

CARDIOSPERMUM HALICACABUM LINN. : A COMPREHENSIVE REVIEW OF ITS ETHNOBOTANICAL HERITAGE, PHYTOCHEMISTRY AND MODERN PHARMACOLOGICAL PROFILE

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ABSTRACT

Cardiospermum halicacabum Linn., also known as balloon vine or love-in-a-puff, is a widely distributed medicinal climber belonging to the Sapindaceae family. This species has been used for various medicinal purposes in Ayurvedic, Unani, Chinese, Homeopathic and folk medicines, and has attracted much scientific attention because of its wide pharmacological applications. In Kerala, it is one of the “Dasapushpam” (Ten Sacred Flowers) and has been used to treat inflammatory conditions, rheumatism, diabetes, dermatitis, fever, gastrointestinal disorders, and neurological problems. Phytochemical studies have revealed the presence of flavonoids, phenolic acids, alkaloids, saponins, sterols, terpenoids, triterpenes, glycosides, tannins, fatty acids, and cyanolipids, which together account for its wide pharmacological properties. Experimental studies have established the antioxidant, anti-inflammatory, antidiabetic, anticancer, antimicrobial, antiviral, hepatoprotective, neuroprotective, antiulcer, antidiarrheal, anxiolytic, antifilarial, antiparasitic, wound-healing, and fertility-promoting properties. Toxicological studies have revealed a favourable safety profile at therapeutic doses. This review aims to integrate the botanical features, phytochemical constituents, traditional uses, pharmacological properties, and therapeutic values of *C. halicacabum*, and thus emphasizes its importance as a potential natural source for future drug development.

KEYWORDS: *Cardiospermum halicacabum*, Sapindaceae, Dasapushpam, Phytochemistry, Antioxidant, Anti-inflammatory.

INTRODUCTION

Plant-based drugs have been used in conventional medical practices for treating various diseases. About 75-80% of the population worldwide is dependent on herbal medicines. Various plants have been found to have medicinal properties and have been researched for new and effective compounds. The diversity of phytochemicals found in plants is a major factor in the treatment of life-threatening diseases.^[1,2]

The medicinal plant *Cardiospermum halicacabum* Linn., belonging to the family Sapindaceae, commonly known as balloon vine or love-in-a-puff, is a shrub-like woody vine, branching, ornamental, herbaceous climber that grows up to 10 feet. The species is widely distributed in tropical and subtropical parts of the world and it is

cultivated on African and American plains, as well as in India, Sri Lanka, China, Bangladesh, Malacca, Pakistan and Australia.

Cardiospermum is derived from the Latin word ‘cardio’ meaning heart and ‘sperma’ meaning seed, referring to the white heart-shaped design on the seed. The name *halicacabum* is derived from the Latin word ‘halicacabus,’ referring to a plant with inflated fruits. The species can be an annual or perennial climber and often occurs as a weed throughout India. The plant is one of the ‘Ten Sacred Flowers’ of Kerala, India, collectively referred to as “Dasapushpam”.^[3,4]

The active compounds extracted from the leaves, roots and seeds of this plant in the form of extracts and

powders are used in the preparation of decoctions and infusions in traditional medicine against diabetes mellitus and arthritis.

Cardiospermum halicacabum is used in Ayurvedic medicine to treat snakebite, limb stiffness, and chronic bronchitis. In Unani medicine, the seeds are described as a tonic for treating cancer. In Chinese medicine, it has been used to cure rheumatism, lumbago, neurological disorders and as a demulcent in orchitis and dropsy. *C. halicacabum* has long been used as a hair detergent and laundry soap due to its saponin compounds. In rural areas of Southern India, this plant is sold in local markets as a green vegetable and is a means of livelihood for economically poor families. For centuries, the entire *C. halicacabum* plant has been used as food and medicine due to its nutritional value.^[5,6,7,8]

Cardiospermum halicacabum is used in alternative medicine systems such as Homeopathy, Unani, Chinese, Ayurvedic and folk medicine. Phytochemical analysis of *Cardiospermum halicacabum* reveals the presence of secondary metabolites such as alkaloids, flavonoids, phenolic acids, saponins, sterols, terpenoids, triterpenes, glycosides, tannins and fatty acids. It possesses a wide range of biological & pharmacological properties, including antioxidant, anti-diabetic, anti-viral, anti-convulsant, anti-diarrheal, anti-cancer, anti-bacterial, anti-fungal, anti-inflammatory, antimicrobial, hepatoprotective, neuroprotective, antiulcer, antidiarrheal, anxiolytic, antifilarial, antiparasitic, wound-healing and fertility-promoting properties.^[8,9]

PLANT PROFILE

Table 1: Taxonomical Classification.^[10,11]

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Sapindales
Family	Sapindaceae
Sub-family	Sapindoideae
Genus	<i>Cardiospermum</i>
Species	<i>Cardiospermum halicacabum</i> Linn.

