

**CARDIOSPERMUM HALICACABUM LINN. - A REVIEW**

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**ABSTRACT**

Before the modern day, medicine and its pharmacopeia of synthetic drugs, there were plants and ancient civilizations knew how to use the plants strategically to treat common ailments and even life-threatening diseases. Natural plant-based remedies are used for the both acute and chronic health problems from treating common colds to control blood pressure and cholesterol. Plant medicines were the most widely used medicines in the world because of their safety and very less or no side effects. In this way, the aim of this review article was to summarize the phytochemical and medicinal information of the readily reachable plant *Cardiospermum halicacabum* Linn. This is commonly known as Balloon vine extensively dispersed in tropical and subtropical areas of world. The roots, leaves, stem, and seeds of this plant are employed as herbal medication. The phytochemical analysis confirmed that this herb contains flavonoids, terpenoids, tannins, saponin, protein, carbohydrates, glycosides, variety of fatty acids, and volatile esters. Due to the presence of various compounds, this plant has antibacterial, antifungal, antiparasitic, antidiarrheal, anxiolytic, antioxidant, antipyretic, antirheumatic, anticonvulsant, anti-inflammatory, and anticarcinogenic activities.

**Keywords:** *Cardiospermum halicacabum*, Antibacterial, Antifungal, Antiparasitic, Antidiarrheal, Anxiolytic, Antioxidant, Antipyretic, Antirheumatic, Anticonvulsant, Anti-inflammatory, Neuroprotective, Anticarcinogenic.

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**INTRODUCTION**

Now a days, herbal medicines play a major role in health-care programs in developing countries. Around 80% of world population still depends on medicinal plants for their primary health-care needs [1]. India is recognized as a land of herbal plants; hence, any specific data on such plants could be of clinical importance [2].

*C. halicacabum* Linn. belongs to family Sapindaceae. Common name is Balloon vine. Tamil name Mudakkathan. Annual climber stems with minutely puberulous, tendrils present. Leaves biternate, essentially trifoliate with each part divided again into 3 leaflets, leaflets with coarse serrate teeth. Flowers in the axillary heads usually 3 flowered by abortion, white with a yellowish center. Fruit a membranous, inflated capsule, green, drying to brown more than 2 cm long. Round and black seeds with a broadly heart-shaped or kidney-shaped spot [3].

This plant is extensively dispersed in tropical and subtropical areas of the world. This plant is produced in the plains of Africa, America, Bangladesh, India, and Pakistan [4].

For several centuries, the whole plant has been used for treatment of rheumatism, stiffness of limbs, snake bite, its root for nervous diseases, as a diaphoretic, diuretic, emetic, emmenagogue, laxative, refrigerant, stomachic, and sudorific; its leaves and stalks are used in the treatment of diarrhea, dysentery, and headache and as a poultice for swellings [5]. It is used for the treatment of skeletal fractures in Srilanka [6]. Various products such as gel, cream, shampoo, and spray of *C. halicacabum* is available in market. These products are useful for dry itchy skin and scalp [6]. Many studies show extract of *C. halicacabum* has pronounced anticarcinogenic activity also.

**PHYTOCHEMICAL CONSTITUENTS**

Phytochemical analysis of the *C. halicacabum* showed presence of carbohydrate, protein, lipids, saponins, tannins, flavonoids, alkaloids, glycosides, and steroids [1,3,6,7]. Gas chromatography - mass spectrometry analysis of this plant extract revealed presence of

many active compounds in *C. halicacabum* such as 1,2,4-trioxolane-2-octanic acid, 5-octyl-methyl ester, ethanol, 2-[9-octadecenyloxy], 1,2,4-Trioxolane-2-octanic acid, 5 octyl methyl ester, ricinolenic acid, [1,1-bicyclopopyl]-2-octanic acid, 2-hexyl-methyl ester, 11-octadecenoic acid, methyl ester, 7-methyl-7-tetradecan-1-ol acetate, oleic acid, 9-octadecenoic acid, 1,2,3-propanetriyl ester [8]. (+)- pinitol,  $\beta$ sitosterol,  $\beta$ sitosterol- $\beta$ -o-galactoside, apigenin-7-o-glucuronide, arachidic acid, chrysoeriol-7-o-glucuronide, linoleic acid, luteolin-7-o-glucuronide, and stearic acid [9].

**THERAPEUTIC USES**

Because of the presence of various chemical constituents, extract of this plant showed various medicinal properties such as antibacterial, antifungal, antiparasitic, antidiarrhoeal, anxiolytic, rubefacient, antipyretic, anti-inflammatory, anticonvulsant, and anticarcinogenic.

