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Pharmacological Properties of *Cardiospermum halicacabum*-A Brief Review

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Abstract: The medicinal climber *Cardiospermum halicacabum* L., which is a member of the Sapindaceae family, has been used extensively in traditional medical systems, such as Ayurveda, Siddha, and folk medicine, to treat rheumatism, inflammatory diseases, skin conditions, gastrointestinal disorders, respiratory conditions, and neurological disorders. This review highlights the current knowledge on the taxonomy, botanical characteristics, ethnomedicinal applications, phytoconstituents, and pharmacological qualities of the plant. The phytoconstituents present in the plant, including flavonoids, phenolic compounds, alkaloids, saponins, tannins, glycosides, steroids, and triterpenoids, which are believed to be responsible for its medicinal potential. Numerous pharmacological actions, including antibacterial, antiviral, antidiarrheal, antiulcer, anticonvulsant, anxiolytic, analgesic, antidiabetic, anticancer, antioxidant, fertility-enhancing, and cytoprotective properties, have been shown by experimental data from *in vitro* and *in vivo* investigations. Clinical research is still scarce, despite strong preclinical evidence in favour of *C. halicacabum*'s traditional therapeutic benefits. To establish its therapeutic efficacy, more research is necessary that focuses on the isolation of potent phytoconstituents, clarification of their mechanisms of action, standardization of herbal formulations, thorough safety evaluations, and carefully planned clinical studies. All things considered, *C. halicacabum* is a valuable medicinal plant with significant potential for the creation of safe and efficient phytopharmaceutical agents for the treatment and prevention of a range of human illnesses.

Keywords: *Botanical Description, Cardiospermum halicacabum, Ethnomedicinal Uses, Pharmacological Profile.*

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I. INTRODUCTION

For ages, traditional healthcare systems have relied heavily on medicinal plants, which are being used today to treat a wide range of illnesses worldwide. Nearly 80% of people worldwide are thought to rely on herbal treatments as their main source of healthcare, especially in poor nations with limited access to contemporary medical facilities. Plant-derived medicines have gained popularity in recent years due to their affordability, biocompatibility, and environmental friendliness. Microbial infections are among the many human illnesses that these natural compounds have shown great promise in treating and preventing. As a result, the use of medicinal plants in complementary medicine and ethnomedicine has grown significantly, underscoring their significance as important resources for the development of new therapeutic agents [1,2]. *Cardiospermum halicacabum* L. (Family: Sapindaceae) is a medicinal climber that is found throughout tropical and subtropical regions of Asia, Africa, and South America. It is also referred to as Balloon Vine, Heartseed, or "Mudakathan" in Tamil. The plant has been widely utilized to treat inflammatory conditions, rheumatism, skin conditions, fever, asthma, gastrointestinal issues, and neurological conditions in traditional medical systems such as Ayurveda, Siddha, and folk medicine.

II. BOTANICAL DESCRIPTION[3-5]

The medicinal climber *Cardiospermum halicacabum* is a member of the Sapindaceae family. It is an annual or short-lived perennial herb that can climb over nearby vegetation and fences thanks to its strong growth and thin tendrils. The species is found natively in many tropical and subtropical locations, including as Asia, Africa, Australia, and the Americas. It frequently lives in disturbed habitats such as roadsides, grasslands, cultivated fields, and forest borders.

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The plant's morphology includes a thin, green, highly branched stem that is either smooth or sparsely covered with fine hairs; alternating, bipinnately compound leaves with deeply dissected leaflets that are typically 5–12 cm long; small white flowers that develop in axillary cymes eventually give rise to the plant's distinctive fruit.

The inflated, membrane, three-lobed capsule of *C. halicacabum*, which resembles a tiny balloon and is the source of its popular name, "Balloon Vine," is one of its most distinguishing characteristics. The genus name *Cardiospermum*, which means "Heartseed," was inspired by the prominent white heart-shaped hilum on each of the three round black seeds that are enclosed in each capsule. A thin taproot and several lateral roots that aid in anchoring and nutrition absorption make up the root system.