VERNACULAR NAMES^[11,12]

English	:	Balloon vine, Love in a puff, Heart pea, Heart seed
Sanskrit	:	Indravalli, Sakralata, Jyotishmati
Hindi	:	Kapalphoti, Kanphuti
Kannada	:	Agniballi, Erumballi
Tamil	:	Mudukattan
Telugu	:	Ekkudutige, Budda kakara
Marathi	:	Kakumardanika, Shibjal
Bengali	:	Lataphatkari
Malayalam	:	Katabhi

SYNONYM^[12]

Cardiospermum corundum L.
Cardiospermum glabrum
Cardiospermum inflatum

GEOGRAPHICAL DISTRIBUTION

The medicinal plant *Cardiospermum halicacabum* Linn., belonging to the family Sapindaceae, is an annual or perennial herbaceous climber commonly found as a weed along roadsides and riverbanks, which are widely used for both medicinal and ornamental purposes. The ideal environmental conditions for this herb include marshy flooded areas, waste ground, seasonal climates and moist soils.^[13]

The genus *Cardiospermum* comprises 16 species in Brazil, of which 12 are recorded from South America. *Cardiospermum halicacabum* has a wide pan-tropical distribution and is native to large parts of Africa, Asia, Oceania, Central and South America and the Caribbean. The species has also been introduced to several regions, including North America, Europe, parts of Asia and Australia, where it is often regarded as an alien or invasive plant.^[14]

Cardiospermum halicacabum Linn. is widely distributed across tropical and subtropical regions of Africa, Asia (including India, China, Bangladesh, Malaysia and Pakistan), Australia, North and South America. In India this species is also found in various geographically diverse regions of Karnataka, Tamil Nadu and Kerala. It is one among the "Ten Sacred Flowers of Kerala," collectively known as "Dasapushpam."^[15,16]

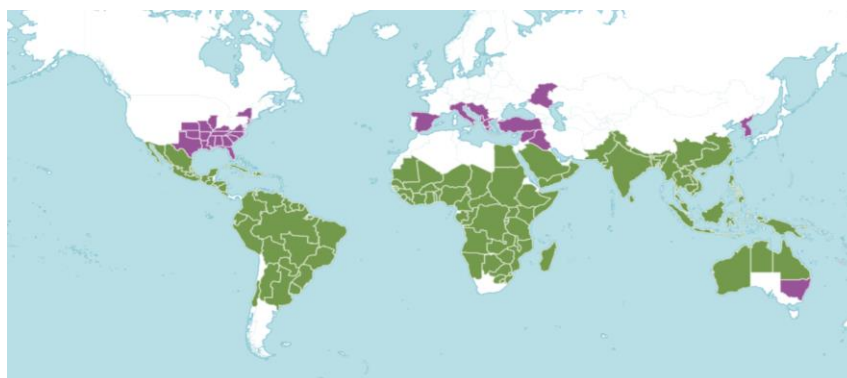


Figure 1: Global distribution of *Cardiospermum halicacabum* L. Green: Native range. Purple: Introduced and naturalized regions. Source: POWO/Kew Science.

MORPHOLOGICAL CHARACTERS^[16,17,18]

Cardiospermum halicacabum Linn. is a slender, climbing herb, either slightly hairy or nearly glabrous, growing annually or perennially with tendrillar hooks for about 3 m long.

Stem: The thin, five-grooved stem might be sparsely hairy or hairless, approximately 3 mm thick, but it can reach a height of up to 2 meters. The stem forms internodes of between 5-10 cm in length.

Leaves: The biternate, trifoliate leaves measure 5 to 9 cm in length, with oblong to lanceolate leaflets that are acuminate on top.

Flowers: Zygomorphic in structure, small, unisexual flower is 2 to 5 cm long, white in colour with a yellowish centre, upper two densely scaly, lower two bearing glands and large, leaf-like scales. The perianth consists

of 4-5 sepals and 4 petals, there are a total of 8 anthers and its flowering time is from July to August.

Fruits: Approximately 3 cm in length, the blown-up capsule is nearly completely spherical and contains the distinctive seeds.

Seeds: The black, round, smooth, kidney shaped, opaque seeds have a white heart shaped patch near the micropyle and its seed maturing season is from the month of August to October.

Root: Slender, cylindrical and branched, with a light to dark brown rough surface showing longitudinal wrinkles and fissures. Internally, it is fibrous with a pale yellow to cream coloured interior and a slightly bitter taste with characteristic odour.

