



Review Article

Review on Multidimensional Application of *Centella asiatica*.

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ARTICLE DETAILS*Article history:*

Received on 11 April 2019

Modified on 10 May 2019

Accepted on 18 May 2019

*Keywords:**Centella asiatica*,

Ethnobotanical,

Mental Ability Triterpenoid,

Pharmacologically Active.

ABSTRACT

Ayurveda is the ancient valuable medical science in India. It deals with to accomplish physical, mental, social and spiritual well-being by practicing preventive, health promoting approach towards life. Now a day's use of herbal products has been tremendously increased in developing countries. *Centella asiatica* has gained a lot of attention in both business and scientific communities due to increased demand in terms of medicines, food, waste management, and agricultural practices. Commercialization and extensive research that is carried on *Centella asiatica* have to lead to the urgent need for the conservation of the plant from the perspectives of pharmacology, dietary, ethnobotanical and biotechnology. Some of the marketed products which have used *Centella asiatica* as the main ingredient which improve mental abilities, vascular support, blood circulation, and psoriasis. The triterpenoid compounds are responsible for the pharmacologically activity of *Centella asiatica*. This review provides its basic character of the plant and significance as an economic plant with medicinal value.

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INTRODUCTION

Most of the medicinally important natural compounds are derived from plants. They are either used directly or indirectly for a variety of functions. Mankind as a whole is dependent on plants for various basic requirements like shelter, medicine, food, and other purposes. Hence plants will remain industrially, environmentally, economically important for the survival of life [1].

Centella asiatica (CA) also called as Gotu kola, asiatic pennywort is a herbaceous frost-tender perennial plant that belongs to the family Apiaceae. *Centella asiatica* occurs in marshy areas like wet lawn, the margin of the ponds and wet ditches up to an altitude of 1800m. It is an odorless, tasteless plant whose leaves are oval in shape, clustered at nodes, has reniform outlines, petiolate and glabrous in nature. Leaves are 1-2 cm long and are held erect. The stem of this plant is soft and hairy (Figure 1). Roots go the soil directly after emerging out nodules [2]. Gotu kola contains the group of triterpenes called asiaticosides that has a strong antioxidant property.

**Figure 1:** *Centella asiatica*.

This herb has the capability of acting against various skin disorders like lupus, leprosy, eczema, psoriasis and can also be employed for improving the memory and relieve anxiety [3]. The whole plant of CA possess medicinal benefits and widely used as a blood purifier as well as for treating high blood pressure. It is the main herb in ayurveda for revitalizing the nerves and brain cells. Eastern healers relied on CA for treating conditions like depression and other emotional disorders. In the middle of 20th century *Centella asiatica* and its alcohol extract has been reported for the leprosy treatment [4].

The Indian government has invested quite a lot of resources in conducting the experiments to know the mechanism of action of CA. However, these researchers revealed the possible

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mechanisms of the herb as an anti-inflammatory, antioxidant, metal chelation and also the cholinergic actions. CA possessing multiple health benefits is the most studied herb in terms of mechanism of action [5].

Table 1: Nomenclature of *Centella asiatica* [6]

| Classification | Name |
|----------------|----------------------------------|
| Kingdom | <i>Eukaryota</i> |
| Subkingdom | <i>Embryophyta</i> |
| Division | <i>Spermatophyta</i> |
| Subdivision | <i>Angiospermae</i> |
| Class | <i>Dicotyledoneae</i> |
| Subclass | <i>Rosidae</i> |
| Superorder | <i>Aralianae</i> |
| Order | <i>Araliales (Umbelliflorae)</i> |
| Family | <i>Apiaceae or Umbelliferae</i> |
| Subfamily | <i>Hydrocotyle</i> |
| Genus | <i>Centella</i> |
| Species | <i>Centella asiatica</i> |