Warm climates with plenty of sunlight and moderate rainfall are ideal for the plant's growth. Seeds are the primary means of propagation, which enables the species to spread quickly in favorable conditions. Many plant parts, such as the leaves, stems, roots, seeds, and the entire plant, have been used extensively in traditional medical systems due to their broad therapeutic usefulness and are still being studied for their pharmacological potential.

➢ *Taxanomy*[6]

- Kingdom: Plantae
- Subkingdom: Tracheobionta
- Division: Magnoliophyta
- Class: Magnoliopsida
- Order: Sapindales
- Family: Sapindaceae
- Genus: *Cardiospermum*
- Species: *halicacabum*

➢ *Common names:* [7]

- English: Balloon Vine, Heartseed, Love-in-a-puff
- Tamil: Mudakathan Keerai
- Hindi: Kanphuti
- Malayalam: Uzhinja
- Telugu: Buddakakara
- Kannada: Agniballi

III. ETHNOMEDICINAL USES[7,8]

For ages, *Cardiospermum halicacabum* has played a significant role in traditional medicine. Different portions of the plant have been utilized to treat a variety of illnesses by indigenous tribes and practitioners of Ayurveda, Siddha, and other traditional systems. While the roots and seeds are saved for certain medicinal uses, the leaves are most commonly used as fresh juice, decoction, or paste.

The herb has long been used to relieve inflammatory conditions, stiff muscles, and joint discomfort. The leaves are frequently used as a medical vegetable in South India to enhance joint mobility and lessen rheumatism and arthritic symptoms. Additionally, leaf paste is applied externally to treat inflammatory skin disorders such as insect bites, dermatitis, edema, sprains, and itching.

Cough, bronchitis, and mild asthma are among the respiratory conditions that have been treated using the aerial parts. Traditionally, decoctions made from the leaves have been used to lower fever and aid in the healing of infectious diseases. Preparations of the plant are also taken in some areas to treat digestive disorders, constipation, indigestion, and discomfort in the abdomen.

In traditional medicine, *C. halicacabum* roots are sometimes used to treat bladder problems and have been described as moderate diuretics. Although these uses vary among cultures, seed formulations have been used in several traditional therapies for neurological problems and overall weakness.

C. halicacabum's extensive ethnomedical profile has garnered significant scientific interest. Experimental pharmacological models have since been used to test several of these traditional claims; several of these models have shown notable biological activity that validates the plant's historical use.

IV. PHYTOCHEMICAL CONSTITUENTS[6,9]

Carbohydrates, proteins, lipids, flavonoids, alkaloids, glycosides, steroids, saponins, and tannins are all present in this plant. Numerous fatty acids, including capric, lauric, myristic, palmitic, and stearic acids, are present in the seed oil. Alanine, arginine, histidine, threonine, and other amino acids are found in the seed proteins, while 3.8% of the seeds are composed of carbohydrates (such as sucrose, fructose, raffinose, etc.). (+)-pinitol, apigenin, and its 7-O-glucoronides, luteolin and chrysoeriol, are found in the leaves. β-sitosterol, phenolics, flavonoids, tannins, and other compounds are present in the root.

V. PHARMACOLOGICAL ACTIVITIES

A. Antidiarrhoeal Activity:[10-12]

Using well-established experimental models, such as castor oil-induced diarrhea, prostaglandin E_2 (PGE_2)-induced enteropooling, and the charcoal meal gastrointestinal transit test in rats, the antidiarrheal activity of whole-plant extracts of *Cardiospermum halicacabum* has been assessed. To guarantee safety during pharmacological evaluation, the doses chosen for the investigation matched one-fifth of each extract's median lethal dose (LD_2^1). In these models, petroleum ether, alcoholic, and aqueous extracts showed notable antidiarrheal benefits. Tannins, flavonoids, saponins, sterols, and triterpenes were found in phytochemical analyses and are thought to be the cause of the activity. The combined effects of these bioactive components, especially flavonoids, tannins, sterols, and triterpenes, are probably responsible for the antidiarrheal effect. They may lessen intestinal motility and fluid output, which would lessen the symptoms of diarrhea.