Pollinator: Pollinated by bees, wasps, flies, and butterflies.

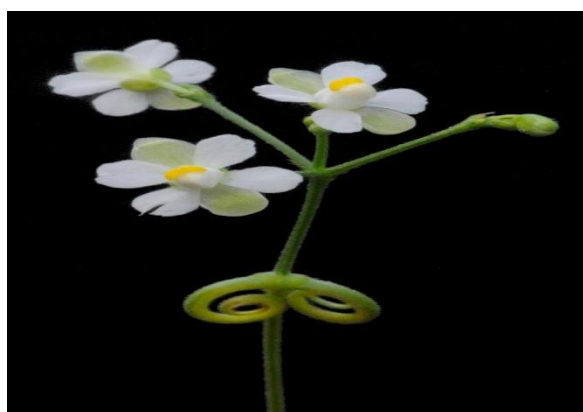


Figure 2: *Cardiospermum halicacabum* whole plant, pods, seeds & flower.

PHYTOCHEMICAL CONSTITUENTS

Cardiospermum halicacabum Linn. is known to have a wide range of biologically active secondary metabolites, which include flavonoids, phenolic acids, alkaloids, saponins, sterols, terpenoids, triterpenes, glycosides,

tannins, fatty acids and cyanolipids. These compounds have been isolated and identified through chromatographic and spectroscopic techniques such as GC-MS, HPLC, LC-MS, and FT-IR analysis, which are responsible for their diverse traditional applications.

Table 2: Phytochemicals and Bioactive Constituents of *Cardiospermum halicacabum*.

Sl. No	Plant Parts	Phytoconstituents	References
1.	Leaves	Flavonoids (quercetin, kaempferol, luteolin, apigenin, rutin, vitexin, quercetin-3-O- α -L-rhamnoside, kaempferol-3-O- α -L-rhamnoside), Flavonoid glycosides (apigenin-7-O- β -D-glucuronide, luteolin-7-O- β -D-glucuronide, chrysoeriol-7-O-glucuronide), Phenolic acids (gallic acid, caffeic acid, ferulic acid, <i>p</i> -coumaric acid, protocatechuic acid, benzene acetic acid), Sterols (β -sitosterol, stigmasterol, Campesterol), Triterpenoids (lupeol, phytol, squalene, friedelin), Sesquiterpenes (caryophyllene), Tannins (catechin, epicatechin), Diterpenes (neophytadiene, cyclohexane derivatives), Aliphatic hydrocarbons (hexadecane, heptadecane, nonadecane, 1-hydrotetradecane, 11-trimethyl-8-methylene, 14-methyl-8-hexadecyne), Nitrogenous compounds (N-methyl tomatidine, 3-methylbutanamide), phenylethyl alcohol, aliphatic esters, pinitol, cardiac glycosides, oxalic acid, amino acids	[19,20,21,22,24]
2.	Stem	Flavonoids (quercetin, kaempferol, luteolin, apigenin), Phenolic acids (gallic acid, caffeic acid, ferulic acid), Sterols (β -sitosterol, stigmasterol, Campesterol), Triterpenoids (lupeol, α -amyrin, β -amyrin, friedelin), and terpenoids (phytol, neophytadiene)	[19,21,24]
3.	Root	Alkaloids (indole alkaloids, piperidine derivatives), Flavonoids (quercetin, kaempferol, luteolin), Phenolic acids (gallic acid, caffeic acid, syringic acid, vanillic acid), Sterols (β -sitosterol, stigmasterol), Triterpenoids (lupeol, α -amyrin, β -amyrin), and cardiospermin (cyanogenic glucoside)	[19,24]
4.	Seed (non-oil fraction)	Flavonoids (quercetin, kaempferol, and rutin; Phenolic acids: gallic acid, caffeic acid, ferulic acid, chlorogenic acid), Sterols (β -sitosterol, stigmasterol, campesterol), and terpenoids/triterpenes (lupeol, phytol, squalene, and friedelin)	[19,22,24]
5.	Seed oil	Fatty acids (octanoic acid (4.6%), palmitic acid, oleic acid (30%), linoleic acid, stearic acid, arachidic acid, eicosanic acid (12%), erucic acid (43%), 11-eicosenoic acid), Cyanolipids (55%), Sterols (β -sitosterol), fatty acid methyl esters	[19,23,24]

TRADITIONAL USES^[24,25]

Cardiospermum halicacabum Linn., also referred to as "Kanphuti," has long been used in Ayurvedic and traditional medicine to treat fever, cough, rheumatism, snakebite, eczema, osteoarthritis, psoriasis and neurological diseases.

