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Centella asiatica: A Comprehensive Pharmacological Review of its Therapeutic Potential

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Abstract

Centella asiatica, also referred to as gotu kola, is a well-known medicinal herb that has been used for more than 3,000 years in Chinese and ancient Indian Ayurvedic medicine. It has recently attracted interest from all around the world due to its several medicinal advantages. The pharmacological characteristics, chemical makeup, and therapeutic uses of *Centella asiatica* are examined in this paper. The plant, which is abundant in bioactive substances like triterpenoids and saponins, has strong anti-inflammatory, anticancer, anticonvulsant, and antioxidant properties. Among other advantages, its medicinal potential includes improving memory, reducing anxiety, and encouraging wound healing. Although its natural sources make it a desirable therapeutic alternative, the way it is administered and the patient's specific medical condition will determine its safety and efficacy. The IUCN has classified *CA* as endangered due to the alarming loss in its natural populations caused by uncontrolled exploitation. This underlines how urgently sustainable farming methods and more study are required to properly realize its therapeutic potential.

Keywords: *Centella asiatica*, Gotu Kola, Traditional Medicine, Bioactive Compounds, Pharmacological Properties

Introduction

The traditional Indian medical system known as Ayurveda is becoming more and more well-known for its ability to effectively treat a wide range of chronic illnesses. After a diagnosis, many individuals combine traditional drugs with Ayurvedic therapy.In order to fully comprehend the impact of food, spices, and medicinal herbs, one must understand their impacts. Although ayurvedic plants and spices are generally healthy for society to use, concentrated items made from individual plants like teas or tablets cause issues. Polyherbal medications work very differently from synthetic or single-substance medications. Although ayurvedic medicines are natural, their safety is dependent on how they are used and are tailored to meet the needs of each patient and particular medical condition.Plant-based medicines are the core of Ayurvedic medicine because of their powerful ability to balance the body's energies, or doshas, and possibly even reverse the course of disease [1].

Centella asiatica, a valued medicinal herb that has historically been praised in the East, is currently becoming more well-known in the West [2].*Centella asiatica*, sometimes called Asiatic pennywort, gotu kola, or centella, is a herbaceous plant that belongs to the Apiaceae family of flowering plants. The plant might be affected by frost [3].

Indian pennywort *(CA)* is member of Apiaceae family, which is used to be referred to as the Umbelliferae. *Bacopa monnieri* along with *Centella asiatica* were once mistaken in India because both were marketed by similar names, "brahmi", Now that this distinction has been made clear, *CA* is known as mandookaparni and Bacopa monnieri is known as brahmi [4]. Tribal people have traditionally used *C. Asiatica* (Linn), a plant endemic to places like Madagascar, Malaysia, South Africa, and Sri Lanka, for its therapeutic qualities. It has been an essential component of Indian Ayurvedic therapies for more than 3,000 years and a pillar of Chinese herbal therapy for almost 2,000 years [5].

Since *CA* has been used for a variety of health and cosmetic purposes from ancient times,making it a beneficial commercial product. According to European Pharmacopoeia, German Homeopathic Pharmacopoeia, Indian Herbal Pharmacopoeia, and Pharmacopoeia of the People's Republic of China,*CA* is a recognized medication [6].

Centella asiatica, often known as gotu kola, is used in Indian medicine to treat nervous system diseases, skin conditions, and memory impairment [7]. In recent years, there is notable increase due to the worldwide interest in medicinal plants utilized in traditional medical systems. Particular attention has been paid to *Centella asiatica*, a herb that has been used for a very long time in China, Sri Lanka, Nepal, Madagascar, and the Indian subcontinent. *CA* is suggested by the Indian Pharmacopoeia to cure a number of skin conditions, such as lupus, leprosy, varicose ulcers, psoriasis, and eczema. It is also utilized for its remarkable wound-healing qualities and to treat ailments like diarrhea, fever, irregular menstruation, and abnormalities of the female reproductive system [8]. Natural populations of *Centella asiatica* have declined significantly as a result of overharvesting, insufficient cultivation, and poor restoration efforts. The species has been formally designated as endangered by (IUCN). Its natural populations have been drastically reduced by widespread and uncontrolled harvesting, with little effort made toward cultivation or replenishment, despite being acknowledged by the Export-Import Bank of India as a medical plant of worldwide significance [9, 10].

