



A Comprehensive Review on *Cardiospermum halicacabum*

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Abstract

Medicinal plants are natural sources of bioactive phytochemical constituents that can be utilized to treat a variety of ailments due to the marked physiological effects they have on the human body. India, with its diverse ethnic groups and unique biodiversity, has a centuries-old ethnobotanical history for health promotion and treatment of illness. Among the medicinal herbs, the plant *Cardiospermum halicacabum* belonging to the family Sapindaceae is a climber with inflated fruits and seeds with a white heart-shaped pattern. Alcohols, phenols, alkynes, flavonoids, alkanes, and aliphatic esters are the major phytochemical components present in this plant. The phytochemical examination revealed that the herb contains terpenoids, flavonoids, tannins, proteins, saponin, glycosides, carbohydrates, volatile esters, and fatty acids. *Cardiospermum halicacabum* has been demonstrated to exhibit anti-oxidant, anti-viral, anti-ulcer, anti-diabetic, anti-convulsant, antipyretic, anxiolytic, anti-cancer, anti-bacterial, anti-arthritic, anti-fungal, anti-parasitic and fertility activities. The decoction of this plant is used in the treatment of dysentery, diarrhea, cold, asthma and pertussis. Various traditional uses of the plant include its usage as a refrigerant, emetic, stomachic, diuretic, laxative, wound healing and in treating earache. This review summarizes the wide range of phytochemical constituents, pharmacological activities along with microscopical, macroscopical characteristics and traditional uses of *Cardiospermum halicacabum*.

Keywords: Anti-Oxidant, Anti-Viral, Anti-Filarial, Adulticidal, Sapindaceae

1. Introduction

Drugs from plant sources have been used to treat different ailments in the conventional system of medicines. Around 75-80% of the world population mainly depend on herbal medicines. Most of the plants have medicinal value and were examined for new and effective compounds. The various phytochemicals in plants play a major role in the treatment of life-threatening diseases. *Cardiospermum* is derived from the Latin word “cardio”, which means heart, and “sperma”, which means seed, and refers to the seed’s white heart-shaped pattern. The name *halicacabum* derives from the Latin word “halicacabus”, which refers to a plant with inflated

fruits¹. The plant *Cardiospermum halicacabum* belongs to the family Sapindaceae commonly known as balloon vine (Table 1). It is a climber widely distributed in tropics and subtropics. Balloon-vine is native to the Bermudas, Florida, and Texas. This plant is found in tropical forests of East Africa and is distributed in Africa and Asia and found throughout India. It is a woody perennial, branching, herbaceous climber which grows up to 10 feet. The various parts of the plant have been used to treat stiffness of limbs, snake bite, and rheumatism. In Ayurveda and folk medicine, this plant is used to treat fever, lumbago, and earache. It is also used as stomachic, rubefacient, and diuretic². It possesses pharmacological activities such as antioxidant, anti-diabetic, anti-viral, anti-convulsant, anti-diarrheal, anti-cancer, anti-bacterial, and anti-fungal. This herb is

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useful for the production of commercial drugs because of the existence of constituents such as beta-sitosterol along with its D-glucoside, amino acids, oxalic acid, saponins, quebrachitol, oleic acid, eicosonic acid, erucic acid, octanoic acid, n-hexadecenoic acid, and rich in triterpenoid³. *Cardiospermum halicacabum* is used in unique systems of medication along with Homeopathy, Unani, and Ayurveda medicine. The presence of several phytoconstituents such as flavonoids, tannins, and alkaloids were detected during the preliminary phytochemical analysis. In extracts, the concentration of phenols ranged from 29.697 ± 0.232 to 187.372 ± 0.615 mg pyrogallol equivalent/g, and the concentration of flavonoids ranged from 27.833 ± 0.412 to 139.261 ± 0.412 mg quercetin equivalent/g⁴. This plant also has cortisone effects and studies were conducted for its therapeutic efficacy. In the Southern part of India, *C. halicacabum* is used as a green vegetable. The presence of saponins results in foam formation when agitated with water and hence, it is used as hair detergent and soap for laundry. Each part of the plant is beneficial and is used as food and for the treatment of specific diseases. The complex chemical structure and wide range of applications of this plant have captured the interest of researchers who have verified the validity and safety of its utilization in the treatment of several diseases using modern methodologies⁵. The medicinal plant *Cardiospermum halicacabum* is known as 'karnasphota' in the traditional system of medicine (Table 2). In Ayurvedic pharmacopoeia, the root of this plant is officially included due to its medicinal uses in *jvara*, *kusta*, *ksaya*, and *sandhivata*⁶.