Morphology

Centella asiatica is a prostrate, faintly aromatic, stoloniferous, perennial, creeper herb, attains height up to 15cm (6 inches). The stem is glabrous, striated, rooting at the nodes. *Centella asiatica* flourishes extensively in shady, marshy, damp and wet places such as paddy fields, river banks 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 regeneration. The leaves, 1-3 from each node of stems, long petioles, 2- 6cm long and 1.5-5cm wide, orbicular-renaliform, sheathing leaf base, crenate margins, glabrous on both sides. Flowers are in fascicled umbels, each umbel consisting of 3-4 white to purple or pink flowers, flowering occurs in the month of April- June. Fruits are borne throughout the growing season in approx 2 inches long, oblong, globular in shape and strongly thickened pericarp. Seeds have pedulous embryo which is laterally compressed [6]. Nomenclature of *Centella asiatica* is given in Table 1.

Chemical Constituents of *Centella asiatica*

The characterization studies have reported that the primary active constituents of *Centella asiatica* are saponins. It is also called triterpenoids. Which include asiaticoside, linked to anaglyconeasiatic acid, madecassoside and madasiatic acid [6]. In addition, the plant contains the following chemical constituents which are

given in Table 2, structure in Figure 2 and Table 3.

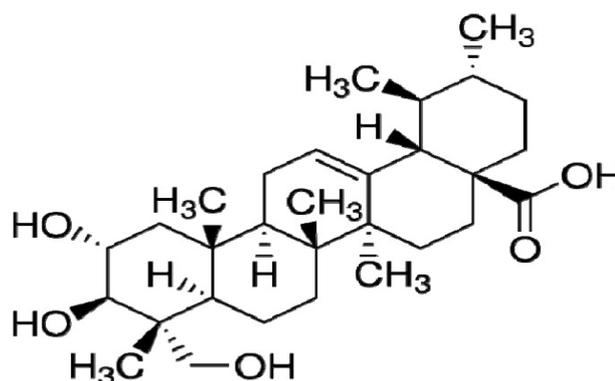


Figure 2: Structure of asiatic acid and other derivatives.

Table 2: Chemical constituents of *Centella asiatica* [6]

| Main Group | Constituents |
|---|--|
| Essential oil (0.1%) | Terpene acetate, germacrene, caryophyllene, P-cymol, pinene |
| Triterpenic acids | Asiatic acid, 6- hydroxyasiatic acid, madecassic acid, madasiatic acid, betulinic acid, thankunic acid, isothankunic acid |
| Triterpenic acid sugar esters (saponins or pseudo saponins) | Asiaticoside (major components) Asiaticoside A, asiaticoside B, Madecassoside A & B, braminoside, brahmoside, thankuniside, isothankuniside. |
| Flavone derivatives | Quercetin glycoside, kaempferol, glycoside and in free form astragalin |
| Sesquiterpenes | Caryophyllene, elemene and bicycloelemene, trans- farnese, ermacrene- D |
| Triterpenic steroids | Stigmasterol, sitosterol |
| Carbohydrate | Glucose, mesoinositol, centellose, pectin, arabinogalactan |
| Vitamins | Ascorbic acid, nicotinic acid, β -carotene |
| Minerals | Calcium, phosphorus, iron, potassium, calcium, magnesium, manganese, zinc, |
| Amino acids | Alanine, arginine, aspartic acid, glutamic acid, leucine, iso-leucine, valine, methionine, lysine, histidine, tyrosine, phenylalanine, threonine, glycine, serine, |

Table 3: Main chemical constituents and its basic structural groups [6]

| | R1 | R2 | R3 | R4 | R5 | R6 | R7 |
|-------------------------|-----------------|----|--------------------|--------------------|----|-----------------|-----------------|
| Asiatic acid | COOH | H | CH ₂ OH | CH ₃ | OH | CH ₃ | CH ₃ |
| Madescassic acid | COOH | OH | CH ₂ OH | CH ₃ | OH | CH ₃ | CH ₃ |
| Madasiatic acid | COOH | OH | CH ₃ | CH ₃ | OH | CH ₃ | CH ₃ |
| Ursolic acid | COOH | H | CH ₃ | CH ₃ | H | CH ₃ | CH ₃ |
| Asiaticoside | COO-glu-glu-rha | H | CH ₂ OH | CH ₃ | OH | CH ₃ | CH ₃ |
| Tankunic acid | COOH | OH | OH | CH ₂ OH | H | CH ₃ | H |