Fig 1: *Centella asiatica* [30]

Table 1: Scientific classification of *CA*

Kingdom	**Plantae**
Subkingdom	Spermatophyta
Division	Angiospermae
Subdivision	Spermatophytina
Class	Dicotiledoneae
Subclass	Rosidae
Order	Umbelliferae
Family	Apiaceae
Genus	*Centella*
Species	*Asiatica Linn*

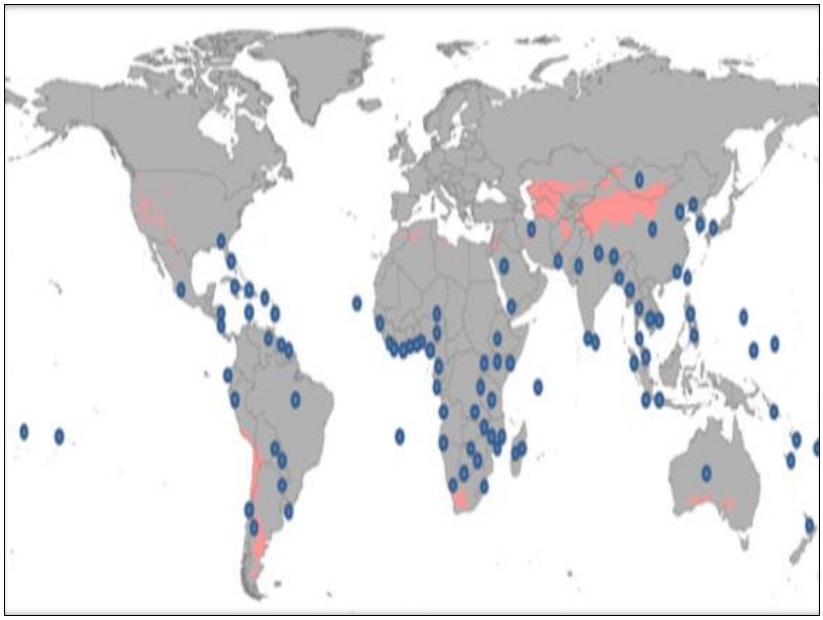

Fig 2: Distribution of *CA* [30]

Nomenclature of plant species in diverse region

CA is produced extensively in India's tropical and subtropical areas, up to 600 meters in height [11]. Herb is commonly recognized as Indian pennywort in India. Nonetheless,*CA* goes by several regional terms in various parts of India and by diverse vernacular names across the world [12, 13, 14, 15] such names are listed in (Table 2).

Region/language	Vernacular name
Hindi	Brahmemanduki,Mandookparni,Gotukola, Khulakhudi
Mizoram	Lambak
Malayalam	Kodangal, Kodagam, Kutakm, kuttanal, Muthal, Muttil
Manipur	Phuk
Telgu	Bokkudu, Saraswataku, Saraswati plant, Bekaparnamu
Kanarese	Bhramisoppu,Urage,Vandelaga-illikiwigidda, Vondelaga
Sanskrit	Bhekaparni,Brahmananduki,Manduki,Supriya, Tvasthi
Meghalaya	Bat-meina
Sinhalaese	Hingotukola
Marathi	Karinga, Karivana
Deccan	Vallarai
Oriya	Thalkudi
Kerala	Mayalchevi
Tripura	Thankuni, Thunimankuni
Tamil	Babassa, Vallarai
Assam	Manimuni
Gujarati	Barmi, Moti Brahmi
Bihar	Chokiora
Urdu	Brahmi
Bengal	Thankuni, Tholkuri
Bombay	Karivana
Bangladesh	Dhol manik
China	Fo-ti-tieng, Chi-hsueuh-ts'ao
USA	Marsh pennywort, Indian Pennywort
Tonga	Tono
Hawai	Pohe kula
Cook Islands	Kapu kapu
Tahiti	Tohetupou
Nepal	Gho tapre
Sri-Lanka	Thankuni sak
Fiji	Totodro
Samoa	Tono

