known as the miracle herb, is utilized by Indian tribes to heal bone fractures, diabetes, and obesity, wound healing, stomach upset, allergies, weak bones. Aim of current review is to examine the literature for updated pharmacological characteristics of Cissus species (vitaceae). The assembled data may be useful to researchers in focusing on the priority areas of study that have yet to be identified. The plants complete information has been gathered from numerous books and periodicals. The study concluded with a specific of pharmacological activity, continuing and developing fields of research of this plant, particularly in the real of pharmaceuticals.

Keywords: *Cissus, Vitaceae, pharmacological activities, pharmaceuticals*

Introduction

The word “medicinal plant” refers to different types of plant with medicinal activity. The term “herb” is derived from the Latin word, “herba” and an old French word “herbe”. Herbs are referred as a group of plants, except vegetables and other types of plants which are used for macronutrients or aromatic or fragrances which are used for flavoring or decoration of food and for medicinal property. Herbs are distinguished from spices by Culinary use. Herbs are the flowering or leafy green parts of a plant either fresh or dried, while spices are dried and they are obtained from other parts of the plant which includes bark, roots seeds and fruits. Any parts of the plant might be regarded as “herbs”, which includes leaves, roots, flowers, seeds, root, bark resin and pericarp. Herbs have been used for various purposes such as culinary, healing, and fragrant and they are used for spiritual in some cases. The general application of the term “herb” differs between culinary herbs and medicinal herbs whether in healing or spiritual use.

Ultramodern pharmaceuticals had their origins in crude herbal drugs, presently, some medicines are still uprooted as fractionate or separate composites from raw herbs and also purified to meet pharmaceutical norms.¹

The method of treatment by using herbal drugs is the curative experiences of development of traditional physicians for over hundreds of years. Herbal drug has gained accumulative popularity even in present’s medical practice. The rise in the use of herbal products is due to their cultural sufficiency, accessibility, affordability, effectiveness and safety.²

Herbal medicine, sometimes referred to as botanical medicine or herbalism, involves the use of plants or parts of plants, to treat injuries or illnesses³. Herbal medicines are the study or use of medicinal herbs to prevent and treat diseases and ailments or to promote health and healing⁴. It is a medicine or preparation derived from a plant or plants part and used for any of the mentioned uses. Herbal medicines are the oldest form of health care known to mankind⁵.

Plant description

Cissus quadrangularis reaches a height of 1.5 m (4.9 ft) and has quadrangular-sectioned branches with internodes 8–10 cm (3–4 in) long and 1.2–1.5 cm (0.5–0.6) wide. Along each angle is a leathery edge. It has a

toothed trilobe leaves of 2–5 cm (0.8–2.0 in) wide appear at the nodes. It consists of racemes of small white, yellowish, or greenish flowers; globular berries are red incolor when fully ripe.

Cissus quadrangularis is an evergreen climber and perenninal growing to 5 m (16 ft) a fast rate. It is hardy to zone. Suitable at: light (sandy), medium (loamy) and heavy (clay) soils, grows in well-drained soil and can grown in nutritionally poor soil. Suitable pH at acid, neutral and basic (alkaline) soils and can grow in very acid and very alkaline soils. It cannot grow in the shade.⁶



Figure.1 : Stems of *Cissus quadrangularis*.

Scientific classification⁷

Scientific name: *Cissus quadrangularis*.

Kingdom: Plantae

Subkingdom: Tracheobionta-Vascular plants.

Superdivision : Spermatophyta- Seed plants

Division: Magnliopsida- Dicotyledons

Subclass: Rosidae.

Order: Rhamnales.

Family: Vitaceae- Grape family.

Genus: *Cissus* L.-Treebine.

Species : *Cissus quadrangularis*.

Synonyms: Veldt grape, pirandai, hajpod, devils backbone, asthisamharaka.

General description⁸

English Name: *Cissus quadrangularis*.

Kannada Name: Mangaravalli, sanduballi.

Telugu Name: gudametige, nalleru, vajravalli.

Tamil Name: pirantai, arukani.

Malayalam Name: changalampareanda

Hindi Name :asthibhanga, harajora,
Parts Used: roots, leaves, fruits, stems.