2. Description

Table 1. Scientific classification

Kingdom	Plantae
Subkingdom	Viridiplantae
Infrakingdom	Streptophyta
Superdivision	Embryophyta
Division	Tracheophyta
Subdivision	Spermatophytina
Class	Magnoliopsida
Superorder	Rosanae
Order	Sapindales
Family	Sapindaceae
Genus	<i>Cardiospermum</i>
Species	<i>halicacabum</i>

Table 2. Vernacular names

English	Balloon Vein, Heart's Pea
Sanskrit	Indravalli, Sakralata
Hindi	Kapalhoti, Kanphuti
Bengali	Lataphatkari
Marathi	Kakumardanika, Shibjal
Guajarati	Ghisdoda
Telugu	Ekkudutige, Buddakakara
Tamil	Mudukattan
Kannada	Agniballi
Malayalam	Karuttakunni

3. Morphology

The plant *Cardiospermum halicacabum* is an herbaceous vine with bi-ternate leaves. The leaflets are ovate-lanceolate in shape with a glabrous texture, a smooth surface, and dentate margins. The leaf is 3-5 cm long and 1.5-2 cm width. The stem of this plant is green in colour with 0.2-0.3 cm width. The petiole is about 1.5-2.5 cm. tetramerous irregular flowers with 2+2 sepals and 2+2 equal petals and 8 unequal stamens. Tricarpellary ovary and each carpel have one ovule. Trifid stigma and globose fruits with winged bloated capsule (Figures 1 and 2).



Figure 1. *Cardiospermum halicacabum* plant.

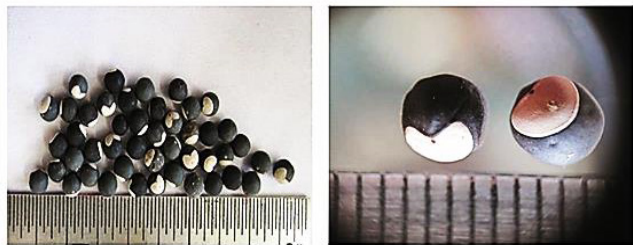


Figure 2. *Cardiospermum halicacabum* seeds.

4. Microscopy

4.1 Microscopy of Leaf

The leaf has a prominent midrib that projects adaxially and abaxially, as well as a thin dorsiventral lamina. The adaxial portion of the midrib is thick and pyramid-like, while the abaxial portion is semicircular with an undulating outline. Midrib is about 350 mm thickness. The thickness of the lamina is about 60-70 mm. The adaxial epidermis is narrow and cylindrical, whereas the abaxial epidermal cells are thin and elliptical.

4.2 Microscopy of Stem

Sectional view reveals pentagonal stem with continuous epidermis layers that consists of spindle shaped cells with prominent cuticle. Appearance of darkly strained cells. The parenchyma tissues are wider, and cells are enlarged within the ridges. Thick sclerenchyma tissues with several layers of small cells running all around the stem. The vascular cylinder constitutes of wider cylinder of phloem enclosing inner xylem cylinder. Thick walled and lignified fibers with wide lumen.

4.3 Powder Microscopy

The microscopical evaluation of powder exhibited various inclusions. Presence of capitate type of glandular trichomes with one celled stalk and glandular body with 2 upper and 2 lower cells. Unicellular, unbranched, and straight non-glandular trichomes. Lamina is fragmentary and vein-terminations are visible. Various types of xylem elements are present in the powder, most common elements are xylem parenchyma, xylem fibers and vessel elements. Parenchyma cells are long, scale like, thin-walled and their main function is storage. Wide and narrow fibers are in the powder. Primary xylem has close spiral lateral, wall thickenings, whereas secondary xylem has dense, multiseriate lateral wall pits⁶.

5. Geography

Cardiospermum halicacabum, also known as balloon vine, is a genus of 17 shrub, subshrub, climber, and erect species. Most of the species occur in tropical and subtropical regions and few are arid-adapted. These species are distributed in Brazil, Argentina, Paraguay, and Mexico. *Cardiospermum halicacabum* is distributed in Europe and Asia. This plant is regarded as being native in South and Central America. This plant is described as either alien or native in Asia. It is present in China and India. The plant is widely used for medicinal purposes and is considered as non-native in India. In China, this plant is considered as common weed seen in grasslands, forest areas, and cultivated areas⁷.