Multidimensional Potential and Utilities of *Centella asiatica* (CA)

Nutritional Value

Centella asiatica is consumed in the form of green leafy vegetable in some parts of Asian countries. The nutritional status of CA is quite high and it is extensively used as traditional medicine in Southeast Asia. This plant is found to be rich in medicinally important compounds like carotenoids and triterpenoids. It can be consumed as juices, green leafy vegetables, drinks, and other food products [6]. Macronutrient found in CA includes carbohydrates, proteins, and fibers. It is also rich in vitamin B, C, E, and K vitamins, including minerals like calcium, magnesium, iron, and potassium. It also contains some important phytonutrients like zeaxanthin, neoxanthin, lutein and β carotene which offers the protection to human cells by protecting them from loss of vision and other age-related problems [7].

The whole CA plant is found to have medicinal properties. It has a somewhat bitter and sweet taste. It has been extensively used as a functional food, and there are food products already in the market with Gotu kola as an active ingredient. It has been most widely investigated for the neuro pharmacological property. Saponins and bacosides are responsible for this property of CA [8].

Centella asiatica is rich in dietary fibers where the fibers play a significant role in health conditions like hypertension, obesity, coronary heart diseases, GIT disorders and various other disorders [9]. It's an abundant source of potassium (345 mg) and calcium (171 mg), where potassium intake reduces the risk of kidney diseases and calcium intake is responsible for bone development. A good amount of calcium intake in childhood will help in providing the required bone mass in adulthood. CA can be used as an inexpensive source for both calcium and potassium [10]. Carotenoids found in CA can be converted to

vitamin A in the body which possesses the antioxidant property and helps in preventing some types of cancer, improvement of the immune response to infection and heart diseases. The herb has to be free from any kind of nematode infections before its use [11].

Wound Healing

Triterpenes are the major constituents of gotu kola which are responsible for most of its pharmacological property. Important ones are brahmoside, brahminoside, brahmic acid, asiatic acid, asiaticoside and madecosside. asiaticoside and madecosside possess wound healing properties and these constituents predominate in leaves. Traditionally CA extracts have been used for wound healing and even the research conducted is in support of this claim. Sunil kumar *et al.* conducted the study to evaluate the extract of CA on the open wounds of rats. Different formulations of CA (cream, gel, and ointments) were applied to the open wounds of rats three times daily (24 days), which resulted in increased collagen synthesis and cellular proliferation at the wound site which leads to increase in the rate of contraction of wounds and also the epithelialization. The gel formulations showed better healing when compared to that of cream and ointments [12].

Asiaticoside, an important constituent of CA is said to possess the wound healing property by increasing angiogenesis and collagen formation. QiangHou *et al.* conducted the study to know the wound healing property of *asiaticoside* and madecassoside. This study showed that both play a role in the wound healing by reducing the oxidative stress, promoting collagen production and vasodilation [13]. Since antioxidants have been shown the significant action in the wound healing process Shukla A *et al.*, investigated the possible effect of asiaticoside on the levels of antioxidants in the wound. In this experiment, asiaticoside was applied for seven days twice daily (0.2%, topical) to excision type cutaneous

wounds in rats. This led to increase the enzymatic and non-enzymatic antioxidants in newly formed tissues. However, when the treatment was continued for 17 days, it showed no significant increase in the antioxidant levels. The present study concluded that asiaticoside might lead to the induction in the antioxidant levels in the primary stage of wound healing procedure, which is an important contributory factor for healing [14].

Suguna L *et al.* experimented to know the effects of alcoholic extract of CA on rat dermal wound healing. CA extract was administered orally and topically to know the healing action. This showed to increase the collagen synthesis and cellular proliferation on the wound site which was witnessed by the increase in the content of protein, DNA and collagen content in the granulation tissue site. When compared to the control groups the rate of wound contraction was faster in the CA treated groups. The results indicated that CA extracts showed different actions on the various phase of wound healing [15].