Traditional uses

The roots and stems were most used for healing of fracture of the bones. The stem is bitter when tasted. A paste of stem is used for muscular pains. The different parts of plant have been documented in Ayurveda for the treatment of osteoarthritis, rheumatoid arthritis and osteoporosis. The stem juice is used to treat scurvy, menstrual disorders, otorrhoea and epistaxis. The use of sap with tamarind has been used in East Africa for the treatment of gonorrhoea. The plant is fed to cattle to induce flow of milk. The ash of plant is used as a substitute for baking powder. A paste of stem is used in treatment of asthma, burns and wounds, bites of poisonous insects and for saddle sores of horses and camels.⁹

Morphology of the plant¹⁰

Cissus quadrangularis is a perennial herbaceous climber; stems are thick, quadrangular, succulent, quadrangular. It is known as aggressive fast growing vine that has been cultivated as a medicinal and ornamental plant. *Cissus quadrangularis* is a vigorous vine that spreads both vertically and horizontally forming dense monospecific stands that outcomplete native vegetation. It climbs over trees and shrubs covering them completely by blocking light where it restricts the growth and regeneration of native plants. *Cissus quadrangularis* is a fast growing vine that can be used as medicinal plant. This species are found in dry forests, coastal thickets, forest edges, warm temperatures in the world.

Phytochemical investigation

The plant contains potassium, calcium, zinc, sodium, iron, lead, cadmium, copper, magnesium, calcium ions, phosphorous, saponins and phenol.

Other constituents of the plant consists of resveratrol, piceatannol, pannonol, Parthenocissus, calcium oxalate, methyl triacontanoic acid, taraxeryl acetate, taraxerol, iso-pentadecanoic acid, ketosterol, tannin, carotene, vitamin.¹¹

Pharmacological activity of *Cissus* species

The various invitro and invivo Pharmacological studies of *Cissus* Species are tabulated below. (Table 1, 2 & 3)

Table.1: Antioxidant Activity of *Cissus* Species

| Name of the plant | Parts of plant used | Extract | Antioxidant activity | Reference |
|------------------------------|---------------------|-------------------|--|-----------|
| <i>Cissus quadrangularis</i> | Aerial part | Hydroethanol | Superoxide radical scavenging, hydroxyl radical scavenging, metal chelating activity | 12 |
| | Stem | Ethyl acetate | DPPH, beta carotenelinoleic acid | 13 |
| | Aerial part | Ethanol, methanol | DPPH, nitric oxide, hydroxyl, superoxide scavenging activity, ABTS, ferric reducing activity | 14 |
| | Stem | Ethanol | Nitric oxide, DPPH and hydroxyl radical scavenging assays. | 15 |

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|--------------------------|------------------------------|---|---|----|
| | Root, stem, leaves, tendrils | Methanol, pet.ether, chloroform, acetone, ethyl acetate | DPPH, ABTS, superoxide anion, hydrogen peroxide, hydroxyl scavenging activity, ferric reducing antioxidant activity | 16 |
| <i>Cissus sicyoides</i> | Stem | Water | ABTS | 17 |
| <i>Cissus cornifolia</i> | Leaf & root | Ethanol and aqueous | Ferric reducing antioxidant power assay, DPPH | 18 |

