Review Article

An update on the ayurvedic herb *Centella asiatica*

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ABSTRACT

Plants have been demonstrated extraordinary source of medicine and recently focus on medicinal plant research has increased. For its traditional usage and medical benefits in the treatment of numerous ailments, *Centella asiatica* is widely known. The utilization of this plant as a whole and isolated bioactive chemical are both commonly employed to cure a variety of human illnesses, according to published research. According to reports, *Centella asiatica* has a range of pharmacological properties, including antibacterial, anticancer, wound-healing, neuroprotective, immunomodulatory, anti-inflammatory, hepatoprotective, insecticidal, and antioxidant properties. Asiatic acid, asiaticosside, and madecassoside are among the several flavonoids and terpenoid chemicals found in *Centella asiatica*, each of which is known for its pharmacological importance. The significant medicinal plant *Centella asiatica* is identified and described as bioactive components, pharmacological characteristics, in vitro propagation, and traditional usage was all succinctly covered in the present review.

Keywords: *Centella asiatica*, Medicinal plants, Triterpenes, Terpenoids phytochemistry, Pharmacology.

For hundreds of years, Malaysia and other countries of Asia have employed the traditional herbal remedy *Centella asiatica* (L) Urban (Umbelliferae) [1]. In Malaysia, it is referred to as pegaga, and in America, gotu kola and pennywort. In addition to its typical usage as a medicine, it is consumed fresh as a salad, cooked as a vegetable, and blended as a beverage [2].

It is also utilized in nutraceutical products, making it a crucial commercial plant. Even though its primary use has been to promote wound healing, this tropical plant has reportedly been used for a variety of medical conditions, including the treatment of wounds, asthma, ulcers, leprosy, lupus, vein diseases, memory improvement [3], as an antidepressant [4], antibacterial [5], antifungal [6], psoriasis [7], and anti-cancer agent. Even though its primary use has been to promote wound healing, this tropical plant has reportedly been used for a variety of medical conditions, including the treatment of wounds, asthma, ulcers, leprosy, lupus, vein diseases, memory improvement, as an antidepressant, anti- bacterial, antifungal, psoriasis, and anti-cancer agent [1].

According to numerous studies, the triterpenes in this plant are thought to be its biologically active components and the presence of several triterpenes, including asiatic acid, madecassic acid, asiaticosside, and madecassoside is primarily responsible for this plant's medicinal properties [8]. Triterpenes, which make up the majority of *Centella asiatica*, have been identified as potential biomarker components [2].

Asiatic acid was the only triterpene component proven to stimulate collagen formation in human fibroblasts in cell culture experiments. Other studies have demonstrated that the plant's asiatic acid, madecassic acid, and asiaticosside, as well as their mixtures, were able to stimulate collagen synthesis in skin fibroblast culture whereas the plant's asiaticosside and madecassoside, respectively, stimulated type-I collagen and type-III collagen. The same three triterpenes, asiatic acid, madecassic acid, and asiaticosside, were present in a titrated extract of *Centella asiatica*, which increased the synthesis of fibronectin and collagen by 20–35% [9]. *Centella asiatica* has been utilized in skin care products to improve the appearance of skin and restore skin firmness and elasticity because of its capacity to increase collagen [10].

When topical extract formulations were used on rats with experimental wounds, the epithelia grew more quickly and the rate of contraction during healing increased [11]. Moreover, in patients with venous hypertension, *Centella asiatica* extract increased capillary permeability and the microcirculation effect. Moreover, the extract was observed to influence lipolytic activity, which increased the amount of cyclic adenosine monophosphate (cAMP) in human adipocytes and had a slimming effect on people [12].