6. Phyto-chemical Constituents

The studies conducted on the ethanolic leaf extract of plant *Cardiospermum halicacabum* indicated the presence of alcohols, phenols, alkynes, flavonoids, alkanes, and aliphatic ester by FT-IR spectrum. Twenty-four compounds have been analyzed by GC-MS. Cyclohexane-1, caryophyllene, neophytadiene, 4, 5-triol-3-one-1-carboxylic acid, phytol, and benzene acetic acid were the major constituents identified. Various other chemical constituents present in the plant are 1-hydrotetradecane, 11-trimethyl-8-methylene, N-methyl tomatidine, 3-methylbutanamide, Phenylethyl alcohol, hexadecane, nonadecane, heptadecane, benzene acetic acid, 14-methyl-8-hexadecyne, 5-dinitrobenzene, hexadecenoic acid, and octadecanoic acid⁸. Another study conducted using the *Cardiospermum halicacabum* indicated the presence of carbohydrates, proteins, tannins, saponins, flavonoids, lipids, alkaloids, steroids, and glycosides. Many active constituents in *C. halicacabum* were identified by gaschromatography-massspectrometryanalysis, including 1, 2, 4-trioxolane-2-octanic acid, 2-[9-octadecenyloxy], ethanol, 5-octyl-methyl ester, ricinolenic acid, apigenin-7-o-glucuronide, 11-octadecenoic acid, methyl ester, -2-octanic acid, 9-octadecenoic acid, oleic acid, 1, 2, 3-propanetriyl ester, β -sitosterol- β -o-galactoside, β -sitosterol, chrysoeriol-7-o-glucuronide, stearic acid, linoleic acid, arachidic acid and luteolin-7-o-glucuronide⁹. Seed oil was extracted with petroleum ether and GC-MS was used to analyze it. There were about 27 different components in the oil. Octanoic acid (4.57%), n-hexa

decanoic acid, erucic acid (43%), eicosanic acid (12%) and oleic acid (30%) are the primary ingredients of the oil¹⁰.

7. Pharmacological Activity

The plant *Cardiospermum halicacabum* exhibited anti-oxidant, anti-viral, anti-ulcer activity, anti-diabetic, anti-convulsant, antipyretic, anxiolytic, anti-cancer, anti-bacterial, anti-arthritic, anti-fungal, antiparasitic, anti-diarrheal, adulticidal, anti-filarial, anti-malarial, anti-inflammatory, anti-sickling, and fertility activities (Figure 3).

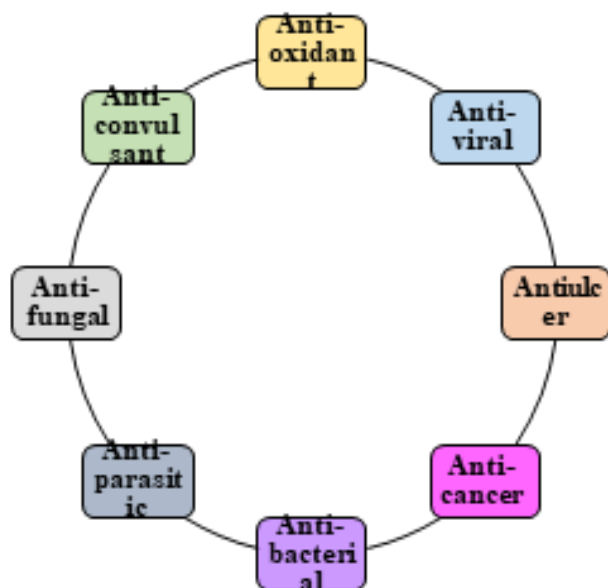


Figure 3. Pharmacological activities of *C. halicacabum*.

7.1 Anti-Oxidant Activity

Chronic disorders including cancer, arteriosclerosis, rheumatism, and other age-related concerns have all been linked to reactive oxygen species. The anti-oxidant property of the plant *Cardiospermum halicacabum* was investigated using its methanol extract by various *in vitro* methods such as the superoxide nitric oxide radical scavenging, β -carotene-linoleate model system, reducing power, 1, 1-diphenyl-2-picrylhydrazyl (DPPH), and iron ion chelating activity. The methanolic extract revealed significant inhibitory activity towards β -carotene-linoleate model system and demonstrated a moderate concentration dependent inhibition of DPPH radical. This extract also possesses reducing power, nitric oxide scavenging activity, superoxide scavenging ability, and

ferrous ion chelating ability which in turn revealed its multiple anti-oxidant activity. The result obtained in these models indicated the antioxidant property of the methanolic extract of *Cardiospermum halicacabum*¹¹. Another study was conducted out using chloroform and ethanolic extracts of the plant. The nitric oxide scavenging, DPPH, hydrogen peroxide scavenging, reducing power assay, ABTS, and superoxide scavenging activity were the free radical models used for screening the anti-oxidant activity. The result concluded that the chloroform extract of the plant possesses notable anti-oxidant properties when compared to the ethanol extract¹².