Morphological features

The spreading, faintly scented perennial plant *Centella asiatica (L.*) Usually reaches a height of 15 cm (6 inches) and produces stolons [10]. Due to the presence of essential oils or resin in their tissues, the plants typically emit a pleasing scent [16].

Stem: The stem of *Centella asiatica* grows in damp, marshy, and shady areas, such rice banks and paddy fields, where it forms a thick, verdant carpet [17].

Leaves: *CA* has alternating leaves with long petioles that range in length from 2 to 6 cm along the stem nodes. With a base that encloses the stem and slightly toothed margins, the orbicular or reniform leaves resemble a kidney or shallow bowl. The leaves have smooth upper and lower surfaces [10, 16, 18].

Flower: Each of the tiny umbels that make up *CA* blossoms has three to four flowers. The blooms usually bloom from April to June and might be pink, purple, or white [10].

Fruits: Fruit is regularly produced by CA throughout the growth season. Fruits have a thicker outer layer (pericarp) and are spherical, oblong, approximately 2 inches long. A laterally flattened pendulous embryo is present in the seeds [10].

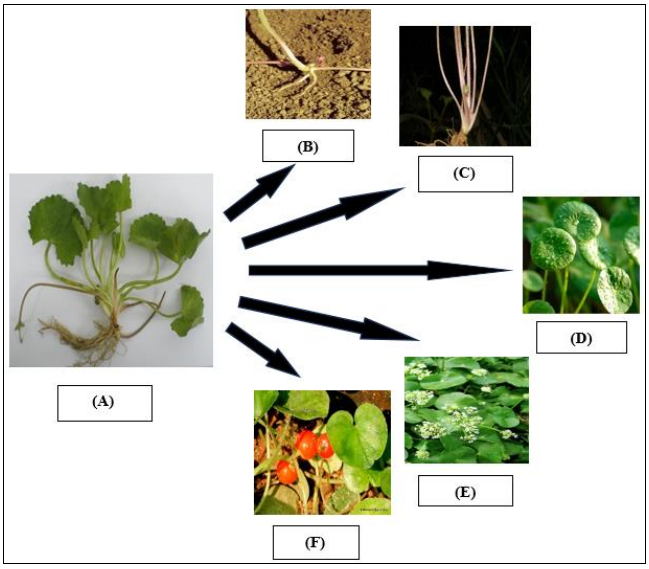

Fig 3: Morphology of *CA* A) Whole plant [31] B) Root [32] C) Stem [33] D) Leaves [34] E) Flower [35] F) Fruit[36]

Chemical composition

The main components of *CA*, triterpenoids and saponins, are responsible for the plant's therapeutic qualities and are well-known for their numerous health advantages [2]. Centelloids are group of pentacyclic triterpenoid saponins that are produced by *Centella asiatica.* These terpenoids, including madecassoside, brahmoside, brahminoside, thankuniside, sceffoleoside, centellose, asiaticoside, centelloside, asiatic acid, and madecassic acid, are produced in the plant's metabolic system, particularly through the isoprenoid pathway.

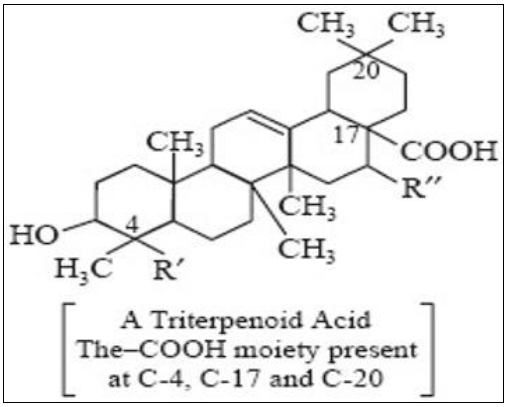

Fig 4: Triterpenoid's structure [37]

These have hydrophilic sugar chain (glycone) connected to a hydrophobic triterpenoid core (aglycone).The plant's medical uses and therapeutic qualities depend mainly on these bioactive compounds [19].

