Journal of Medicinal Plants Studies
www.PlantsJournal.com

ISSN (E): 2320-3862
ISSN (P): 2394-0530
https://www.plantsjournal.com
JMPS 2024; 12(3): 67-70

Received: 01-03-2024
Accepted: 06-04-2024

Drisya MK
Assistant Professor, Nehru College of Pharmacy Kerala, India

Selishya C Luies
Final Year B Pharm Student, Nehru College of Pharmacy, Kerala, India

Aleena C Raphy
Final Year B Pharm Student, Nehru College of Pharmacy, Kerala, India

Anusree V
Final Year B Pharm Student, Nehru College of Pharmacy, Kerala, India

Rashitha VU
Final Year B Pharm Student, Nehru College of Pharmacy, Kerala, India

Sandrima Sali
Final Year B Pharm Student, Nehru College of Pharmacy, Kerala, India

Corresponding Author:
Drisya MK
Assistant Professor, Nehru College of Pharmacy Kerala, India

Review on ethnobotany and pharmacological activities of *Centella asiatica* (Apiaceae)

Drisya MK, Selishya C Luies, Aleena C Raphy, Anusree V, Rashitha VU and Sandrima Sali

Abstract
Researchers are interested in discovery, medication, mainly related to traditional remedies based on plants. Traditional ayurvedic medicine *Centella asiatica* is a medicinal herb (Gotu kola) is used extensively in India and throughout Asia. Triterpenoid saponins such as Asiatic acid, centelloside, madecassoside and asiaticoside are the active chemical contents that offer broad therapeutic potential in area of anti inflammatory, anticancer, neuroprotective, antioxidant and wound healing actions. Aerial portions and roota are used for medicinal purpose. An overview of *Centella asiatica*'s phytoconstituents, bioactive chemicals and pharmacological actions are given in this review.

Keywords: *Centella asiatica*, pharmacological action, triterpenoids, wound healing, asiaticoside

Introduction
Centella asiatica, also known as "Gotukola," "Indian Pennywort," or "Mandookaparni" in India, is a significant traditional medicinal plant that belongs to the Apiaceae family. Found in tropical and subtropical nations including Bangladesh, Sri Lanka, and India, it is a significant perennial medicinal herb. It thrives in wet, clayey or sandy soils up to 600-18,000 meters above sea level in India, where it forms a dense carpet of greenery. The glabrous stem of *Centella asiatica* is paired with long, fleshy, petiolated leaves that root at nodes. This plant has a delicate scent and can grow up to 15 cm in height. The smooth stem allows for roots at the nodes. It is widely distributed in moist, swampy, and damp areas, and it flowers with white, purple, or pink blooms from April to June. Many triterpenes, saponins such as asiaticoside and asiatic acid, sapogenins, madecassic acid, vellarin, adecassoside, glycosides, and centelloside are found in *C. asiatica*. The entire plant is used medicinally and is frequently used to cure high blood pressure, promote longevity, improve cognition, and purify blood. Antileprotic, antifeedant, antistress, anti-tuberculosis, wound-healing, antibacterial, and fungicidal action are only a few of its many beneficial qualities. In 1997, Srivastava *et al*. Leprosy, wounds, cancer, fever, allergies, abscesses, asthma, catarrh, convulsions, dysentery, eczema, gonorrhea, hypertension, headaches, pleuritis, jaundice, rheumatism, ulcers, spasms, TB, urethritis, and other conditions are among those for which it is used. This plant's therapeutic value has led to its application in the production of silver nanoparticles. The Chinese referred to *Centella asiatica* as "elixir of life". She lists the constituents as "vellarine, having the odor and bitter persistent taste of the fresh plant, resin, some fatty aromatic body, gum, sugar, albuminous matter, salts, mostly alkaline sulphates and tannin."

Taxonomical classification

- **Kingdom:** Eukaryota.
- **Subkingdom:** Embryophyta.
- **Division:** Spermatophyta.
- **Subdivision:** Angiospermae.
- **Class:** Dicotyledoneae.
- **Subclass:** Rosidae.
- **Superorder:** Aralianae.
- **Order:** Araliales (Umbelliflorae).
- **Family:** Apiaceae or Umbelliferae.
- **Subfamily:** Hydrocotyle.
- **Genus:** *Centella*.
- **Species:** *Centella asiatica*.

Synonyms

- *Hydrocotyle asiatica*.
- *Hydrocotyle cordifolia*.
- *Hydrocotyle hebecarpa*.
- *Hydrocotyle lunata*.