7.2 Anti-Viral Activity

Researchers have reported the plant bioactive compounds extracted using various solvents were analyzed for anti-HBV and anti-HIV, activity. All HBsAg (79%) and HIV-RT (91%) were suppressed by extract using methanol which contains 11 constituents. According to the recommendations of the earlier research, a Reverse Transcriptase assay was utilized to test the inhibitory activity of the extracts on HIV-1 reverse transcriptase. The anti-HBsAg activity of the extract was assessed using an Enzyme-Linked Immunosorbent Assay (ELISA). Among the constituents, benzene dicarboxylic acid has a docking score of -4.71 against HBV receptor and -4.85 against HIV receptor. The findings suggested that *C. halicacabum* bioactive principles could be used to develop new HBV and HIV co-infection-controlling therapies¹³.

7.3 Anti-Ulcer Activity

An ulcer is a severing of the stomach or duodenum mucosa's continuity to pepsin and gastric acid. It is caused by an imbalance between the mucosal protective and aggressive mechanisms, or by the combination of several endogenous factors such as hydrochloric acid and pepsin, as well as exogenous factors such as tobacco, alcohol, NSAIDs, and *Helicobacter pylori* infection. The anti-ulcer activity of the drug was evaluated using the ethanolic extract of *Cardiospermum halicacabum* against Indomethacin-induced gastric ulcer model in male Wistar rats, 200 and 400 mg/kg of ethanolic extract of *Cardiospermum halicacabum* were given orally 30 mins before inducing ulcer. The standard drug used was omeprazole 10 mg/kg/day by oral administration. The anti-ulcer activity was determined by calculating the

ulcer index in both the test and the standard drug-treated groups. In the ulcer-induced models, ethanolic extract demonstrated a significant dose-dependent reduction in the extent of gastric mucosal damage. This study suggested that the antiulcer activity of plant may be due to the existence of active substances such as phenols, flavonoids, saponins, tannins, phenols, and caffeic acid¹⁴.

7.4 Anti-Diabetic Activity

Diabetes mellitus is a complex condition marked by significant loss of homeostasis of glucose along with disruptions in carbohydrate, protein, and lipid metabolism caused by defects in production of insulin, action of insulin, or both. The anti-diabetic activity or the glucose uptake was investigated using the n-hexane, aqueous, methanol, and ethanol leaf extracts of the plant. Using a standard *in vitro* procedure, the leaf extracts were tested for their ability to inhibit glucose utilization. In this experiment, 1 ml of crude extracts in 1% CMC and 1 ml of 0.15M NaCl with 0.22M D-glucose were added to a dialysis tube. The dialysis tube has been closed on both ends before being placed in a centrifuge tube of 50 ml containing 45 ml of 0.15M NaCl. The dialysis tubes were kept at room temperature by being shaken on an orbital shaker. At predetermined time intervals, the amount of glucose that entering the external solution was measured. The results revealed that among the various extracts of leaf, the methanol extract at a concentration of 50 g plant extract/liter was observed to be more active than the other extracts, with the lowest mean glucose levels of 201.69 mg/dl. Thus, study concluded that extract using methanol exhibited a strong inhibitory effect on glucose uptake¹⁵.

7.5 Anti-Convulsant Activity

Epilepsy is a common neurological disorder and the anticonvulsant activity of the plant *Cardiospermum halicacabum* was investigated on a pharmacological basis using its alcoholic root extract and the mechanisms were studied. Various murine models were used for this study. Before testing, mice (male Swiss albino) were given orally at doses - 300, 100, and 30 mg/kg of the plant's root extract. After two days of the administration, the levels of monoamines in the brain were measured. At a dose of 100 and 300 mg/kg, the alcoholic root extract of *Cardiospermum halicacabum* slowed down the emergence

of clonus and tonus in convulsions induced by isoniazid, pentylenetetrazol, and picrotoxin. It also decreased the extension of tonic hind limb as compared to the vehicle control in the maximal electroshock model. On administration of higher doses, i.e., 900 mg/kg, there was no evidence of substantial motor toxicity. An increase in GABAergic activity in C+ (in the cerebellum) and C- (except cerebellum) was explained by HPLC analysis of brain monoamines. The findings demonstrated that the alcoholic root extract had anticonvulsant properties while causing minimal motor damage. Additional research is required to understand exact mechanism¹⁶.