Chemical Compounds in *Centella asiatica*

Triterpenoids: Contains substances such as brahmoside, brahminoside, brahmic acid, asiatic acid, centelic acid,

madecassic acid, thankuniside, isothankunic acid, centellose, asiaticoside, centelloside, and madecossoside. Brahmic acid has melting point of 293°C and is defined as 2,6-hydroxy, 23-hydroxy-methyl ursolic acid. The concentrations of madecassoside and Asiaticoside are lower in the roots and higher in the leaves.

Essential and Fatty Acids: Glycerides of palmitic, stearic, lignoceric, oleic, linoleic, and linolenic acids are present in the fatty oil.

Alkaloids: It has hydrocotylin, an alkaloid with the chemical formula $C_{22}H_{33}NO_8$.

Glycosides: Centelloside, madecassoside, and asiaticoside are present. Triterpene acids such asiatic acid, madecassic acid, and centellic acid (with centellic acid absent in its free state).

Flavonoids: Some of the flavonoids found in *CA* leaves are 3-glucosylquercetin, 3-glucosylkaempferol, and 7-glucosylkaempferol..

Other components: Includes sugars, resin, inorganic acids, and tannins. A-alanine, phenylalanine, glutamic acid, glycine, and aspartic acid are among the amino acids found in the plant. Minerals like calcium, magnesium, sodium, potassium, iron, phosphate, sulfate, and chloride are abundant in its ash. The leaves also contain high levels of vitamins B, C, and G [10, 21].

Pharmacological Activity of *CA*

Main Compounds: Mostly triterpene sections.

Benefits: By promoting collagen synthesis and deposition, these substances aid in wound healing and provide a number of therapeutic and preventive benefits [10, 20].

CA is identified for it's extensive range of pharmacological activities:

Anti-inflammatory activity: By blocking cytokines like TNF-α, interleukins IL-6 and IL-1β, and enzymes like inos and COX-2, Asiatic acid and madecassic acid suppress inflammation.. This down-regulation happens when LPS-induced macrophage cells block NF-κb activation. In mice, madecassoside has been successful in avoiding arthritis caused by collagen II. Rats was administered with 100 mg/kg body weight of *C. Asiatica* ethanolic extracts that demonstrated anti-inflammatory effects similar to those of ibuprofen. Additionally, several *C. Asiatica* preparations have demonstrated efficacy in treating rats with inflammatory bowel illness. Asiaticoside reduced fever and inflammation carried on by LPS in experimental mice, influencing the generation of PGE (2), liver MPO activity, brain COX-2 expression, and serum TNF-α and IL-6. In macrophage cells activated by LPS, Asiaticoside G also showed anti-inflammatory qualities.

Anticancer activity: It has been demonstrated that certain *C. Asiatica* extracts have anti-cancer qualities. Methanolic extracts enable human breast cancer cells to undergo apoptosis, according to *in vitro* research conducted on cell lines like hela, hepg2, SW480, and MCF-7. Aqueous extracts have been demonstrated to chemoprevent colon carcinogenesis in mice and to cause apoptosis in colonic crypts. Human melanoma and colon cancer cells undergo apoptosis when exposed to Asiatic acid. Components in methanol extracts prevent the growth of uterine, gastric, and melanoma cells, while Asiaticoside increases anti-tumor action of vincristine in cancer cells.

Anticonvulsant activity: Rats suffering from seizures, oral treatment of *CA* extracts at dose of 200 mg/kg for a week raised acetylcholine levels and lowered acetylcholinesterase activity, showing anticonvulsant effects because of alterations in cholinergic system.