Additionally, it treats dropsy and acts as a demulcent for orchitis. The herb has stomachic, rubefacient and diuretic effects. A decoction of its leaves and stems is used to treat diarrhoea, dysentery, and migraines and a poultice of them is used to treat swelling. It is used as a hair detergent and a laundry soap in its native regions due to the presence of saponins. Its juice has long been used to treat hardened tumours and ease earaches. The leaves decoction, when mixed with pepper and jaggery, is used to alleviate fever and cough. The seeds serve as a fever tonic and diaphoretic, while the mucilaginous root is used for its laxative, antirheumatic and emetic properties. Every part of this herb is beneficial, both as food and as a medicine.

PHARMACOLOGICAL ACTIVITY**1. Anticancer Activity**

Cardiospermum halicacabum Linn. seeds were tested for cytotoxicity to explore their anticancer properties as plant-based drugs. Seed extracts were obtained by Soxhlet extraction and tested on human cancer cell lines

such as colorectal (HT-29, HCT-15), skin (SK-MEL-2), and breast (MCF-7) cancer cells, with doxorubicin as the reference drug. The n-hexane extract of the seeds showed strong cytotoxicity against MCF-7 cells with a GI₅₀ value of 12.8 μ g/mL, suggesting strong anticancer properties.^[26]

The leaf extracts of *Cardiospermum halicacabum* L. have been found to possess significant *in vitro* anticancer properties. In Ehrlich Ascites Carcinoma (EAC) cells, the chloroform extract showed higher cytotoxicity IC₅₀ = 140 μ g/mL compared to the ethanolic extract (IC₅₀ = 150 μ g/mL) in trypan blue exclusion and MTT assays.^[27] In HepG2 liver cancer cells, the ethanol and ethyl acetate extracts showed dose-dependent antiproliferative activity with IC₅₀ values of 49.70 μ g/mL and 51.12 μ g/mL, respectively. The results can be attributed to the presence of bioactive compounds such as flavonoids, alkaloids, saponins, and phenolics, thus establishing the plant's role as a potential natural anticancer drug source.^[28]

2. Anti-Oxidant Activity

Reactive oxygen species have been linked to various chronic conditions such as cancer, accumulation of vascular plaques, arthropathies and other age-related issues. The antioxidant properties of the ethanolic extract of the aerial parts of *Cardiospermum halicacabum* L. have been evaluated using various *in*

vitro models such as DPPH (IC₅₀=34.06 µg/mL), ABTS (IC₅₀=21.45 µg/mL), nitric oxide (IC₅₀=25.16 µg/mL), superoxide (IC₅₀=35.16 µg/mL), and hydroxyl radicals (IC₅₀ 28.56 µg/mL), ferrous ion chelation capacity (IC₅₀=19.56 µg/mL), and inhibition of lipid peroxidation (IC₅₀=33.12 µg/mL), which gives an indication that this herb is a promising natural antioxidant source for the management of disorders related to oxidative stress.^[29]

3. Anti Diabetic Activity

In streptozotocin-induced diabetic rats, administration of the ethanolic leaf extract of *Cardiospermum halicacabum* (50–200 mg/kg for 45 days) significantly reduced blood glucose and HbA1c, restored the level of insulin to normal, and restored the disturbed activities of glucose-6-phosphatase and fructose-1,6-bisphosphatase, with the highest dose of 200 mg/kg having the most significant effect.^[30] Similarly, chrysoeriol, a purified flavonoid (20 mg/kg for 45 days), significantly enhanced glycaemic control by reducing plasma glucose and HbA1c, increasing insulin sensitivity, downregulating gluconeogenic enzymes, upregulating glycolytic enzymes, increasing hepatic glycogen stores, and regenerating pancreatic β-cells. It also showed a binding affinity comparable to that of glibenclamide in the molecular docking analysis, establishing it as a potent antidiabetic agent.^[31]

4. Anti-Convulsant Activity

The anticonvulsant activity of the alcoholic root extract of *Cardiospermum halicacabum* L. (Sapindaceae) was evaluated in various murine models of epilepsy. Oral treatment of male Swiss albino mice with the extract at doses of 30, 100, and 300 mg/kg showed significant anticonvulsant activity at 100 and 300 mg/kg doses, as evidenced by the delayed onset of clonic and tonic seizures in models involving pentylenetetrazol, isoniazid, and picrotoxin-induced seizures. In the maximal electroshock seizure (MES) model, the extract significantly reduced tonic hind limb extension compared with the vehicle-treated controls. There was no appreciable motor toxicity even at a dose of 900 mg/kg.