The preliminary phytochemical assay were carried using solvents of different polarity namely water, 50% hydroethanol, ethanol, acetone, chloroform and petroleum ether showed the presence of secondary metabolites like flavanoids, alkaloids, tannins, triterpenoids, carbohydrates, saponins, glycosides, lignins and inulins. Among all different the extracts, hydroethanol extract showed the presence of more secondary metabolites. Hence it was taken for further antioxidant assays like superoxide radical scavenging activity, hydroxyl radical scavenging activity and metal chelating activity. These results revealed that the 50% hydroethanol extract of *Cissus quadrangularis* L. stem possessed potent antioxidant properties.¹² *Cissus quadrangularis* L. extracts were tested for antioxidant activity by β -carotene linoleic acid model and also by 1,1-diphenyl-2-picrylhydrazyl model. The ethyl acetate fraction of both fresh and dry stem extracts at a concentration of 100 ppm showed 64.8% antioxidant activity in the β -carotene linoleic acid system and 61.6% antioxidants the 1,1-diphenyl-2-picrylhydrazyl system. The ethyl acetate fraction showed the presence of sterols, vitamin C, and tannins as phytoconstituents.¹³ In vitro antioxidant analyses were performed for the ethanolic extract of *Cissus quadrangularis* (L). (EECQ) and methanolic extract of *Cissus quadrangularis* (L). (MECQ) using different free radical scavenging assays such as DPPH, nitric oxide, superoxide, metal chelation, and hydrogen peroxide radical scavenging assays.¹⁴ The present study aim was to isolate flavonoid fraction from the aerial parts of *Cissus quadrangularis* and to evaluate its antioxidant potential using *in vitro* assay system and *in vitro*, antioxidant activity of the ethanol extract and isolated flavonoid fraction was investigated by nitric oxide, DPPH and hydroxyl radical scavenging assays.¹⁵ An important medicinal plant *Cissus quadrangularis*, belonging to the family Vitaceae was used in the present study to estimate antioxidant properties of different extract (root, stem, leaves and tendrils). The antioxidant properties of the petroleum ether, chloroform, ethyl acetate, acetone and methanol extracts of *Cissus quadrangularis* were screened and results showed considerable antioxidants in all the extracts.¹⁶ *Cissus sicyoides* contain several bioactive compounds with high antioxidant activity, such as phenolic compounds, which are compounds that prevent or delay oxidative stress, acting as free radical scavengers, and thus reduce the onset of cardiovascular disease, cancer, epilepsy, cancer, diabetes, stroke.¹⁷ The study was intended to explore the antioxidant potential and phytochemical content of the ethanol and aqueous extracts of the leaf and root samples of *Cissus cornifolia* (Baker) Splanck (Vitaceae) across a series of four *in vitro* models. The results showed that all the extracts had reducing power ($\text{Fe}(3+) - \text{Fe}(2+)$) and DPPH, hydroxyl and nitric oxide radical scavenging abilities to varying extents.¹⁸

Table.2: Invitro Activity Of Cissus Species

| Latin name of plant | Plant part used | Extract | Model | Pharmacological activity | Reference |
|---------------------|-----------------|----------|--------------------|--------------------------|-----------|
| | Stem | Methanol | Cytotoxicity assay | Anticancer | 19 |

| | | | | | |
|------------------------------|--------------|------------------|--|--------------------------------|----|
| <i>Cissus quadrangularis</i> | Stem | Ethanol | Flow cytometric analysis, Western blot analysis | Bone fracture healing activity | 20 |
| | Aerial parts | Methanol | Egg hatch inhibition assay, Adult motility assay | Anthelmintic | 21 |
| | Fresh stem | Methanol & water | inhibition of protein denaturation method by bovine serum albumin method and egg albumin method inhibition of protein denaturation method by bovine serum albumin method and egg albumin method Inhibition of protein denaturation method by bovine serum albumin and egg albumin method | Antiarthritic | 22 |

The anticancer effects of *Cissus quadrangularis* leaf extract against MG63 human osteosarcoma cell line. MG63 cells were obtained from NCCS, Pune. The methanolic extract of *Cissus quadrangularis* was utilized to perform anticancer activity in cell lines using Mossman method of cytotoxicity assay. The cell viability of MG63 cells ranged between 29.65% and 73.59% at an extract concentration from 1000 µg/ml to 7.8 µg/ml. The IC₅₀ of extract revealed by this cytotoxicity assay was around 100 µg/ml. This study showed anticancerous activity of *C. quadrangularis* leaf extract against MG63 cells, which can be further characterized by future studies and aid in treatment of bone tumors.¹⁹ Fracture healing involves complex processes of cell and tissue proliferation and differentiation. Many factors are involved, including growth factors, inflammatory cytokines, antioxidants, bone breakdown (osteoclast) and bone building (osteoblast) cells, hormones, amino acids, and uncounted nutrients. Study was carried on the osteogenic potential of *Cissus quadrangularis* (CQ), a plant that has been customarily used in the Indian subcontinent to hasten the process of healing in bone fractures.²⁰ The study aimed to evaluate the anthelmintic activity of crude methanolic extracts of aerial parts of *Cissus quadrangularis* against *H. contortus*. **Methods.** Adult motility test and egg hatching inhibition assay were employed to investigate the *in vitro* adulticidal and egg hatching inhibitory effects of the extracts.²¹ The present investigation deals with the study of *in vitro* anti-arthritis activity by inhibition of protein denaturation method by bovine serum albumin method and egg albumin method.