The antioxidant ability was found to be neuroprotective and able to shield the rat brain from oxidative damage caused by aging [13]. Several studies have revealed that *Centella asiatica* extracts have antioxidant effects [14]. Asiaticosside and

flavonoids have reportedly been linked to the induction of antioxidant levels during the healing of wounds [15]. No reports are indicating that *Centella asiatica* extracts can block UV rays. The purpose of this investigation is to assess the triterpene makeup of *Centella asiatica* and its biological activity about the enhancement of its anti-inflammatory, antioxidant, lipolytic, and UV protection characteristics [16]. Vernacular names are [17] – Mandookaparni (Hindi), Gotukola (Kannada), Vallarai (Tamil), Kodagam (Malayalam), Bekaparanamu (Telugu) and Thankuni (Bengali) (Table 1).

Taxonomical Classification

Table 1. Taxonomical classification of *Centella asiatica* [17]

Kingdom	Plantae
Division	Tracheophyta
Class	magnoliopsida
Order	apiales
Family	Apiaceae
Genus	Centella
Species	*C. asiatica*

Habitat

Centella asiatica is found throughout tropical and subtropical regions of India up to an altitude of 600m. The plant is indigenous to Southeast Asia, India, Sri Lanka parts of China the western South Sea Islands, Madagascar, South Africa, the southeast USA, Mexico, Venezuela, Columbia, and eastern South America [18].

Botanical Description

Stem: glabrous, striated, rooting at the nodes. Flourishes extensively in shady, marshy, damp, and wet places such as paddy fields, and riverbanks forming a dense green carpet, and rather than clayey soil, the sandy loam (60% sand) is found to be the most fertile soil for its generation.

Seed: pendulous embryos which are laterally compressed [19].

Leaves: 1-3 from each node of stems, long petioles, 2-6 cm long and 1.5-5cm wide, orbicular-reniform (Figure 1).

Figure 1: *Centella asiatica* leaf

Flowers: fascicled umbels, each umbel consisting of 3-4 white to purple or pink flowers, flowering occurs in the month of April-June (Figure 2).

Figure 2: *Centella asiatica* flower

Fruits: borne throughout the growing season in approx. 2 inches long, oblong, globular in shape, and strongly thickened pericarp (Figure 3).

Figure 3: *Centella asiatica* fruit

Phytochemistry

C. asiatica contains a variety of amino acids, flavonoids, terpenoids, essential oils, alkaloids, and other compounds. Most phytochemical studies focused on leaves, and the constituents differ depending on geographical distribution. For a very long period, *C. asiatica* has been utilized as a natural source of medicine. Pentacyclic triterpenes, such as Asiatic acid, madecassic acid, asiaticosside, and madecassoside, among others, are the primary active components of *C. asiatica*. To date, isoprenoids (sesquiterpenes, plant sterols, pentacyclic triterpenoids, and saponins) and derivatives of phenylpropanoid have been found as phytochemicals from *C. asiatica* (eugenol derivatives, caffeoylquinic acids, and flavonoids) [19].

Pharmacological Activity

Antiulcer activity: An Acute toxicity study was carried out in which the animals were treated with the rhizome extract at a dose of 2 and 5 g/kg of *C. asiatica* leaf extracts and were kept under observation for 14 days. All the animals remain alive and did not manifest any significant visible signs of toxicity at these doses. At any point during the observation period, there were

no unusual behaviors, macroscopic findings, symptoms, or body weight changes. The hematology and serum biochemistry parameters like triglycerides, creatinine, urea and hemoglobin, AST, ALT, and ALP of the extract-treated rats showed no significant change compared to the control normal rats. The oral lethal dose (LD50) for the male and female rats was larger than 5 g/kg body weight, suggesting that the extract is fairly safe even at these higher concentrations and had no acute toxicity [20].