7.6 Anti-Pyretic Activity

Cardiospermum halicacabum has traditionally been used to treat fever. The anti-pyretic property was demonstrated using the alcohol, n-hexane, and aqueous extracts of this plant. The anti-pyretic activity of the various extracts was determined against yeast-induced pyrogenesis in adult male Wistar rats. Paracetamol was used as standard and Tween80 as control. Plant extracts are orally administered. At 400 mg, all the extracts demonstrated varying degrees of anti-pyretic activity. The most effective extract was alcohol, which was followed by n-hexane. The anti-pyretic activity was significantly greater at the higher dose of 400 mg/kg than at the lower dose of 200 mg/kg. At 2 hours after the drug treatment, the efficacy of paracetamol 100 mg/kg was similar to that of 400 mg/kg extract. Results suggested that all the extracts of *Cardiospermum halicacabum* possess anti-pyretic properties without any known adverse effects¹⁷.

7.7 Anxiolytic Activity

The anxiolytic or anti-anxiety effects of the plant *Cardiospermum halicacabum* were studied using the alcoholic and aqueous root extracts in mice. A 100 or 300 mg/kg of the aqueous and alcoholic extract of the plant were administered orally to the mice before 1 hour of subjecting the mice to various models of anxiety. Elevated Plus Maze (EPM), Open Field Test (OFT), and Light-Dark Model (LDM) were the models used for studying the anti-anxiety effects. Researchers observed that there is an increase in time spent in the open arm and total locomotion time in animals treated with alcoholic and aqueous extracts in the elevated plus-maze model. In the light-dark model, these extracts increased the time

spent in the light compartment, whereas in the open field test, these extracts increased the time spent in the central compartment. These findings imply that *Cardiospermum halicacabum* alcoholic and aqueous extracts have anti-anxiety properties¹⁸.

7.8 Anti-Cancer Activity

Cancer is the uncontrolled proliferation of genetically altered cells that is a major health problem. Despite the numerous strategies used to deal with those conditions, herbal drug treatments are in excessive call for because of their vast outcomes as immune enhancers and healing retailers and less aspect outcomes. The examiner turned into undertaken to assess the cytotoxic impact of seeds of *C. halicacabum* primarily based totally on conventional claims. Various extracts of *C. halicacabum* seeds have been acquired the use of an Soxhlet extractor. The cytotoxic impact of numerous extracts on HCT-15 colon carcinoma, MCF-7 breast carcinoma, HT-29, and SK-MEL-2 pores skin carcinoma turned into evaluated using Sulforhodamine B colorimetric assay and the standard drug used is Doxorubicin. The current study discovered that n-hexane extract of *Cardiospermum halicacabum* seeds had a powerful cytotoxic interest towards the MCF-7 breast most cancers line with a 50% increase inhibition value (GI50) of 12.8 g/ml, however that different extracts had less effects in different examined cell lines. The outcomes discovered the capability of the seeds with the very best extractive yield as an anti-cancer agent¹⁹. The ethanol and chloroform extract of the plant turned into examined for anti-cancer property. Against the Ehrlich Ascites Carcinoma cell line, *in vitro* cytotoxic experiments inclusive of trypan blue dye exclusion and MTT assays have been performed. The chloroform extract of *Cardiospermum halicacabum* has significantly higher anti-cancer activity than the ethanolic extract, according to the findings of this study¹².

7.9 Anti-Bacterial Activity

The antibacterial screening was carried out using the crude extracts of stem and leaf of *C. halicacabum* in different solvents against selected gram-negative and gram-positive bacteria. The screening was performed using alcohol, chloroform, acetone, benzene, and aqueous extracts of leaf and stem. Various cultures of stock such as *Bacillus subtilis*, *Citrobacter freundii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*,

Streptococcus aureus, and *Salmonella typhi* used. Nutrient agar and nutrient broth were the growth media. Disc diffusion method was employed for the evaluation of antibacterial efficacy. All of extracts had varying degrees of inhibitory potential against all the bacteria tested. The extracts using acetone and chloroform of the leaf showed greater inhibitory activity against *Salmonella typhi* and *Streptococcus subtilis*. The maximum inhibitory action was shown by acetone extracts of the stem against *Salmonella typhi* whereas the moderate inhibitory action was shown by benzene extracts of the stem against *Escherichia coli*²⁰. Another study conducted revealed that the ethanolic leaf extract of the plant *Cardiospermum halicacabum* screened for the antibacterial activity against the different strains of bacteria showed minimum inhibitory concentration ranging from 80 to 125µg of extract. The extract was found to be effective against *Staphylococcus aureus*, *Escherichia coli*, and *Aeromonas hydrophila*, a fish pathogen. Some of the multidrug-resistant bacteria examined showed moderate efficacy against the ethanolic extract of *Cardiospermum halicacabum*⁸.