Neurochemical analysis by HPLC showed an increase in GABAergic activity, particularly in the cerebellar areas, suggesting that the anticonvulsant activity could be mediated through the modulation of GABA neurotransmission.^[32]

5. Anti-Inflammatory Activity

The ethanolic extract of *Cardiospermum halicacabum* was evaluated for its anti-inflammatory potential using lipopolysaccharide (LPS)-stimulated human peripheral blood mononuclear cells and RAW 264.7 macrophage cells, as well as an *in vivo* model of carrageenan-induced paw edema in mice. The results revealed significant inhibition of tumor necrosis factor-alpha (TNF-α) production (IC₅₀ = 70 µg/mL), as well as nitric oxide (NO) release (IC₅₀ = 90 µg/mL), in a concentration-dependent manner without any evidence of toxicity using

a cell viability MTS assay. The ethanolic extract also exhibited a significant reduction of carrageenan-induced paw edema. Furthermore, there was a reduction in TNF-α and NO levels, as well as malondialdehyde (MDA) content in paw tissue, and a concomitant enhancement of endogenous antioxidant enzyme activity, i.e., catalase, superoxide dismutase, and glutathione peroxidase. The results of this study indicate that the anti-inflammatory potential of *Cardiospermum halicacabum* ethanolic extract is due to the downregulation of TNF-α and NO release, as well as a reduction of oxidative stress, and therefore support its traditional use in the treatment of inflammatory diseases.^[33,34]

6. Anti-Bacterial Activity

The ethanolic, acetone, benzene, chloroform, and aqueous extracts of the leaves and stems of the *Cardiospermum halicacabum* plant have been found to possess significant antibacterial properties against both Gram-positive and Gram-negative bacteria, as determined by the disc diffusion method. Among these, the ethanolic extracts were found to have pronounced inhibitory activity, especially against *Staphylococcus aureus* and *Bacillus subtilis*, while the acetone extracts had the maximum inhibitory effect against *Salmonella typhi*. Also, the ethanolic extracts from wild and commercial sources have been found to possess significant antibacterial activity, with zones of inhibition ranging from 8.3 to 21.7 mm, and the MIC, MBC, and IC₅₀ values ranging from 116.7 to 366.7 µg/mL, 233.3 to 358.3 µg/mL, and 102.7 to 200 µg/mL, respectively. The antibacterial activity was found to be more pronounced against *Streptococcus pyogenes* and *Staphylococcus aureus*, and the wild extracts were found to have more potency compared to the commercial powder.^[35]

7. Anti-Fungal Activity

Dermatophytosis, mainly caused by *Trichophyton rubrum* and *Trichophyton mentagrophytes*, was investigated to evaluate the antifungal efficacy of *Cardiospermum halicacabum* against *T. rubrum* using *in vitro* and *in silico* approaches. The whole plant extract at a concentration of 31.25 to 500 µg/ml showed significant fungistatic activity at higher concentrations (250 to 500 µg/ml). The computational studies revealed high binding affinity of luteolin and rutin to fungal Hsp90, a key protein involved in pathogenicity and antifungal resistance. Although both compounds showed measurable antifungal activity, it was found to be lower compared to the whole plant extract. The results of this study provide conclusive evidence for the potential therapeutic use of *C. halicacabum* in dermatophytosis, which acts through Hsp90-mediated pathways.^[36]

8. Analgesic Activity

The aerial parts of *Cardiospermum halicacabum* was extracted with petroleum ether, chloroform, ethyl acetate and ethanol and evaluated for analgesic activity using the thermal stimulus model in albino mice. Among the extracts, the petroleum ether extract showed the highest

analgesic effect, producing 34% and 58% inhibition at 0.15 and 0.3 mg/ml, respectively, compared to morphine, and 48% and 82% inhibition at the same concentrations compared to paracetamol.

The activity may be attributed to the presence of flavonoids, alkaloids, sterols, and saponins identified during phytochemical screening.^[37]

9. Anti-Ulcer Activity

The antiulcer activity of the aerial part extracts was assessed using the pylorus ligation model in rats. The ethanol extract at a dose of 75 mg/kg, p.o. exhibited the most significant antiulcer activity (48.2%) compared to ranitidine at 50 mg/kg (67.2%). The extract reduced gastric volume, total acidity, free acidity, and ulcer index, indicating moderate gastroprotective potential likely associated with bioactive phytoconstituents such as flavonoids and saponins.^[37]

The gastroprotective and antiulcer properties of *Cardiospermum halicacabum* were investigated using experimental rat models of gastric ulcer induced by ethanol and indomethacin. In the ethanol-induced ulcer model, oral dosing with the ethanol extract (200-600 mg/kg) significantly and dose-dependently reduced ethanol-induced gastric mucosal lesions and gastric acidity, while increasing mucosal resistance as evidenced by increased levels of gastric glutathione and reduced activity of alkaline phosphatase.^[38]