Anti-diabetic activity: Alloxan monohydrate solution of 10 mg/ml was prepared in ice-cold citrate buffer (0.1M); the pH of the ice was kept at 4.5 and was administered to the rats within 5 mins at a dose of 50 mg/kg body weight intraperitoneally. The fasting blood sugar levels of each of the rats were checked every day with an autoanalyzer (Glucometer) glucose kit. After 8 days, animals with fasting blood sugar levels of 250 mg/dl and above were considered to be diabetic and were used for the study and assigned into five groups of five rats each. Group I served as the negative control and received tween 80 solution (solvent used to dissolve the extract) (10 ml/kg), group II–IV received the *C. asiatica* extract at the dose of 250, 500, and 1000 mg/kg respectively while group V served as the positive control and received the standard reference drug glibenclamide (2 mg/kg) all by gastric gavage. The blood glucose levels of the rats were measured at 0, 1, 2, and 3 h after administration of the drug and extracts. Blood samples were collected by tail snip and the blood glucose was measured with an autoanalyzer (Glucometer) glucose kit. At the end of the experiment percentage reduction of the glucose levels of the rats at the 3rd hour was calculated [21].

Anti-inflammatory activity: This study investigated the antipruritic and anti-inflammatory effect of *Centella asiatica* extract in rats and anti-allergic in vitro using sheep (*Capra hircus*) serum method and compound 48/80 induced mast cell degranulation method, compared with standard drug ketotifen fumarate. Orally administered *Centella asiatica* extract was tested for its ability to treat pruritis in rats. Chlorpheniramine maleate was used as the standard medication, and carrageenan paw-induced inflammation was used to test the plant's ability to treat inflammation. The results show that the extracts of *Centella asiatica* exhibited antiallergic, anti-pruritic, and anti-inflammatory activities [22].

Cytotoxic and anti-tumor activity: The antioxidant activity of AE of *Centella asiatica* was evaluated by its ability to scavenge DPPH free radicals. The radical scavenging activity of the compounds can be measured by the decolorizing effect following the trapping of the unpaired electrons of DPPH. The AE showed high antioxidant activity, with an IC_{50} value of 31.25 µg/mL. Ascorbic acid and butylated hydroxytoluene (BHT) produced IC_{50} values of 2.50 µg/mL and 7.58 µg/mL, respectively. Previous research suggests that the presence of compounds with free hydroxyls may be the cause of the potent antioxidant action of polar extracts. Since they contain a lot of hydroxyls that act as hydrogen donators, flavonoids have a perfect structure for scavenging free radicals in this context, making them significant antioxidant agents [23].

Neuroprotective activity: The neuroprotective effect of *C. asiatica* and its major triterpene saponosides has been extensively studied through different experimental models on animals such as passive avoidance and elevated-plus labyrinth tests for memory enhancing effect. By administering the extract at doses of 100, 200, and 300 mg/kg (b.w.), the extract was tested in rats to see how it affected intra-cerebrovascular streptozocin-induced memory linked to the sporadic type of AD. Oxidative stress markers like glutathione, superoxide dismutase (SOD), and catalase (CAT) were also measured. While a clear dose-dependent improvement was observed in memory-related behaviors in the rat group administered the extract at 200 mg/kg (b.w.) dose, a serious decrease in malondialdehyde (MDA) and an increase in glutathione and CAT levels was recorded, which led to a final suggestion by the authors that *C. asiatica* extract has a positive effect on memory that is also related to its remarkable antioxidant effect. The same research group subjected this extract to passive avoidance and spontaneous locomotor activity behavioral tests using pentylenetetrazole-(PTZ-) induced memory loss in rats at 100 and 300 mg/kg (b.w.) doses. After the behavioral tests, the rat brains' MDA and glutathione levels were assessed as oxidative stress markers, which are strongly linked to neurodegeneration. As a result, all test parameters significantly improved when the extracts were administered at the specified levels [24].

Cardioprotective activity: Laboratory-bred Sprague–Dawley rats of either sex weighing 200–350 g were selected. The rats were maintained under standard laboratory conditions at 25±2 °C, relative humidity. In Group-I (control) animals, the percentage of left ventricular necrosis was reported to be 50.911.90. PLVN was considerably and dose-dependently reduced in the treated groups. Lipid peroxide concentrations were observed to be 27.571.42 nmol ml1 in serum and 109.242.77 nmol g1 in cardiac tissue in Group-I animals. Whereas in the treated groups, the lipid peroxide levels were found to be 17.68±0.91 nmol ml^{-1}, 12.20±0.86 nmol ml^{-1}, and 5.85±0.5 nmol ml^{-1} in serum [25].