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B. Antiulcer Activity:[13]

Rats with ethanol-induced stomach ulcers have been used in experiments to show the gastroprotective properties of the ethanolic extract of *Cardiospermum halicacabum* Linn. (Sapindaceae). Gastric ulcer formation was reduced in a dose-dependent manner when the extract was administered orally at doses between 200 and 600 mg/kg. Significant increases in stomach glutathione (GSH) levels and decreases in alkaline phosphatase (ALP) activity were linked to the protective effect, suggesting improved antioxidant defense and maintenance of gastric mucosal integrity. Furthermore, the extract demonstrated potent antioxidant qualities *in vitro* by efficiently scavenging hydroxyl radicals and preventing lipid peroxidation. The ethanolic extract did not cause any notable acute or short-term toxic effects in experimental rats, according to toxicological evaluation, indicating a positive safety profile.

C. Anticonvulsant Activity:[14]

Using maximum electroshock (MES), pentylenetetrazol (PTZ), picrotoxin (PT), strychnine (STN), and isoniazid (INH)-induced seizure models, the anticonvulsant potential of the alcoholic root extract of *Cardiospermum halicacabum* (ARECH) was assessed in Swiss albino mice. Oral dosages of 30, 100, and 300 mg/kg of the extract were given. Particularly at dosages of 100 and 300 mg/kg, ARECH demonstrated broad-spectrum anticonvulsant action by considerably delaying the onset of clonic and tonic seizures in PTZ-, PT-, and INH-induced convulsions and reducing tonic hind limb extension in the MES paradigm. It did not, however, provide much protection against seizures brought on by STN, indicating that its anticonvulsant action is not dependent on glycine-mediated neurotransmission. Flavonoids, phenolics, tannins, saponins, phytosterols, triterpenoids, fixed oils, lipids, proteins, and carbohydrates were found through phytochemical examination. Gamma amino butyric acid (GABA) levels significantly increased without changing dopamine, serotonin, or noradrenaline, according to brain monoamine studies, suggesting that GABAergic neurotransmission augmentation is the primary mechanism behind the anticonvulsant action.

D. Antimicrobial Activity:

- *Antibacterial Activity:*[15,16]

The effectiveness of *Cardiospermum halicacabum*'s broad-spectrum antibacterial activity against both Gram-positive and Gram-negative bacteria varies depending on the extraction solvent. Strong action against *Bacillus subtilis, Bacillus cereus, Staphylococcus aureus, Staphylococcus epidermidis, Enterococcus (Streptococcus) faecalis, Escherichia coli,* and *Citrobacter freundii* was demonstrated by aqueous and ethanolic extracts. *Micrococcus luteus, Klebsiella pneumoniae, Salmonella typhi, Salmonella paratyphi B, Shigella boydii*, and *Enterobacter* species were also shown to be inhibited by ethyl acetate, butanol, chloroform, benzene, and acetone extracts. However, against multidrug-resistant *Shigella* species, *Salmonella typhi, Klebsiella pneumoniae, Enterobacter*, and *Pseudomonas* species, only modest or negligible action was seen. The solvent utilized has a significant impact on the antibacterial potency, which reflects variations in the extract's phytochemical makeup.

- *Antifungal Activity:*[17]

Cardiospermum halicacabum has a strong antifungal effect on a number of harmful fungus. Methanolic extracts had a dose-dependent fungistatic action against *Trichophyton rubrum*, but ethanolic extracts successfully inhibited *Saccharomyces cerevisiae, Aspergillus niger*, and *Candida albicans*. While little to no action was seen against *Trichophyton longifusis, Trichophyton tonsurans*, and *Microsporum canis,* seed oil also demonstrated activity against *Microsporum gypseum* and *Trichophyton mentagrophytes*. Additionally, molecular docking studies revealed a possible mode of action for flavonoids including luteolin-7-O-glucoside and rutin, which may interact with fungus Hsp90 to provide antifungal effects.