Centella asiatica in Alzheimer's

Chemical constituents such as brahminoside, brahmoside, brahmnic acid and isobrahmnic acid show anticonvulsant, sedative and psychotropic activity and the poly herbal formulation called "mentat" helps to increase the memory power and concentration in children. CA (*Centella asiatica*) is the most studied herb for its nootropic action, and it is believed to be a promising agent for treating alzheimers in future because of its anti-amyloid property, cholinergic and antioxidant property. Oxidative damage is the main reason for many for the age-related disorders, and free radicals like hydroxyl (OH), hydrogen peroxide, peroxy nitrite, and superoxide dismutase are responsible for this kind of damages. Our body itself has several enzymatic and nonenzymatic mechanisms to act against these free radicals. The imbalance between the production of free radicals and protective mechanisms are responsible for the damage in elderly people [16].

Dhanasekaran M *et al.* studied the effect of CA extract on the beta-amyloid levels in the hippocampus of Alzheimer's disease in the animal models. This study investigated whether the CA extract can change the amyloid pathology in mice starting at two months of age before the onset of detectable amyloid deposition and continued for 2-8 months. The study resulted in

the decrease in amyloid beta with 2.5mg/kg of CA extract for the treatment period of 8 months, and it also confirmed CA extract acts an antioxidant agent *in-vitro* by scavenging the free radicals and offers protection against DNA damage [17].

Anil Kumar *et al.* investigated the effect of *Centella asiatica* against Colchicine-Induced Cognitive Impairment in rats. Colchicine was administered to the rats, and later various biochemical parameters were analyzed. Intracerebro ventricular Colchicine resulted in oxidative stress and memory impairment. Chronic Treatment pattern with *Centella asiatica* (150-300mg/kg) for 25 days beginning from 4 days prior to the administration of colchicine resulted in the reduction of the oxidative stress and memory loss significantly. Thus this result concluded the protective action of CA against colchicine-induced memory loss [18].

Gastric Ulcer

Cheng CL *et al.* studied the effect of CA extract on the prevention of the gastric lesions that was induced by the administration of ethanol in rats. The transmucosal potential difference in the gastric *ex vivo* chamber was reduced by the ethanol administration, and CA helped in the acceleration of recovery and on the other hand when CA was given by orally before ethanol administration inhibited the formation of gastric lesions. This experiment concluded that the CA prevents the gastric lesions by reducing the devastating effects of free radicals and strengthening the mucosal barrier [19].

Mahmood A A *et al.* investigated the anti ulcer activity of CA extract against the ethanol-induced injury of gastric mucosa. One hour before the administration of ethanol, rats were orally administered with carboxymethyl cellulose (ulcer control group), omeprazole (reference group) and different doses of CA leaf extract (experimental group). Results showed that pretreatment of rats with CA leaf extract showed prominent protection from the gastric mucosal injury when compared to that of the ulcer control group which showed a severe injury. Additionally, even histological studies showed that the experimental groups pretreated with CA offered protection of gastric mucosa with the absence of edema and leucocytes infiltration [20].

Antidepressant Activity

Centella asiatica is a multipurpose miraculous herb that has several significant therapeutic

actions (such as hypnotic and sedative activity.) Padmavathi golla *et al.* investigated the antidepressant activity of *Centella asiatica* in mice by using the forced swimming test. It was found out doses of 10 mg and 20mg/kg of *Centella asiatica* decreased the immobility activity in treatment groups when compared to that of control and standard group, thereby proving the antidepressant action. Moreover, the dose of 20mg/kg (*C.asiatica*) showed the antidepressant action that is almost similar to 10mg/kg of imipramine (standard drug) [21].