Antidepressant activity: *CA's* total triterpenes rectified amino acid imbalances and reduced immobility time in mice's forced swimming tests, suggesting possible antidepressant effects. Additionally, these triterpenes decreased blood corticosterone levels, increased brain levels of monoamine neurotransmitters, and improved hypothalamic-pituitary-adrenal axis function [21].

Antioxidant activity: In rats' brains, *Centella asiatica* has potent antioxidant qualities that aid in neuroprotection and the reduction of age-related oxidative damage. It boosted the activity of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (gshpx), and catalase in malignant mice., when exposed to methanol extracts of C. Asiatica. Furthermore, aqueous extracts reduced oxidative stress caused by lead in rats, and the flavonoids in these extracts exhibited potent antioxidant properties. Potential advantages as natural food additives and herbal teas are suggested by these qualities. In rats with lymphomas, a raw methanolic extract of Centella asiatica demonstrated substantial antioxidant activity and notable neuroprotective benefits, successfully shielding rat brains from age-related oxidative damage.The extract's simultaneous treatment dramatically decreased the oxidative stress caused by arsenic in the brain, kidneys, and liver. *C.asiatica* exhibits significant neuroprotective qualities and is efficient in reducing age-related oxidative damage in rat brains, despite the fact that it lacks chelating characteristics [21, 22, 23, 24, 25].

Antiulcer activity: Centella asiatica provides strong protection against pyloric ligation, stress, aspirin, and ethanol-induced stomach ulcers in rats. Asiaticoside-containing water extracts lessen the size of acetic acid-induced stomach ulcers.

Anxiolytic activity: In humans, a single oral dose of *C.asiatica* dramatically decreased the auditory startle response. Pure asiaticoside, methanol, and ethyl acetate extracts, and standardized extracts all showed anxiolytic effects in rats. Patients who received treatment with a concentrated extract of *C.asiatica* experienced a considerable reduction in anxiety, stress, and associated depression.

Cardioprotective activity: In rats, alcoholic extracts of *C.asiatica* dramatically decreased cardiac necrosis. Additionally, extracts showed cardioprotective effects on the antioxidant defense system when the heart was damaged by drugs. In rats and rabbits, myocardial ischemia-reperfusion injury was protected by madecassoside.

Hepatoprotective activity: Rat's liver fibrosis was significantly reduced by *C.asiatica's* total glucosides extract. Hepatoprotection against acute liver damage brought on by toxins was offered by Asiaticoside.

Effect on Skin: Asiaticoside is advised for the treatment of keloids and hypertrophic scars because it promotes the production of collagen in human skin cells. Pruritis and other skin conditions can benefit by *C.asiatica's* alcoholic extracts. Herbal creams contain extracts that lower melanin content while increasing skin hydration, sebum production, and elasticity. Asiaticoside decreases the expression of UV-damaging enzymes and encourages skin cell activities necessary for wound healing.

Immunomodulating activity: Mice's phagocytic activity and white blood cell count are increased by the immunomodulatory actions of *C.asiatica's* triterpenoid saponins. In human blood cells, water extracts promote the growth and synthesis of IL-2 and TNF-α, whereas ethanol extracts have the opposite effect. Human cytochrome P450 isoforms are inhibited by asiatic acid and certain extracts.

Radioprotective activity: *C. Asiatica* aqueous extracts provide greater radioprotection against radiation-induced behavioral alterations in rats than conventional medications. Mice were protected against liver damage and radiation-induced DNA damage by extracts given prior to irradiation.*CA* inhibits UVB induced skin damage via controlling cell division and cell death, according to mirna studies.

Wound healing activity: Multiple studies indicate Centella asiatica's capacity to heal wounds. Rat's wound contraction rates are improved and healing is accelerated when aqueous extracts are included into ointments, lotions, and gels. Additionally, these extracts have been used to heal diabetes patients' wounds without creating any negative side effects. Asiaticoside has been demonstrated to promote wound healing in a number of animal models and facilitate periodontal tissue recovery. In rabbit corneal cells, low doses of aqueous extracts encourage the repair of epithelial wounds. Extracts added to cellulose fiber mats also promote the formation of collagen for use in wound dressings and stay stable for months.