In the indomethacin-induced ulcer model, the extract (200 and 400 mg/kg) significantly protected against gastric mucosal damage, with the 400 mg/kg dose providing 60.94% protection, close to that of omeprazole (70.61%). The protective activity is due to the strong hydroxyl radical scavenging and lipid peroxidation inhibition, and the presence of bioactive compounds such as flavonoids, tannins, phenols, saponins, and caffeic acid. These compounds can stimulate the secretion of mucus and prostaglandins, and inhibit oxidative stress. The extract lacks acute and short-term toxicity, thus is safe and has potential as a natural gastroprotective and antiulcer agent.^[39]

10. Anti-Diarrhoeal Activity

The antidiarrhoeal activity of whole-plant extracts of *Cardiospermum halicacabum* was evaluated using experimental rat models, with the use of petroleum ether, alcoholic and aqueous extracts. Acute toxicity studies showed the absence of lethal effects at a dose of 2000 mg/kg, which indicated a positive safety profile. At a dose of 400 mg/kg, oral administration of the three extracts significantly reduced fecal output in castor oil-induced diarrhea ($P < 0.01$), reduced intestinal fluid accumulation in prostaglandin E2-induced enteropooling, and prevented gastrointestinal transit in the charcoal meal test. Phytochemical analysis indicated the presence of sterols, tannins, flavonoids, saponins, carbohydrates, and triterpenes, which may contribute to the

antidiarrhoeal activity. These findings provide scientific evidence for the use of *Cardiospermum halicacabum* in the treatment of diarrheal diseases.^[40]

11. Hepatoprotective Activity

The ethanolic extract of *Cardiospermum halicacabum* (ECH) showed significant hepatoprotective activity against CCl₄-induced hepatotoxicity in Wistar rats. The hepatoprotection was evident by the normalization of disrupted serum parameters (AST, ALT, ALP, bilirubin, and total protein), reduction of liver lipid peroxidation ($P \leq 0.05$) and improvement of antioxidant levels. Histopathological analysis also supported the reduction of liver damage and DNA damage, similar to that of standard drug silymarin.^[41]

12. Anxiolytic Activity

The ethanolic root extract of *Cardiospermum halicacabum* showed significant anxiolytic activity in mice using the elevated plus-maze (EPM) and light-dark transition models. Among the nineteen master fractions, MF-14, MF-16, and MF-17 (10-30 mg/kg) caused significant increases in open arm entries and time spent in the light compartment, reaching a level of efficacy equivalent to that of diazepam (1 mg/kg). These fractions also caused a reduction in behaviors reflecting anxiety, such as closed arm preference and dark compartment preference. The active anxiolytic principle was separated from MF-14 and found to be cardiospermin, a cyanogenic glucoside, which is responsible for the use of roots in the treatment of anxiety and other CNS disorders.^[42]

13. Anti-Viral Activity

Plant bioactive compounds of *Cardiospermum halicacabum* were isolated using various solvents, and the methanolic extract with eleven compounds exhibited strong anti-HBV and anti-HIV effects. The methanolic extract inhibited the hepatitis B surface antigen (HBsAg) by 79% and HIV-1 reverse transcriptase by 91%, as measured by ELISA and reverse transcription assays, respectively. Molecular docking studies also revealed that benzene dicarboxylic acid had strong binding affinities to HBV and HIV receptors with binding scores of -4.71 and -4.85, respectively, suggesting the potential use of this compound in the treatment of HBV and HIV dual infections.^[43]

14. Anti-Pyretic Activity

The ethanol and n-hexane extracts of *Cardiospermum halicacabum* whole plant, given orally at a dose of 400 mg/kg, showed potent antipyretic effects in yeast-induced fever in rats. The ethanol extract caused a dose-dependent reduction in fever at 100, 200, and 400 mg/kg, which was similar to paracetamol at 100 mg/kg. Both simultaneous and delayed treatments with the extract were effective, while the aqueous extract caused minimal activity.^[44]

15. Wound Healing Activity

The ethanolic leaf extract of *Cardiospermum halicacabum* (Sapindaceae) showed marked wound-healing potential in excision wound models using Wistar rats. Ointment preparations with 10% and 20% (w/w) concentrations of the plant extract significantly accelerated wound contraction and reduced the time for epithelialization compared to the control and povidone-iodine-treated groups. The wound-healing potential of the plant is due to its phytoconstituents, such as alkaloids, flavonoids, saponins, tannins, steroids, and glycosides, which could have a positive effect on collagen synthesis.^[45]