7.10 Anti-Arthritic Activity

Rheumatoid arthritis is an inflammatory disease resulting in the progressive destruction of the articular and periarticular structure. It is known as leading source of morbidity worldwide. The ethanolic extract of the leaves *Cardiospermum halicacabum* was used to study the anti-arthritic effect. The extract was orally administered to rats at a dose of 125 mg/kg and 250 mg/kg on arthritis induced by FCA (Freund's complete adjuvant). Various haematological measures such as haemoglobin (Hb) content, White Blood Cell Count (WBC), total Red Blood Cell (RBC) count, and erythrocyte sedimentation rate are used to evaluate the treatment (ESR). The extract decreased FCA-induced arthritis in a dosage-dependent manner, with the impact being more significant (($p < 0.001$) with a 250 mg/kg dose and standard drug used is Indomethacin (10 mg/kg). When compared to FCA-induced arthritic animals, extract administration improved body weight considerably. The results obtained concluded that the ethanolic extract possesses anti-arthritic properties²¹.

7.11 Anti-Fungal Activity

Dermatophytosis is an infection caused by fungi that affects the stratum corneum, nails and hair. It is a major public health problem because of its increased frequency

and accompanying morbidity. The pathogens responsible for this infection are *Trichophyton mentagrophytes* and *Trichophyton rubrum*. The extract *Cardiospermum halicacabum* was evaluated for antifungal activity against *T. rubrum*, implying that a possible interaction with Hsp90 is significant in susceptibility and pathogenicity. Varying concentrations of *C. halicacabum* (from 500 to 31.25 g) were tested *in vitro* against *T. rubrum* isolate, the interaction between several active chemicals of *C. halicacabum* and the fungal Hsp90 was investigated computationally. The result revealed distinct antifungal activity at the highest concentrations of the plant extract (250 and 500 µg). The molecules like rutin and luteolin were found *in silico* as the most potential Hsp90 inhibitors among all tested compounds of *C. halicacabum*. Individual assessment of rutin and luteolin were carried out for their anti-fungal activity. Rutin and luteolin individually displays anti-fungal effect but lesser than that of the total plant extracts. This study indicates that *C. halicacabum* has a substantial fungistatic impact against *T. rubrum*, demonstrating its pharmacological activity in the treatment of dermatophytosis. The substances rutin and luteolin are Hsp90 interactors, which explains the fungistatic action²². A study conducted using the ethanolic extract of *Cardiospermum halicacabum* revealed anti-fungal activity against the *Candida albicans*. The Minimum Inhibitory Concentration for *Candida albicans* was 190 µg extract/ml⁸.

7.12 Anti-Parasitic Activity

Strongyloides stercoralis is a parasitic worm that can infect humans. In a human host, it can live for years and inflict a deadly illness. Anti-parasitic drugs must therefore be used effectively and promptly. *In vitro* testing was performed on extracts from the medicinal herb *Cardiospermum halicacabum* against *Strongyloides stercoralis* third-stage larvae. Using the agar plate culture method, *S. stercoralis* larvae were generated from cultures of dog faeces. At 37 °C with 5 % CO₂, the larvae (1,000 larvae/ml) in phosphate buffer saline solutions were subjected to *C. halicacabum* alcoholic and aqueous extracts (2,000 µg/ml). The standard drug used was piperazine (2,000 µg/ml) and ivermectin (250 µg/ml). The survival of *Strongyloides* larvae was determined every day for 7 days based on their motility. When the larvae were exposed to piperazine, ivermectin, and *C. halicacabum* solutions, they were able to survive, but many of them were becoming immobile within 72 and 48 hours, after exposed to extracts of *C. halicacabum*,

whereas ivermectin took 72 to 144 hours and piperazine took more than 7 days. The results suggested that the plant *Cardiospermum halicacabum* decreased the viability of *S. stercoralis*²³.

7.13 Anti-Filarial Activity

Lymphatic Filariasis (LF) is a mosquito-borne worm infection that causes persistent and gradual oedema of the limbs and testis resulting in substantial deformity and impairment. In tropical and subtropical nations, it is still a major cause of irreversible impairment. Lymphatic dysfunction results from a long-term infestation with vector-borne filarial worms, leading to progressive, permanent inflammation of the breasts, limb, and genitals²⁴. Adult worms and microfilariae of *Brugia pahangi* were investigated *in vitro* using aqueous and ethanolic preparations of the *Cardiospermum halicacabum*. The motility of microfilariae, worms and microfilariae release from female worms were all evaluated daily with or without extracts in the culture medium. The MTT assay was used to test the vitality or damage to tissue of adult worms following 7 days of culture. Adult worm motility was reduced, and the sequence of microfilariae release from female worms was time and dose dependent. The ethanol extract reduced microfilariae motility quickly, and the aqueous extract of *C. halicacabum* had a weak but definite direct activity on *B. pahangi*, according to the findings²⁵.