**Antibacterial activity**

In recent years, the rate of infection and resistant against antibiotics has been increased. The presence of antibacterial substances in the plant show good antibacterial activity without producing any side effects. Antibacterial activity of *C. halicacabum* Linn. was investigated by well diffusion technique (Farrukh *et al.*, 2008) against the selected human pathogens. This extract showed varying degrees of inhibition zones against Gram-positive bacteria (*Staphylococcus aureus*, *S. aureus* AB 188, *Staphylococcus epidermis*, *Streptococcus pyogenes*, *Streptococcus fecalis*, *Bacillus subtilis*, *Bacillus cereus*, *Bacillus stearther*, *Micrococcus luteus*, *Corynebacterium hofmanu*, and *Pneumococci*) and Gram-negative bacteria (*Shigella boydii*, *Shigella dysenterae*, *Salmonella typhi*, *Salmonella paratyphi A*, *Salmonella paratyphi B*, *Shigella flexneri*, *Proteus flexneri*, *Proteus mirabilis*, *Proteus vulgaris*, *Escherichia coli*, *Klebsiella pneumonia*, *Enterobacter*, and *Pseudomonas aeruginosa*) [2,5,7,9-11].

**Antifungal activity**

Antifungal activity of plant extract was carried out according to Mahmud *et al.*, 2009 by agar dilution method. The extract of *C. halicacabum* Linn. showed significant antifungal activity against human pathogens (*Aspergillus niger*, *Candida albicans*), animal pathogens (*Microsporidium*

*gypsiccus*, *Trichophyton mentagrophyte*) and plant pathogens (*Saccharomyces cerevisiae*, *Penicillium* sp.) [1,2,11].

#### Antiparasitic activity

Extracts of *C. halicacabum* were tested in *in vitro* for their effectiveness against third-stage larvae of *Strongyloides stercoralis*. This is an important parasitic nematode which persists for years in the human host and it may disseminate and cause fetal infection. Aqueous extract of *C. halicacabum* exerted more rapid effect on larval motility than that of the alcohol extract. To attain 50% non motility or dead it took <24 hrs and more than 36 hrs for aqueous and alcohol extract of *C. halicacabum*, respectively [12].

#### Anti-inflammatory activity

$\lambda$ -Carrageenan hind paw edema model was used for determination of anti-inflammatory activity [13,14]. The L-arginine-NO pathway has been proposed to play an important role in the carr-induced inflammatory response. The expression of inducible isoform of NO synthase is an important mediator of inflammation. Therefore, the NO level has been increased during inflammation.

Tumor necrosis factor (TNF- $\alpha$ ) is a major mediator in inflammatory responses. It induces innate immune responses by activating T cells and macrophages and increase the secretion of other inflammatory cytokines [13,14].

The ethanolic extract (100, 200, and 400 mg/kg) significantly decreased the NO level in serum and TNF- $\alpha$  level in serum after 5 hrs of post-Carr injection [13]. By inhibiting the NO and TNF- $\alpha$  production, *C. halicacabum* expressed its anti-inflammatory activity [15].

Extract of *C. halicacabum* Linn. contained rutin. Rutin is a flavonol glycoside comprised flavonol quercetin and the disaccharide rutinose. Rutin was shown to increase the colonic glutathione level, thus reducing oxidative tissue damage and thus reduce the inflammation [16].

#### Antioxidant activity

Reactive oxygen species affects various molecular components of the cell such as fatty acids, proteins, and DNA. An excess production of reactive oxygen species leads to cell degeneration and death [17]. Methanolic extract of *C. halicacabum* exhibited inhibition of 2,2-diphenyl-1-picrylhydrazyl radical and possessed reducing power, superoxide scavenging ability, nitric oxide scavenging activity, and ferrous ion chelating potency [9,18,19]. Large quantities of phenolic compounds in *C. halicacabum* extract makes it a strong free radical scavenger, which indicates that the extract has good potential as a source for natural antioxidants to prevent free radical-mediated oxidative damage [20].

#### Antipyretic activity

Antipyretic activity of the *C. halicacabum* Linn. extract was studied in rat models. For this, pyrexia was induced by pyrogen administration. Ethanolic and n-hexane extract of the *C. halicacabum* showed significant antipyretic activity at a higher dose of 400 mg/kg. The efficacy of 100 mg/kg paracetamol was almost equal to that of 400 mg/kg of the extract [1,21].