Regional names

- **English:** Indian pennywort.
- **Hindi:** Gotukola.
- **Sanskrit:** Bhekaparni.
- **Malayalam:** Kodagam.
- **Tamil:** Vallarai.
- **Telungu:** Bokkudu.

Plant Description

Centella asiatica (CA) is a clonal, perennial herbaceous creeper that grows up to 1800 meters in elevation in damp areas of India. It is a member of the Umbellifere (Apiceae) family. It grows in swampy places in most tropical and subtropical nations, including sections of Madagascar, South Africa, South America, Pakistan, India, and Eastern Europe. The majority of tropical or moist pantropical regions, including rice fields, as well as rocky, higher altitudes, are home to about 20 species related to CA [4]. This plant, which grows near water, has no flavour or smell. It grows small oval fruit and has small fan-shaped green leaves. The flowers are white, light purple to pink, or both. There are medical uses for the entire plant. It is frequently used as a blood purifier, to treat hypertension, to improve memory, and to lengthen life. One of the key herbs in Ayurveda for reviving the nerves and brain cells is CA. Eastern healers used CA to treat emotional diseases like depression, which they believed had their origins in physical issues. CA and its alcohol extracts were reported to have showed promising effects in the treatment of leprosy in Western medicine around the mid-1900s.

Ethnomedical uses: Numerous scientific studies have shown evidence for *Centella asiatica*'s potential to enhance cognitive and other brain functions. Rats treated with plant extracts were observed to have better cognitive function and less oxidative damage. Leaf powder has been demonstrated to reduce 3-nitropropionic acid-induced oxidative stress in mitochondria *in vitro* and to have an anti-oxidant impact in brain areas of pre-pubertal mice *in vivo*. The plant possesses a neuroprotective effect against oxidative stress, mitochondrial dysfunction, and intracerebroventricular colchicine-induced cognitive impairment. Similarly, D-galactose-induced cognitive impairment also exhibits this effect. The plant's capacity to improve memory has also been assessed in connection to its antioxidant characteristic. It has been discovered that giving the plant to mice at the postnatal stage improves their memory and learning. It has been shown that giving rats fresh leaf extract improves their capacity for learning and memory retention. After the plant was administered, healthy older human participants showed improvements in their mood and cognitive function. Because the plant extract has been demonstrated to increase phosphorylation of cyclic AMP response element binding protein (CREB) in neuroblastoma cells expressing amyloid beta peptide - a component of amyloid plaques associated with Alzheimer's disease - it may prove beneficial for patients with the disease. It should be mentioned that as the disease progresses, amyloid beta peptide in Alzheimer's disease dramatically inhibits the phosphorylation of CREB by protein kinase A (PKA), which may result in cognitive impairment. Indeed, it has been shown that a plant extract reduced the levels of amyloid beta in the hippocampus of an animal model of Alzheimer's disease.

Pharmacological activities

Antibacterial activity

The antibacterial activity of *Centella asiatica* leaves was evaluated using a hot methanol extract, and the disc diffusion method was used to determine the minimum inhibitory concentration (MIC) value of 2 µg/disc and the zone of inhibition. According to Sankar *et al*., there was no antibacterial activity demonstrated by acetone, chloroform, or hexane extract against the three Vibrio species, V. harveyi, V. alginolyticus, and V. parahaemolyticus, when it came to the methanolic extract of *Centella asiatica*.

According to a study, essential oil extract exhibited antibacterial activities with MIC values ranging from 1.25 to 0.039 mg/ml against Gram-positive (Bacillus subtilis and S. aureus) and Gram-negative (Escherichia coli, Pseudomonas aeruginosa, and Shigella sonnei) bacteria. In order to investigate the antibacterial activity of *C. asiatica* under both normal and osmotic stress conditions, Bacillus cereus and Listeria monocytogenes 10403S were chosen. Under conditions of osmotic stress, antibacterial activity was twice improved at 95% ethanolic extract. Methanol extracts of the leaf and callus showed the greatest inhibitory action against the investigated species, B. cereus, E. coli, S. aureus, and P. aeruginosa.