7.14 Anti-Inflammatory Activity

Inflammation occurs when infectious microbes, viruses, or fungi infect the body, settle in specific tissues, and/or circulate in the bloodstream. It can also occur due to tissue damage, cell death, malignancy, degeneration, and ischemia. In most cases, both the innate and adaptive immune responses are associated with development of inflammation²⁶. The anti-inflammatory potency of the plant was investigated using ethanolic and aqueous extracts. The anti-inflammatory properties of ethanolic extract were tested in mice with carrageenan-induced paw oedema. Extract using ethanol prevented the development of paw oedema generated by Carrageenan in the anti-inflammatory testing and enhanced the activities of (glutathione peroxidase) GPx, (superoxidase dismutase) SOD and CAT (catalase) in the liver tissue. The findings suggested that ethanolic extract could act as a potential anti-inflammatory agent²⁷.

7.15 Anti-Diarrheal Activity

Diarrhoea is a common and serious issue in many tropical areas of the world, leading to 4-5 million fatalities per year. The aqueous and alcoholic leaf extract of the plant *Cardiospermum halicacabum* was used to investigate the anti-diarrheal effect in different models. Castor oil induced diarrhoea was used to test the anti-diarrheal efficacy. In experimental models, the extracts of *Cardiospermum halicacabum* lowered defecation rate and weight of moist faeces, including the charcoal meal propulsion through the digestive tract. This extract also decreased the volume of oedema in the intestine of the animals treated with drugs. The studies concluded that the extracts possess potential anti-diarrheal activity²⁸.

7.16 Fertility Activity

The fertility test was carried out using the aqueous extract of the plant *Cardiospermum halicacabum* on male rats. The aqueous extract was administered at a dose of 100 and 200 mg/kg body weight for about 30 days. This resulted in a rise that is dosage dependent in the count and mobility of sperms in caput and cauda regions. The serum testosterone level was also significantly increased in all the doses. The weight of the sex organs and the overall cholesterol level in serum was unchanged. The leaf extract (aqueous) enhanced the number of females inseminated, implantations, and survivable foetuses in pregnant females whereas decreasing the overall number of resorption sites. Despite the lack of evidence of renal toxicity, ALE was found to have a hepatoprotective effect. The study concluded that the aqueous leaf extract of *Cardiospermum halicacabum* was found to increase sperm concentration, motility, and testosterone, resulting in improved fertility²⁹.

7.17 Adulticidal Activity

Mosquitoes are carriers of a variety of diseases that afflict humans and animals all over the world. They are indeed the primary vectors of malaria, filariasis, dengue fever, schistosomiasis, yellow fever, Japanese Encephalitis (JE), and other diseases, leading to millions of fatalities each year. They can also induce allergic reactions including localized skin reactions. The repellent activity of *C. halicacabum* was evaluated using benzene, hexane, methanol, ethyl acetate and chloroform extracts against *Anopheles stephensi*, *Culex quinquefasciatus* and *Aedes aegypti*. The leaf crude preparations were administered in

the exposed area of the forearm, with ethanol as a control. The extracts protected against mosquito bites without causing an allergic reaction in the test subject, and the repellent action was found to be proportional to the strength of the extracts. All three mosquitoes were successfully repelled by the plant extract that was tested³⁰. The adulticidal activity of the plant *Cardiospermum halicacabum* was evaluated using the hexane, ethyl acetate, benzene, chloroform, and methanol extracts against *Anopheles stephensi*, *Culex quinquefasciatus* and *Aedes aegypti*. The WHO method was followed, and bioassay was carried out. After 24 hrs, the mortality of mosquitoes was observed. After the exposure time, adult mosquitoes showed signs of a moderately hazardous effect. The methanolic extract of the plant showed the highest rate of mortality when compared to the other extracts. The result expressed that the crude extract of the plant possessed excellent adulticidal property against all the three mosquitoes³¹.