16. Anti-Arthritic Activity

The ethanolic leaf extract of *Cardiospermum halicacabum* (CEE) showed significant anti-arthritic effects in a rat model of arthritis induced by Freund's Complete Adjuvant (FCA). The anti-arthritic effect was evident as a dose-dependent reduction in paw edema, with highly significant inhibition ($P < 0.001$) at 250 mg/kg, comparable to the anti-arthritic drug indomethacin (10 mg/kg). Moreover, the extract also showed improvement in body weight and hematological abnormalities caused by arthritis, including the normalization of hemoglobin level, red blood cell count, and erythrocyte sedimentation rate, while significantly reducing the elevated white blood cell count. These findings indicate that CEE has the potential to reduce both inflammatory and systemic manifestations of adjuvant-induced arthritis, and thus may be a useful therapeutic agent in the treatment of rheumatoid arthritis.^[46]

17. Anti-Parasitic Activity

The aqueous and alcoholic extracts of *Cardiospermum halicacabum* exhibited significant *in vitro* antiparasitic activity against third-stage larvae of *Strongyloides stercoralis* (1,000 larvae/ml). At 2,000 µg/ml, the alcoholic extract induced complete larval immobilization within 48 hours, while the aqueous extract achieved the same effect within 72 hours. In comparison, ivermectin (250 µg/ml) required 72–144 hours and piperazine (2,000 µg/ml) more than 7 days to produce comparable non-motility. The marked reduction in larval viability over a 7-day period highlights the potent anthelmintic potential of the plant extracts and supports further investigation into their active constituents and mechanisms of action.^[47]

18. Anti-Filarial Activity

The antifilarial activity of *Cardiospermum halicacabum* has been evaluated *in vitro* against adult worms and microfilariae of *Brugia pahangi*. The aqueous extract at concentrations >500 µg/ml significantly reduced adult worm motility within 24 hours and decreased microfilarial release in a concentration and time-dependent manner, demonstrating direct macrofilaricidal activity. The ethanol extract (2 mg/ml) inhibited adult

worm motility and microfilarial release, while 500 µg/ml rapidly reduced microfilarial motility by day 2. Overall, the extracts exhibited dose-dependent macrofilaricidal and microfilaricidal effects, likely attributed to bioactive constituents such as flavonoids, saponins, and other phenolic compounds that may interfere with parasite metabolism and structural integrity. These findings support the traditional use of the plant in parasitic infections and highlight its potential as a source of novel antifilarial agents.^[48]

19. Fertility In Male Rats

The aqueous leaf extract of *Cardiospermum halicacabum* (given orally at 100 and 200 mg/kg for 30 days) caused a significant and dose-dependent increase in both sperm count and motility in the caput and cauda parts of the epididymis, together with a marked increase in serum testosterone. The treatment enhanced male fertility, as evidenced by the increase in the number of pregnant females, implantation sites, and live fetuses, together with a decrease in the number of resorption sites. There were no significant changes in the weights of the reproductive organs and serum cholesterol levels. The extract was non-reno-toxic and had hepatoprotective properties. The results indicate that the aqueous leaf extract of *Cardiospermum halicacabum* has a potential role in the enhancement of male fertility mainly by the induction of spermatogenesis and the consequent increase in androgen secretion.^[49]

20. Neuroprotective Activity

Extracts of *Cardiospermum halicacabum* aerial parts and seeds exhibited significant anti-tyrosinase ($IC_{50} = 10.8$ mg/mL) and butyrylcholinesterase inhibitory activity ($IC_{50} = 57.9$ mg/mL), along with antioxidant effects attributed to flavonoids such as apigenin and luteolin and fatty acids including oleic acid, supporting their potential role in neurological disorder management.^[50]

The methanolic extract of *Cardiospermum halicacabum* (MCH) was evaluated for neuroprotective activity against scopolamine (0.5 mg/kg, i.p.)-induced amnesia in Swiss albino mice. MCH was administered orally at doses of 50, 100, and 200 mg/kg for eight consecutive days, and cognitive performance was assessed using the elevated plus maze and passive avoidance paradigms, with Piracetam (200 mg/kg, i.p.) as the standard. The extract significantly improved learning and memory in a dose-dependent manner, with 200 mg/kg showing effects comparable to piracetam, and markedly reduced whole-brain acetylcholinesterase activity, indicating enhanced cholinergic transmission. Acute toxicity studies confirmed safety up to 800 mg/kg. The observed neuroprotective effect may be attributed to its anticholinesterase, antioxidant, and anti-inflammatory properties, suggesting its potential as a memory-restorative agent in the management of dementia.^[51]

Table 3: The pharmacological activities of *Cardiospermum halicacabum*.