Neuroprotective activity

The primary methods of *C. asiatica*'s neuroprotection are enzyme inhibition, oxidative stress reduction, dopamine neurotoxicity in Parkinson's disease, and prevention of amyloid plaque formation in Alzheimer's disease. According to Ramanathan *et al*., the neurodegeneration caused by monosodium glutamate is prevented by *Centella asiatica* extract. Asiaticoside which is included in the extract

suppressed the activities of phospholipase A2 (PLA2) subtypes in primary cultures of rat cortical neurons. This evaluation was conducted using a water extract of *C. asiatica*. Acute asiatic acid administration resulted in better learning and memory in male Sprague-Dawley rats. Asiatic acid, madecassic acid, brahmaside, and the flavonoids madecassoside and madesiatic acid are among the plant's components with neuroprotective potential in modern medicine. By reducing the alterations in an animal model, such as abnormal neurobehavioral and neurochemical features, the plant is known to employ neuroprotective effects. In the rat, asiaticoside has neuroprotective effects on synaptic function and phosphoinositides-assisted cytodynamics, which includes a kind of ROT-infused hemiparkinsonism.

Antioxidant property

Aging is mostly caused by reactive oxygen species (ROS) and free radicals. Every organism has a defense system against these reactive groups, and free radical scavengers shield the organism. According to a study, asiaticoside dramatically raised the concentrations of catalase, glutathione peroxidase, superoxide dismutase, ascorbic acid, and vitamin E in rats with excision-type cutaneous lesions.

C. asiatica has a wide range of components, including polyphenol, flavonoid, β-carotene, tannin, vitamin C, and DPPH, which all contribute to the herb's noticeably greater antioxidant activity. Mice carrying lymphomas showed a decrease in ascorbic acid levels and an increase in antioxidant enzyme levels after receiving continuous supplementation of crude methanolic extract for 14 days. The antioxidant capacity of *C. asiatica* extracts in a variety of solvents, including water, methanol, ethyl acetate, hexane, acetone, and chloroform, was evaluated.

Wound healing

The literature has been increasingly supportive of the traditional use of C.asiatica extracts (CAE) for wound healing. An increase in collagen content and tensile strength was observed at the wound site as a result of increased cellular proliferation and collagen synthesis.

It has been shown that Asiaticoside, a component of CA aiding in wound healing. As antioxidants have been linked to a function in the healing of wounds, asiaticoside's effects on antioxidant levels were investigated in a laboratory animal study.

Studies have been conducted on the effects of asiaticoside on both normal and delayed wound healing. In both normal and delayed healing models, Asiaticoside demonstrated its potency at 1 wound healing activity when taken orally.

Gastric ulcer

Aqueous extract of CA can effectively prevent stomach ulcers caused by the ingestion of ethanol. The authors came to the conclusion that the CA extract probably reinforced the mucosal barrier lining the stomach and lessened the harmful effects of free radicals. The antiulcer activity was contrasted with sodium valproate (antiepleptic or antiseizure) and famotidine (H2-antagonist).

According to one study, asiaticosides, an ingredient of CA, have an anti-inflammatory effect that is caused by blocking nitric oxide (NO), which promotes ulcer healing. Preclinical and clinical trials conducted by a few other researchers also demonstrated the effectiveness of CA in treating stomach ulcers. Additionally, studies have been conducted to show how CA functions in periodontal therapy.

Memory enhancing

The plant *Centella asiatica* contains brahminoside, brahmic acid, and brahmoside as active constituents, an aqueous extract of CA has been shown to significantly improve memory. Rao et.al shown that Fresh leaf juice of *Centella asiatica* has properties to promote memory retention and improve spatial learning in neonatal rats.

Venous insufficiency

Centella asiatica was thought to have a major impact on connective tissues by fortifying the weaker veins. *Centella asiatica* was suggested to have a potential role in connective tissue maintenance. Because it reportedly increased the development of hyaluronidase and chondroitin sulfate and exerted a balancing effect on the connective tissue, it may also help stabilize connective tissue growth and reduce its formation in the treatment of scleroderma. According to reports, *Centella asiatica* acts on the vascular wall's connective tissues, enhancing microcirculatory parameters and reducing capillary filtration rate in cases of hypertensive microangiopathy and venous insufficiency.

Sedative and anxiolytic properties

It has been reported that *Centella asiatica* has central nervous system (CNS) properties that include stimulating-nervine tonic, rejuvenating, sedative, tranquilizer, and intelligence-promoting qualities. It has been used historically as a sedative; the major ingredients thought to have this action are brahmoside and brahminoside. The cholecystokinin receptors (CCKB), a class of Gprotein coupled receptors that bind the peptide hormones cholesystokinin (CCK) or gastrin, are thought to be partially responsible for the anxiolytic activity. These receptors may also beinvolved in the modulation of anxiety, nociception, memory, and hunger in both humans andanimals.