7.18 Anti-Malarial Activity

The herb *Cardiospermum halicacabum*, which has traditionally been used to cure malaria symptoms in various regions was tested for anti-malarial efficacy *in vitro* and *in vivo*. The aqueous extract of *Cardiospermum halicacabum* was toxic to mice, with none surviving past the fourth day after oral dosing and no evidence of protection against *Plasmodium berghei* malaria. The study shows the possibility of inconsistencies between *in vitro* and *in vivo* plant-derived extract screening, as well as the importance of taking *in vitro* anti-plasmodial results into account³².

7.19 Anti-Sickling Activity

Cardiospermum halicacabum stems and leaves are employed traditional treatment of a variety of disorders, including angina, the common cold and various other diseases. The extracts of *C. halicacabum* created a considerable reversal of crenation in haemoglobin AA blood that had crenated in acidic citrate-dextrose saline. In the addition of the isolate of *C. halicacabum*, haemoglobin AS samples showed a reversal of sickling of RBCs to normal form. In the concentrations employed, the findings were found to be far superior to those achieved with testosterone propionate. At this time, it is unclear that the anti-sickling and anti-crenation actions reported were caused by the extract's direct impact on the

erythrocyte membrane or by the extract's oxygenation of the haemoglobin. Some of the chemical constituents are being isolated and once isolated, the compounds will be examined for anti-sickling properties once more³³.

8. Nutritional Value

Flame Emission Spectroscopy was used to examine the macro element analysis of *Cardiospermum halicacabum*, which included analyses of sodium, potassium, and calcium. Using the Atomic Absorption Spectroscopy method, the trace element analysis of *Cardiospermum halicacabum* was quantified. Additional components were also analysed. Extracts include a wide range of micro and macronutrients that can be used as a nutritional supplement to improve our wellbeing and immunity³⁴.

9. Traditional Uses

The plant *Cardiospermum halicacabum* is used in treating many disorders. Diarrhea and dysentery are relieved by decoction of the leaves. Its juice can be used to help with hemorrhoids. It helps in treating various respiratory disorders. The plant decoction is used for colds, asthma, and pertussis. The roots are used to treat renal disorders since they have diuretic properties. Urinary tract infection, edema, nephritis, and oliguria are all treated with the whole herb³⁵. It can be used as a refrigerant, emetic, diuretic, laxative, stomachic, anti-bacterial, anti-diarrheal, anti-inflammatory, anti-ulcer, wound healing, nerve illnesses, itching, and the fruits can be used to treat boils³⁶. Earache can be treated using the aqueous extract of leaf. The root and stem decoction are used to cure bladder catarrh. Eczema and purities are treated using a leaf decoction³⁷. It is believed that the leaves have been used to wash cloths. Antifeedant and insect resistant qualities are found in the oil obtained from the seeds of the plant³⁸. The extract of the herb has a sedative effect on the central nervous system. It had a lot of anti-inflammatory and analgesic properties. The medication also had Vaso depressant properties, which are thought to be transient. Its anti-spasmodic activity was also discovered *in vitro*. These findings back up Ayurvedic medicine's usage of it³⁹. The tea prepared from the plant would be used to heal itchy skin, and leaves that are salted are applied to swellings as a poultice⁴⁰.

10. Adverse Drug Reaction

There aren't many reports about this plant having an adverse reaction. Skin problems, including itching, rash, and skin irritation, are treated with a formulation containing *Cardiospermum halicacabum* (10%). However, it is advised to avoid using this cream during the period of pregnancy⁴¹.

11. Conclusion

Cardiospermum halicacabum has significant therapeutic potential and is used to cure minor ailments to chronic conditions. It is an uncultivated crop grown that is usually consumed as a leafy vegetable in India. It has a wide range of phytochemical constituents that are responsible for the therapeutic efficacy. It has been proven scientifically to have several pharmacological activities *in vitro*. Additionally, the plant *C. halicacabum* has been recommended as a lead chemical for the formulation of a cost-effective and nontoxic medication. Although studies have shown an association between activities and active components present, additional data is required to extract, identify, and evaluate the nature of bioactive compounds and their underlying mechanisms to develop industrial pharmaceuticals. Various studies conducted revealed the anti-oxidant, anti-viral, anti-inflammatory, anti-filarial, anti-malarial, anti-bacterial, anxiolytic, anti-arthritic, anti-parasitic, anti-cancer, anti-diarrheal, anti-fungal, anti-pyretic, anti-sickling, adulticidal and fertility properties of the plant. The findings confirmed its conventional usage for human diseases and helped to explain its usage in herbal medicine as a significant source of phytochemical compounds, including phenols, steroids, tannins, saponins, terpenoids and flavonoids. As a result, this plant can be used as a substitute for pharmaceuticals. This review provides emphasis on the bioactivity potential of this readily distributed plant that could benefit society.

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