Skin protective activity: During clinical irradiation, *Centella asiatica* may help avoid radiation-induced behavioral abnormalities. The plant extract exhibited radioprotective qualities, and the pretreatment of mice with it before gamma radiation exposure was successful in preventing radiation-induced liver damage. Extractsd obtai- ned under different extraction conditions show different extraction patterns, as well as different extraction yields, possibly due to the different polarities, the solubility of the solvents, and the effects of the extraction temperature [26].

Memory enhancing activity: Results of the preliminary screening showed that oral administration of *C. asiatica* for fifteen days enhanced the learning and memory in three months old mice as assessed by the radial arm maze test. Spatial memory is frequently tested using the radial arm maze. The number of accurate entries increased dose-dependently during the radial arm maze test. It can be shown from this that the extract improved cognitive abilities in young adult mice [27].

Wound healing effect: The effect is observed with a quicker wound contraction, probably owing to the stimulation of fibronectin and collagen I synthesis and matrix remodeling. These two are characteristic of the proliferative stage of the wound healing process. Additionally, it has been discovered that *C. asiatica* is effective in maintaining connective tissue and bolstering veins that are weak. As a result, its use may be advantageous for the treatment of hypertensive microangiopathy and venous insufficiency. Its oral supplementation has been demonstrated to promote fibroblast division after injury in addition to collagen synthesis and cellular proliferation. Additionally, it might improve wound contraction and re-epithelialization in incision model wounds (p 0.001). *C. asiatica* has also been shown to improve the tensile strength of the newly formed skin of the wound in animal studies, which could lead to a decrease in the wound area and faster healing [28].

Hepatoprotective activity: A safety evaluation using rodents to determine appropriate conditions to use. By conducting the 'single and 14-day repeated oral study in rodents', we confirmed that the non-toxic amount of CA-HE50 was 2 g/kg/day. Therefore, a study on the protective effect of CA-HE50 on the liver using CA-HE50 doses of 50, 100, and 200 mg/kg/day. Due to the strain of metabolism on the liver, liver enlargement and edema frequently arise when liver failure is caused. The study found that when APAP was used to cause liver damage, the weight of the liver decreased (p 0.05). When APAP caused liver toxicity, a decrease in liver weight took place between six and twenty-four hours later and was accompanied by a rise in blood ALT and AST values, which suggested liver cell lysis. We gave APAP, just like in the first trial, and weighed the liver 24 hours later. The decrease in liver weight caused by APAP in our study was likely due to liver cell injury (lysis) caused by APAP toxicity. Provision of 200 mg/kg CA-HE50, however, prevented the APAP-induced decrease in liver weight. Thus CA-HE50 helps to protect against liver injury [29].

Anti-cancer activity: Asiatic acid was evaluated for antiproliferative effect in lung cancer cells using MTT assay. Oral administration of AA inhibited weight and tumor volume significantly in the lung cancer xenograft model. In a different study, asiatic acid demonstrated dose-dependently triggered apoptosis and lowered viability in human melanoma SK-MEL-2 cells. It reduced the focal adhesion kinase (FAK) expression levels, and the probable mechanism of AA may be connected to the suppression of signal transduction carried out by FAK. Asiatic acid, asiaticoside, and madecassic acid was the major component of the titrated extract of *C. asiatica*, and asiaticoside reduces melanogenesis in B16F10 mouse melanoma by checking tyrosinase mRNA expression [30].