Memory enhancing activity: *CA* has been used historically which improve's cognitive function with intelligence. When extracts were given orally to mice at different phases of development, their brain function improved. Patients' working memory and mood were enhanced by higher dose treatment. It has been demonstrated that the Asiatic acids found in *C.asiatica* improve memory and learning in rats.

Burns: The active ingredients and extracts of *C.asiatica* are beneficial in treating burns caused by exposure to gas, electric current, or boiling water. Antibiotic combinations provide anti-infective properties and aid in the healing process. Low asiaticoside dosages aid in the healing of burn wounds [21].

Gastric ulcer healing: In rats, Asiaticoside successfully inhibited the development of stomach ulcers brought on by cold. Asiaticoside dramatically decreased stress-induced ulcers when taken orally. A plant extract significantly reduced stomach ulcers in Charles-Foster rats brought on by cold and restraint stress; this decrease was associated with a dose-dependent rise in GABA levels in the brain. Additionally, by strengthening the mucosal barrier and lowering free radical damage, *CA* decreased ethanol-induced stomach mucosal lesions. The plant's fresh juice significantly protected experimental ulcer models by strengthening mucosal defense systems. Both Asiaticoside and the plant's aqueous extract had therapeutic efficacy in rats with stomach ulcers caused by acetic acid [25].

Anabolic effect: *Centella asiatica* decreased the death rate from severe protein shortage in albino rats by a low-protein diet. It prevented fatty acid buildup in the liver and increased blood protein nitrogen levels. The rise in hemoglobin content was both statistically significant and large. It also decreased the average blood urea levels [25, 26].

Antiprotozoal activity: *Centella asiatica* as a whole showed antiprotozoal efficacy against Entamoeba histolytica in an alcoholic extract [27].

Antifilarial activity: In dogs naturally infected with *Dirofilaria immitis*, a combination of ethanol extracts from *Acacia auriculiformis, A. Cunn*., and *Centella asiatica* dramatically reduced the filarial levels [28].

Slimming effects: *In vitro*, slimming liposomes which contained extracts of *CA* and esculoside, two microcirculation activators, significantly increased the levels of cyclic adenosine monophosphate (camp) in human adipocytes. A possible *in vivo* slimming impact in human volunteers was suggested by this increase, which was linked to an increase in non-esterified fatty acids in the incubation medium [29].

Conclusion

Centella asiatica, often known as Indian pennywort or gotu kola, has been used for a very long time in traditional medicine in many different cultures, particularly in Chinese herbal medicine and Ayurveda. The plant has several pharmacological effects, including anti-inflammatory, antioxidant, anticancer, and wound-healing qualities, due to its large variety of bioactive components, comprising of triterpenoids, saponins, flavonoids, and alkaloids.

As modern study continues to support these traditional use, *C.asiatica* has gained international attention and is now listed in a number of pharmacopoeias. Nevertheless, the plant is now considered a vulnerable species due to rising demand and unsustainable harvesting methods. In order to guarantee the continuous supply of this priceless plant, conservation initiatives and sustainable farming methods are required.

C.asiatica has demonstrated potential in therapeutic settings for treating chronic illnesses, boosting mental clarity, and promoting healthy skin. When used appropriately and according to a patient's needs, its safety and effectiveness highlight its potential as a supplemental therapy in modern medicine. To completely comprehend its methods of action, maximize its therapeutic application, and guarantee its sustainable supply, additional research is necessary.

The incorporation of *Centella asiatica* into contemporary medical treatments marks a substantial breakthrough in the search for safe and efficient remedies for a range of illnesses. It is a useful tool in the ongoing investigation of plant-based medications because of its extensive pharmacological profile and historical relevance.

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