Sl. No	Activity	Plant Part Used	Type of Extract	Method/Model	References
1	Anticancer activity	Seeds	n-Hexane extract	Cytotoxicity assay on cancer cell lines	[26]
2	Anticancer activity	Leaves	Chloroform, ethanolic, ethyl acetate extracts	EAC cells, HepG2 cell line	[27,28]
3	Antioxidant activity	Aerial parts	Ethanolic extract	DPPH, ABTS and free radical scavenging assays	[29]
4	Antidiabetic activity	Leaves	Ethanolic extract	STZ-induced diabetic rats	[30]
5	Antidiabetic activity	Isolated flavonoid	Chrysoeriol	STZ-induced diabetic rats, molecular docking	[31]
6	Anticonvulsant activity	Roots	Alcoholic extract	PTZ, MES and seizure models in mice	[32]
7	Anti-inflammatory activity	Whole plant	Ethanolic extract	LPS-stimulated cells and carrageenan paw edema	[33,34]
8	Antibacterial activity	Leaves and stems	Ethanolic, acetone, benzene, chloroform, aqueous extracts	Disc diffusion antibacterial assay	[35]
9	Antifungal activity	Whole plant	Whole plant extract	Antifungal assay against <i>T. rubrum</i>	[36]
10	Analgesic activity	Aerial parts	Petroleum ether, chloroform, ethyl acetate, ethanol extracts	Thermal stimulus model in mice	[37]
11	Antiulcer activity	Aerial parts	Ethanol extract	Pylorus ligation ulcer model	[37]
12	Antiulcer activity	Whole plant	Ethanol extract	Ethanol-induced ulcer model	[38]
13	Antiulcer activity	Whole plant	Ethanol extract	Indomethacin-induced ulcer model	[39]
14	Anti-diarrhoeal activity	Whole plant	Petroleum ether, alcoholic, aqueous extracts	Castor oil-induced diarrhea model	[40]
15	Hepatoprotective activity	Whole plant	Ethanolic extract	CCl ₄ -induced hepatotoxicity in rats	[41]
16	Anxiolytic activity	Roots	Ethanolic extract and fractions	Elevated plus maze and light-dark model	[42]
17	Antiviral activity	Whole plant	Methanolic extract	Anti-HBV and anti-HIV assays	[43]
18	Antipyretic activity	Whole plant	Ethanol and n-hexane extracts	Yeast-induced pyrexia model	[44]
19	Wound healing activity	Leaves	Ethanolic extract ointment	Excision wound model in rats	[45]
20	Antiarthritic activity	Leaves	Ethanolic extract	FCA-induced arthritis model	[46]
21	Antiparasitic activity	Whole plant	Aqueous and alcoholic extracts	<i>Strongyloides stercoralis</i> assay	[47]
22	Antifilarial activity	Whole plant	Aqueous and ethanol extracts	<i>Brugia pahangi</i> assay	[48]
23	Fertility enhancement in male rats	Leaves	Aqueous extract	Sperm motility and sperm count in both cauda and caput regions in male rats	[49]
24	Neuroprotective activity	Aerial parts and seeds	Extracts	Anti-tyrosinase and cholinesterase assays	[50]
25	Neuroprotective activity	Whole plant	Methanolic extract	Scopolamine-induced amnesia model	[51]

CONCLUSION

Cardiospermum halicacabum Linn. is a versatile medicinal herb with a wide range of ethnomedicinal uses and pharmacological properties that have been scientifically validated. This herb contains a wide range of bioactive phytoconstituents, including flavonoids, phenolics, saponins, and triterpenoids, which contribute to its wide range of pharmacological properties. Preclinical studies have shown strong scientific evidence for its traditional use in the treatment of inflammatory diseases, metabolic disorders, infections, neurological disorders, gastrointestinal problems, and parasitic diseases. In addition, its antioxidant and cytoprotective actions also add to its therapeutic potential.

Despite the promising experimental findings, most of the existing studies are limited to in vitro and animal studies. Therefore, clinical trials, standardization of extracts, toxicity studies, and mechanism of action studies are required to determine its safety, efficacy, and dosage regimens in human patients. Future studies focusing on the isolation of active principles, understanding the molecular mechanisms, and developing formulation technologies may help to integrate *C. halicacabum* into conventional evidence-based medicine. In summary, this ancient herb has a wide range of potential as a natural, inexpensive, and versatile therapeutic agent.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This work does not contain any studies involving human and animal subjects.

CONFLICT OF INTEREST

The authors of this work declare that they have no conflicts of interest.

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