Antidepressant properties: Total triterpenes from *Centella asiatica* were found to have antidepressant effects on the content of amino acids in mouse brain tissue and the immobility period in forced swimmingmice. *Centella asiatica*'s antidepressant action was confirmed by the reduction of immobilitytime and the amelioration of amino acid imbalance caused by imipramine and total triterpenes.

Radioprotection

During clinical irradiation, *Centella asiatica* may be helpful in avoiding radiation-induced behavioral abnormalities. At a sublethal dosage, the plant extracts' radio protective qualities were also examined. When compared to the mice that received radiation alone, the animals in the drug-treated group lost much less body weight

Central Nervous system

The derivatives of asiaticosides reduce or avoid the effects of beta amyloid neurotoxicity, decrease the concentration of intracellular free radicals, and lessen the death caused by H2O2. It was discovered that *Centella asiatica* extract raised GABA levels in the brain.

Anticancer activity

The anti-cancer activity of *C. asiatica* was demonstrated by aqueous extracts, which caused apoptosis in colonic crypts and had a chemo preventive effect on colon tumorigenesis in male F344 rats. The growth of human gastric adenocarcinoma (MK-1), human uterine cancer (HeLa), and murine melanoma

(B16F10) cells was suppressed by components in the methanol extract of *C. asiatica*. Methanolic extract caused human breast malignant MCF-7 cells to undergo apoptosis, according to an *in vitro* investigation using the HeLa, HepG2, SW480, and MCF-7 cell lines. Human colon cancer SW480 cells and melanoma SK-MEL-2 cells underwent apoptosis when exposed to aspartic acid.

Effect on skin

Asiaticoside increases skin cell migration rates, improves initial skin cell adhesion, and causes an increase in the number of normal human dermal fibroblasts, all of which promote skin cell behaviors involved in wound healing.Four medicinal plants - Curcuma caesia, Areca catechu, Cinnamon zeylanicum, and Tamarindus indica - as well as a hydroalcoholic extract of *C. asiatica* were utilized to make herbal lotions that improved skin moisture, sebum production, viscoelasticity, and melanin content.

Antiepileptic activity

Asian CA's antiepileptic qualities come from its increased brain GABA levels, which accounts for its historical use as an anxiolytic and anticonvulsant. Leprosy has been treated using the plant's separated steroids [31]. In one investigation, pentylenetetrazole (PTZ) kindled rats were used to assess the effects of aqueous CAE (100 and 300 mg/kg) on the course of kindling development, kindling-induced learning impairment, and oxidative stress markers. Animals were given PTZ for 24, 48 hours, and their entire brains were examined for oxidative stress markers like glutathione and malondialdehyde (MDA) as well as for the passive avoidance test and spontaneous locomotor activity. When CA (300 mg/kg, p.o.) was administered, the number of PTZ-kindled seizures decreased, and the seizure score also revealed improvement in the learning deficit caused by PTZ kindling.

Antinociceptive

It has been documented how CA affects inflammation and pain (antinociception) in mouse models. Rats' paw edema caused by prostaglandin E2 was used to investigate the anti-inflammatory effects of CA, while mice's acetic acid-induced writhing and hot-plate technique was used to examine the antinociceptive effects of the aqueous CAE (10, 30, 100, and 300 mg/kg). Significant antinociceptive effect, comparable to aspirin but less strong than morphine, and significant antiinflammatory action, comparable to mefenamic acid, were both demonstrated by the aqueous CAE in both models. These findings supported the traditional use of this plant in the treatment of rheumatism or inflammatory disorders by indicating that the aqueous CA extracts have antinociceptive and antiinflammatory properties.

Conclusion

The used of the medicinal plants or herbs was still based on traditional nostrum. In which in order to increase value of herbal products and medicinal plants, a knowledge-based scientific proved should be conducted. This research conducted tests on 3 different aspects of *C. asiatica*. There were antibacterial activity, antioxidant activity and chemical profiling. The result obtained showed that different extraction solvents affect all 3 aspects. For antibacterial, overall comparison showed no different between gram positive and gram negative bacteria. Ethanolic and chloroform extract showed slightly different in antibacterial activity. However hexane extract showed lowest antibacterial activity. In antioxidant part, ethanolic extract showed highest antioxidant activity (FRAP) and total phenolic content. In chemical profile, from identified peak, hexane extract showed widest variety of chemical compounds. Overall finding showed that *C. asiatica* would be a promising antibacterial and antioxidant activity source.

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