#### Antidiarrhoeal activity

Diarrhea is a very common and major national problem in many tropical countries which results in 4-5 million deaths throughout the world annually [22]. Diarrhea was induced by castor oil to the animal models. The alcoholic and aqueous extract of the *C. halicacabum* exhibited the antidiarrhoeal activity against the castor oil induced diarrhea by reducing the frequency of defecation and decrease the intestinal secretion [23,24].

#### Antiarthritic activity

Rheumatoid arthritis is an autoimmune disease which results in a chronic, systemic inflammatory disorder that causes pain, swelling,

stiffness, and loss of function in joints [25]. Liquid chromatography – mass spectrometry analysis of *C. halicacabum* indicated the presence of anti-inflammatory compounds Luteolin-7-o-glucuronide, Apigenin-7-o-glucuronide, and Chrysoeriol [26-28]. Extract of the *C. halicacabum* exhibited therapeutic effects against Freund's complete adjuvant-induced arthritis in rat models by decreasing the production of proinflammatory cytokines such as TNF- $\alpha$ , interleukin-1 [29] and inhibition of protein denaturation, membrane stabilization and proteinase inhibition [30,31].

#### Anxiolytic activity

The state of anxiety involves disturbances in coordination of different neurotransmitters, for example, gamma amino butyric acid (GABA), serotonin, noradrenalin, dopamine, opioid peptides, endocannabinoids, corticotrophin-releasing hormone, neuropeptide Y, and oxytocin in various brain pathways [32]. GABA is a major inhibitory neurotransmitter in the central nervous system and activation of GABA<sub>A</sub> receptors results in significant increase in chloride conductance across the cell membrane which causes neuronal failure to generate an action potential and leads to inhibition. *C. halicacabum* extract has various bioactive compounds such as flavonoids, sterols, triterpenoids, saponin, tannins, and xanthoproteins [33-35]. Anxiolytic activity of the extract may be due to binding of any of these phytochemicals to the GABA<sub>A</sub>-BZD<sub>5</sub> complex [32].

#### Antidiabetic activity

Diabetes mellitus is a metabolic disorder which is characterized by a loss of glucose homeostasis with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion or insulin action or both. Management of diabetes without any side effect is still challenge to the medical community [36,37]. Antihyperglycemic effect of ethanolic extract of *C. halicacabum* leaf was examined against streptozotocin-induced diabetic rats. This extract has several flavonoids such as apigenin, pinitol, and luteolin which are reported as the antidiabetic principles [38,39]. This extract showed significant antihyperglycemic activity at the dose of 200 mg/kg by decreasing the plasma glucose and HbA<sub>1c</sub> and increasing the level of insulin and hemoglobin. This extract increased the activity of glucokinase and decreased the activity of glucose 6 phosphatase and fructose 1,6 phosphatase in the liver [38,40]. Thus, this extract showed antidiabetic activity [41].

#### Anticonvulsant activity

Alcoholic extract of the petroleum ether fraction of *C. halicacabum* in the dose of 350 mg/kg body weight was effectively reduced the extensor and flexor component of tonic convulsions in electroshock-induced convulsions in Wistar rats [1,41,42].

#### NEUROPROTECTIVE ROLE

Dementia is a progressive brain dysfunction which leads to a gradually increasing restriction of daily activities. It is characterized by difficulties in memory, disturbances in language, psychological and psychiatric changes, and impairment in routine activities. Methanolic extract of *C. halicacabum* potentially improved memory and reversed amnesia induced by administration of scopolamine. It also significantly decreased the whole brain acetyl cholinesterase activity [43].

#### Anticancer activity

Cancer is a second major cause of deaths after cardiovascular diseases. The available anticancer therapies not only kill the cancer cells but kill the normal cells also [9]. Due to the presence of phytochemicals, the extract of *C. halicacabum* showed anticancer activity. Methanolic extract of the *C. halicacabum* showed remarkable anticancer potential against the breast cancer cell lines [44,45]. Chloroform extract of *C. halicacabum* Linn. showed significant anticancer activity against Ehrlich Ascites carcinoma cell line [9]. Methanolic extract of *C. halicacabum* has profound effect in controlling Hep-G2 cell proliferation at lower

concentration [8]. Evaluation of cytotoxic activity of *C. halicacabum* using MTT assay revealed that *C. halicacabum* extract is a potential material for the treatment of cancer [46].

## CONCLUSION

*C. halicacabum* Linn. has enormous medicinal value which is used to treat simple ailments to chronic diseases because of presence of their bioactive phytochemical constituents. This review throws light on the bioactivity potential of this easily available plant which may be beneficial to the society.

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