- *Antiparasitic Activity:*[18-20]

Additionally, *Cardiospermum halicacabum* exhibits encouraging antiparasitic action. *In vitro* antiplasmodial efficacy against chloroquine-resistant *Plasmodium falciparum* was moderate to good for both dichloromethane–methanol (1:1) whole-plant extracts and ethyl acetate leaf extracts. The aqueous shoot extract did not significantly protect against malaria in a mouse model, despite having poor *in vitro* antiplasmodial efficacy. Additionally, both ethanolic and aqueous extracts showed antifilarial activity against *Brugia pahangi*; at higher concentrations, the ethanolic extract quickly inhibited both adult worm movement and microfilarial release, while the aqueous extract decreased both.

E. Fertility Enhancing Activity:[21]

Without changing the weights of reproductive organs, oral administration of Aqueous leaf extract at doses of 100 and 200 mg/kg body weight for 30 days markedly and dose-dependently raised serum testosterone levels, sperm motility, and epididymal sperm count. A greater number of pregnant females, more implantation sites and viable fetuses, and decreased fetal resorption were all indicators of improved reproductive performance in treated males. The extract showed hepatoprotective action by lowering alkaline and acid phosphatase levels, but it did not change the blood cholesterol or lipid profile or cause any indications of renal or hepatic damage. Flavonoid's antioxidant qualities and the plant's saponin's ability to increase testosterone were blamed for the fertility-boosting benefits. According to the study's overall findings, the aqueous leaf extract of *Cardiospermum halicacabum* is a safe and efficient natural way to increase male fertility by boosting sperm quality and reproductive potential.

F. Anticancer Activity:[22,23]

Using consecutive n-hexane, chloroform, ethyl acetate, methanol, and hydroalcohol extracts made by Soxhlet extraction, the anticancer activity of *Cardiospermum halicacabum* seeds was assessed. Using doxorubicin as the reference medication, cytotoxic activity was evaluated using the Sulforhodamine B (SRB) assay against four human cancer cell lines: HT-29 and HCT-15 (colon cancer), SK-

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MEL-2 (skin cancer), and MCF-7 (breast cancer). With a GI^{21} value of 12.8 µg/mL, indicating significant cytotoxicity, the n-hexane seed extract showed the strongest, selective antiproliferative activity against the MCF-7 breast cancer cell line, outperforming the other extracts in terms of extractive yield (24.18% w/w). Bioactive phytoconstituents, such as phenolics, flavonoids, amino acids, glycosides, and essential fatty acids (omega-3, omega-6, omega-9, oleic acid, erucic acid, eicosenoic acid, and n-hexadecanoic acid), were found to have an anticancer effect. These compounds may have cytotoxic effects by modulating inflammation, apoptosis, and cell-cycle regulation. It stated that the n-hexane seed extract had promising antineoplastic potential, especially against breast cancer, and suggested that its active chemicals might be further isolated, characterized, and their mechanisms of action investigated.

G. Antidiabetic Activity:[24]

Glibenclamide (600 µg/kg) was the conventional medication, and the ethanolic leaf extract was given orally at a dose of 200 mg/kg body weight for 45 days. By lowering plasma, liver, and kidney levels of hexose, hexosamine, and fucose while bringing sialic acid levels back to normal, treatment dramatically decreased high blood glucose levels and restored aberrant glycoprotein metabolism. Improved glycemic control and the presence of bioactive flavonoids with antihyperglycemic, antioxidant, and aldose reductase inhibitory properties, like apigenin and luteolin, were linked to the antidiabetic impact. By controlling glucose metabolism and minimizing tissue damage caused by hyperglycemia, *C. halicacabum* may help avoid diabetic complications and guard against glycoprotein abnormalities brought on by diabetes, according to the findings.

H. Analgesic Activity:[25]

Using the thermal stimulus (analgesiometer/hot plate) method kept at 55°C, the analgesic potential of the aerial portions of *Cardiospermum halicacabum* was assessed in albino mice. Morphine (10 mg/kg) and paracetamol (15 mg/kg) were used as standard medications, while petroleum ether, chloroform, ethyl acetate, and ethanol extracts were examined at 7.5 and 15 mg/kg (equal to 0.15 and 0.3 mg/mL). The petroleum ether extract demonstrated the most effectiveness among the extracts, all of which showed dose-dependent analgesic action. Petroleum ether extract demonstrated 58% analgesic action when compared to morphine and 82% when compared to paracetamol at 0.3 mg/mL, whereas ethanol, chloroform, and ethyl acetate extracts demonstrated 45%, 42%, and 40% activity when compared to morphine, respectively. The plant's phytoconstituents, including flavonoids, sterols, alkaloids, and saponins, may be responsible for its analgesic effects, as seen by the longer reaction time and lower frequency of paw-licking.