Ceremuga TE *et al.* investigated the antidepressant as well as the anxiolytic property of CA in the male Sprague rats. The potential of the asiatic acid in the modulation of the GABAA receptors was studied. The rats were administered with Asiatic acid extract just before 30 mins of testing via intraperitoneal route, and it was tested for the elevated plus maze and forced swim test. Results suggested that Asiatic acid modulates the benzodiazepine site on GABAA receptors suggesting its antidepressant activity [22].

Antifertility

Irfan yunianto *et al.* investigated the antifertility properties of *Centella asiatica* in treated male rats as a contraceptive agent to identify the sperm proteomic changes. Treated groups received around 300mg/kg of an ethanolic extract of *Centella asiatica* for 42 days. Soon after the treatment period number of implantation sites was recorded and proteomic changes in the sperm were analyzed. Results showed that the number of implantation sites, as well as the percentage of infertile rats, decreased in the treatment group. This revealed the infertility activity in male rats with the administration of *Centella asiatica* and the proteins that were obtained could help in understanding the adverse effect of the same [23].

Other Economic Utilities

Centella asiatica is thought to be an ideal plant for monitoring the contamination of soil and water because of its high sensitivity. It has been reported for phytoremediation due to its hyperaccumulation ability. Heavy metal poisoning will cause serious harm to human health; hence the pollutant cleanup is an important step in controlling heavy metal risk. Conventional steps for the clean-up comes with a huge amount of economic loss and ineffective in some cases. Phytoremediation is one such

technique which is effective with minimal cost. Since these plants grow in the aquatic ecosystem especially which are used for waste disposal of industrial effluents and sewage disposal they are exposed to heavy metal pollution. It's been reported as an accumulator for lead, manganese, and chromium from an artificially contaminated soil. One of the studies conducted by Fazilah Abd Manan to evaluate the phytoremediation potential of the medicinal plant CA plant was made to grow in contaminated soil from the industrial area and then the plant growth, as well as the accumulation capacity, was monitored. This study concluded that CA was tolerant towards lead, zinc, and copper and suitable for phytoextraction [24].

Micro Propagation

When compared to conventional propagation method, plant tissue culture techniques is an excellent strategy to get the continuous supply of the plant throughout the year in fixed space and time via clonal mass multiplication. It also serves as a technique for the conservation of the medicinally and economically valuable plant.

According to Gupta Set *al.*, one stop solution for all the major concerns that are related to the overexploitation, disease resistance and increasing the nutritional values of the plant can be met by the *in-vitro* regeneration and multiplication method. It can also be used for the commercial production of metabolites. Therefore all the present research is focused on the optimization of the *in-vitro* propagation methods by using the different parts of the *Centella asiatica* plant for the purpose of meeting all the commercial demands [25].

Study on the micro propagation of *Centella asiatica* has been done by Das Ret *al.*, where the multiple shoot regeneration of high frequencies was obtained from the shoot tip cultured on MS (murashigeskoog) media. Explants for about 10.2 ± 0.38 were obtained on an average. The plantlets that were grown *in-vitro* showed 80% survival rate when they were transferred to natural conditions [26].

The Dose of *Centella asiatica*

The daily dose of CA was reported 600mg per day by dried leaf or by infusion. In the market, capsules with a dose of 300 to 680mg are available which are used as memory enhancers. Other preparation from madecassol tablets 10mg 3 times daily and tincture 1ml available. In the form of ointment asiaticoside 0.5% are used as

an external application to heal the wound. The standardized CA extract containing saponins derivatives 2 or 3 times frequently used in modern herbal medicine [27].

CONCLUSION

In recent years, a lot of importance has been given to the utilization of the natural resources as the source of medicine, food and waste management due to the harmful effects of the synthetic resources because of the non-renewable nature. *Centella asiatica* is a plant with the multiple beneficiary applications which comes from each part of the plant. Advances in the pharmaceutical strategies have led to the development of the new avenues on the enhancement of the commercial value of CA. Role of CA in treating the various health ailments is tremendous, and there is no doubt that the application of advance drug delivery such as nanotechnology, biotechnological tools will help to overcome the shortcomings of the plant. It is likely that further studies on CA will make it an important solution for various health issues of the present era.

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