TABLE 3. In vivo Activity of Cissus Species

| Latin name of the plant | Plant part used | Extract | Model | Pharmacological activity | Reference |
|-------------------------|-----------------|----------|--|--------------------------|-----------|
| | Stem | Methanol | Rifamycin induced hepatotoxicity | Hepatotoxicity | 23 |
| | stem | Acetone | Carragenan induced edema in rats, induction of arthritis | Antiarthritic | 24 |

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|------------------------------|--------------------|--------------------|--------------------------------------|--------------------------|----|
| <i>Cissus quadrangularis</i> | stem | Ethanol | Ovariectomized rat model | Antiosteoporotic | 25 |
| | Stem | Ethyl acetate | Carragenan induced paw edema in rats | Antiinflammatory | 26 |
| | Leaf, stems, roots | Water & chloroform | Formlin test & writhing test | Antinociceptive activity | 27 |

Hepatoprotective activity of methanol extract of *Cissus quadrangularis* evaluated against rifampicin-induced hepatotoxicity in rats. The coarse powder of the shade dried stem of *Cissus quadrangularis* was subjected to successive extraction in a Soxhlet apparatus using solvents petroleum ether (60-80°) and methanol.²³ In the present study, anti-arthritis activity of AFCQ (Active Fraction of *Cissus quadrangularis*) obtained from acetone extract of *Cissus quadrangularis* has been reported by employing CFA (Complete Freund's Adjuvant) induced arthritis model in Wistar rats as an in vivo experimental model. Rat paw edema was induced by carrageenan and altered hematological and biochemical parameters were determined.²⁴ *Cissus quadrangularis* L. (*C. quadrangularis* L.) (Vitaceae) has been reported in Ayurveda for its antiosteoporotic activity. The study separated the phytoestrogen-rich fraction (IND-HE) from aerial parts of *C. quadrangularis* L. and evaluated its effect on osteoporosis caused by ovariectomy in rats.²⁵ The anti-inflammatory activity of *Cissus quadrangularis* Lin. was investigated in carrageenan induced inflammation in Wistar albino rats. Two different doses 250mg/kg and 500mg/kg were administered to the animals. The results showed that both doses had significant reduction in inflammatory condition but dose 500mg/kg showed maximum inflammatory reduction on comparing with control and standard treated groups.²⁶ The plant extract were prepared by using chloroform and distilled water in proportion (20:80), macerated for 72 h with occasional stirring and concentrated under dry vacuum. The extract of *Cissus quadrangularis* was examined for centrally acting analgesics by using the hot plate method, formalin test and acetic acid induced writhing method for peripherally acting analgesics. The doses administered were 250 mg/kg and 350 mg/kg. The animal that administered both the doses showed significant analgesic activity. The animal that administered a dose of 350 mg/kg has shown the maximum analgesic activity which is comparable to the standard.²⁷

Conclusion

Cissus species is a well-known traditional herb that has long been utilized in traditional medicine. To achieve comprehensive wellbeing, the current scientific consensus recommends consuming whole plants rather than isolated components, as nature intended, with full complements of naturally occurring synergistic phytonutrient. According to the information shown above, the plant has been utilized for a variety of therapeutic purposes in the past. Analgesic, anti-inflammatory, hepatoprotective, anthelmintic, antibacterial, cytotoxic, and many other properties of the plant have been discovered. As a result of the current literature review and ayurveda text, it was determined that the plant has a great therapeutic value. Traditional and ethnomedicinal literature revealed that the herb is extremely useful and safe for therapeutic purposes. A strong and safe medicine can be researched from the plant employing reverse pharmacological procedures in natural drug development for many chronic diseases such as liver disorders, cancer, and other inflammatory diseases.

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