Anti-bacterial activity: Methanol hot extract from *C. asiatica* leaves was taken to check the antibacterial activity which was assessed by zone of inhibition and minimum inhibitory concentration (MIC) value (2 µg/disc) by disc diffusion method. In a study, it was discovered that essential oil extract had antibacterial activities against both Gram-positive and Gram-negative bacteria, including Escherichia coli, Pseudomonas aeruginosa, and Shigella sonnei, with MIC values ranging from 1.25 to 0.039 mg/ml. Bacillus cereus and Listeria monocytogenes 10403S were selected to study the antibacterial activity in *C. asiatica* under both normal and osmotic stress conditions. At 95% ethanolic extract, antibacterial activity was enhanced twice under osmotic stress conditions [31].

Anti-fungal activity: The petroleum ether, ethanol, chloroform, n-hexane, and aqueous extract of *C. asiatica* showed activity against Aspergillus niger and C. albicans with a zone of inhibition of 14, 16, 13, 13, and11 mm and 13, 15, 15, 11, and 9 mm, respectively. The control ketoconazole (10 g) demonstrated a 12 mm inhibition. When Aspergillus flavus was exposed to an ethanolic extract of *Centella asiatica*, Penicillium citrinum showed the greatest antifungal activity (% mycelial inhibition = 26.3 mm).100% ethanolic extract of *C. asiatica* showed a zone of inhibition of 15.4 mm against A. niger [32].

Antioxidant: *C. asiatica* extract and powder were evaluated for a reduction in oxidative stress in Sprague-Dawley rats. Results showed a decrease in the generation of ROS and oxidative stress in the rats. Essential oil of *C. asiatica* extracted through steam distillation showed to be an excellent antioxidant for food containing lipids. Its activity was quite comparable with the synthetic antioxidant butyl hydroxyanisole (BHA). Polyphenol, flavonoid, β-carotene, tannin, Vitamin C, and DPPH compounds are readily found in *C. asiatica* contributing to significantly higher antioxidant activity in the herb. Crude methanolic extract on continuous supplementation for 14 days increased the level of antioxidant enzymes and the ascorbic acid level was reduced in lymphoma-bearing mice [33].

Anti-depressant: Compared to diazepam *C. asiatica* possesses an antianxiety effect but does not affect behavioral despair. Total triterpenes and imipramine from *C. asiatica* were evaluated for antidepressant activity using a forced swimming test, the result showed a reduction in stillness duration and regulated amino acid levels. In another study, a decrease in corticosterone levels in serum and enhanced 5-HT, NE, DA, and their metabolites 5-HIAA and MHPG in rat brains were observed. The standardized extract showed a reversal of

physiological and behavioral changes following OBX-induced depression in rats. A forced swim test was performed in male Sprague-Dawley rats treated with asiatic acid [34].

Traditional uses: *Centella asiatica* has traditionally been used to treat a variety of ailments. Triterpene fractions, which make up the majority of *C. asiatica's* constituents, have a wide range of protective and therapeutic benefits. One of these effects is a significant influence on collagen synthesis and deposition during wound healing. Several microcirculatory issues, skin inflammation (eczema, atopic dermatitis, leprosy, varicose ulcers, etc.), fever, intestinal issues, and genitourinary diseases are all treated with titrated extract of *Centella asiatica* (TECA). Due to the presence of several saponin constituents, such as asiaticosside, asiatic acid, madecassic acid, and some other bioactive compounds, *C. asiatica* exhibits a wide range of pharmacological activities, including antibacterial, antidepressant, antiemetic, antineoplastic, antioxidant, antithrombotic, anxiolytic, gastroprotective, immunomo- dulatory, antigenotoxic, nerve regenerative, reproductive, and wound healing.

CONCLUSION

Centella asiatica is a well-known plant in Indian medicine, and folk medicine believes it can help with heart and hepatic problems, ulcers, and other ailments. Plant components including leaves, fruit, stem, and even roots are utilized for a variety of uses. Chemically, *Centella asiatica* includes amino acids, flavonoids, terpenoids, essential oils, and alkaloids among other physiologically active phytoco- nstituents. It is also important in a variety of disorders for which there is plenty of scientific evidence and data. In essence, *Centella asiatica* is a versatile medicinal plant.

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