I. Anxiolytic Activity:[26]

The roots of *Cardiospermum halicacabum* have long been used to treat epilepsy and anxiety. In this investigation, 19 master fractions (MFs) were obtained by fractionating the ethanolic root extract using silica gel column chromatography. Diazepam (1 mg/kg, p.o.) was the standard anxiolytic medication used to assess the anxiolytic activity in Swiss albino mice utilizing the Elevated Plus Maze (EPM) and Light–Dark Transition (LDT) paradigms. MF-14, MF-16, and MF-17 showed notable anxiolytic effects among the studied fractions. In the EPM test, these fractions (30 mg/kg, p.o.) significantly increased the number of open-arm entrances and the amount of time spent in the open arms while lowering the amount of time spent in the closed arms, indicating a decrease in anxiety. Administering 10, 20, and 30 mg/kg of these fractions in the LDT test resulted in a dose-dependent increase in locomotor activity, a decrease in anxiety-related behavior, and an extension of the time spent in the lit compartment. Cardiospermin, a cyanogenic glucoside, was shown to be the main anxiolytic component extracted from MF-14 using bioactivity-guided fractionation. Cardiospermin may be a good lead chemical for the creation of safer plant-derived anxiolytic drugs with fewer side effects than traditional benzodiazepines, according to the study's conclusion that *C. halicacabum* root demonstrated significant anxiolytic activity.

J. Antiviral Activity:[27]

Using various solvent extracts, the antiviral activity of *Cardiospermum halicacabum* was assessed against the hepatitis B virus (HBV) and the human immunodeficiency virus (HIV). With 91% inhibition of HIV-1 reverse transcriptase (RT) and 78.9% inhibition of hepatitis B surface antigen (HBsAg) release, the methanolic leaf extract demonstrated the greatest antiviral activity among the extracts tested, demonstrating substantial activity against both HIV and HBV. The extract did not, however, considerably reduce the activity of HBV DNA polymerase. Steroids, triterpenes, alkaloids, saponins, phenolic chemicals, sugars, and amino acids were found in the active methanolic extract using phytochemical screening. Eleven bioactive chemicals were found by GC-MS analysis; the main antiviral components were identified as phenanthrol, eicosenoic acid, and benzene dicarboxylic acid. Benzene dicarboxylic acid was found to have the strongest binding affinity toward both HIV and HBV target proteins in molecular docking tests, indicating that it is the primary lead chemical responsible for the reported antiviral efficacy. According to these results, *C. halicacabum* is a promising natural source of antiviral drugs and could be a starting point for the creation of new treatments for HIV/HBV co-infection.

VI. CONCLUSION

Cardiospermum halicacabum L.. is a valuable medicinal plant that has long been used in traditional medical systems. Many of its ethnomedical claims are supported by mounting scientific data. Different plant parts have been shown in experiments to exhibit a variety of pharmacological properties, such as anti-inflammatory, analgesic, antibacterial, antiviral, anticonvulsant, anxiolytic, antidiabetic, antiulcer, antidiarrheal, fertility-enhancing, and anticancer effects. Its extensive phytochemical composition, including flavonoids, phenolic compounds, saponins, alkaloids, tannins, steroids, and triterpenoids, is mainly responsible for these medicinal qualities. The majority of the information that is currently available comes from *in vitro*

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and animal research, despite the fact that preclinical investigations have demonstrated encouraging efficacy and favorable safety profiles. Therefore, to determine its effectiveness, safety, and mechanisms of action in humans, carefully planned clinical trials, thorough toxicological assessments, standardization of extracts, and separation of active bioactive elements are crucial. All things considered, *Cardiospermum halicacabum* is a promising source of new therapeutic compounds and merits more investigation to produce safe and efficient phytopharmaceuticals for the treatment of a range of human illnesses.

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