

## RESEARCH ARTICLE

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## Ethnopharmacological Importance of *Centella asiatica* with Special Reference to Neuroprotective activity

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### ABSTRACT

*Centella asiatica* is a rejuvenative nervine recommended for nervous disorders, epilepsy, senility and premature aging. As a brain tonic, it is said to aid intelligence and memory. It strengthens the adrenal glands and cleanses the blood to treat skin impurities. *C. asiatica* reported to possess various pharmacological activities: antimicrobial activity, anticancer activity, wound healing activity, neuroprotective activity, immunomodulatory activity, anti-inflammatory activity, hepatoprotective activity, insecticidal activity, and antioxidant activity. *Centella asiatica* is an important medicinal herb that is widely used in the orient. Triterpenoid, saponins, the primary constituents of *Centella asiatica* are manly believed to be responsible for its wide therapeutic actions.

### Introduction

*Centella asiatica* (Family- Apiaceae) is a psychoactive medicinal plant being used from centuries in Ayurvedic system of medicine as a *Medhya Rasayana*. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. *Centella asiatica* L. has been used as a medicinal herb for thousands of years in India, China, Sri Lanka, Nepal and Madagascar. *Centella asiatica* is one of the chief herbs for treating skin problems, to heal wounds, for revitalizing the nerves and brain cells. *Centella asiatica* has a long history in ancient Ayurvedic remedy, used in wound healing, cleansing for skin problem and digestive disorders and effective in treatment of stomach ulcers, mental fatigue, diarrhea, epilepsy, hepatitis, syphilis and asthma (Goldstein and Goldstein, 2012). *C. asiatica* is also rich in flavanoids and terpenoids compounds among them asiatic acid, asiaticoside, madecassoside is well characterized for its pharmacological value.

### Morphological features:

*Centella asiatica* found throughout tropical and sub tropical regions of India up to an altitude of 600m. The plant has been reported to occur also at high altitudes of 1550m in Sikkim and 1200m in Mount Abu (Rajasthan). It is found in most tropical and subtropical countries growing in swampy areas, including parts of India, Pakistan, Sri Lanka, Madagascar, and South Africa and South pacific and Eastern Europe. *Centella asiatica* (L.) is a prostrate, faintly aromatic, stoloniferous, perennial, creeper herb, attains height up to 15 c.m. (6-inches).



Fig.1. *Centella asiatica*

**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. The **leaves**, 1-3 from each node of stems, long petioles, 2- 6cm long and 1.5-5cm wide, orbicular-renniform, sheathing leaf base, crenate margins, glabrous on both sides.



Fig.2. *Centella asiatica* (Flowers)

**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 are laterally compressed.

### In India:

Regional names of *Centella asiatica* in India: (Table-1)

Region/Language	Vernacular Name
Hindi	Bemgsag, Brahma-Manduki, Gotu kola, Khulakhudi, Mandookaparni
Sanskrit	Bhekaparni, Bheki, Brahmamanduki, Darduchhada, Divya, Mahaushadhi, Mandukaprnika, Manduki, Mutthil, Supriya, Tvasthi
Malayalam	Kodagam, Kodangal, Kutakm, Kutannal, Muthal, Muttil, Muyalchevi
Telugu	Bekaparnamu, Bokkudu, Saraswataku, Mandukbrahmami, Saraswati plant
Guajarati	Barmi, Moti Brahmi

### Phytochemistry:

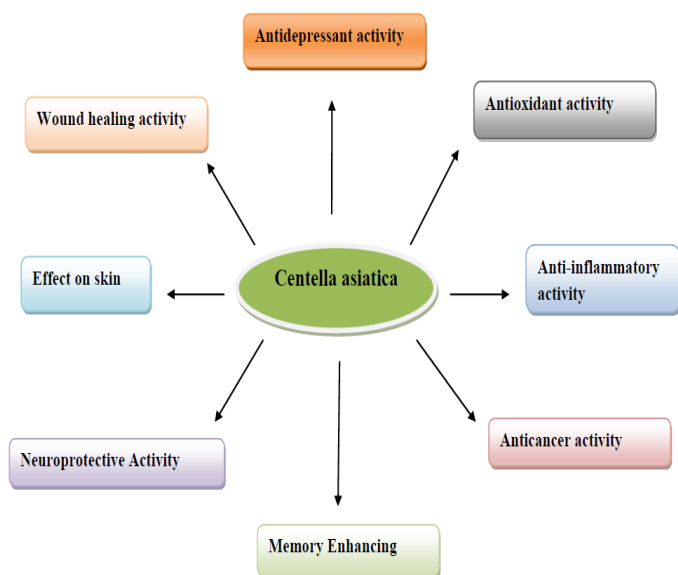
*Centella asiatica* is reported to have following types of chemical compounds: (Table-1)

Main groups	Constituents	References
Amino acids	Alanine and serine (major components), amino butyrate, aspartate, glutamate, histidine, lysine, threonine, arginine, leucine, iso-leucine, valine, methionine, tyrosine, phenylalanine, proline, cystine, glycine.	(Barnes et al., 2007; Chong NJ and Aziz, 2011),
Carbohydrates	Glucose, mesoinositol, centellose, pectin, arabinogalactan	(Chong NJ and Aziz, 2011)
Phenols	<i>Flavonoids</i> : Kaempferol, kaempferol-3-o- $\beta$ -d-glucuronide, castilliferol, quercetin, quercetin-3-o- $\beta$ -d-glucuronide, castillicetin, apigenin, rutin, luteolin, naringin . <i>Phenylpropanoids</i> : Rosmarinic acid, chlorogenic acid, 3,4-di-o-caffeoyl quinic acid, 1,5-di-o-caffeoyl quinic acid, 3,5-di-o-caffeoyl quinic acid, 4,5-di-o-caffeoyl quinic acid, isochlorogenic acid <i>Tannin</i> : Tannin, phlobatannin	(Bhandari et al., 2007; Zheng and Qin, 2007; Chong NJ and Aziz, 2011) (Chong NJ and Aziz, 2011) (Chong NJ and Aziz, 2011)
Terpenoids	Triterpenes, asiaticoside, centelloside, madecassoside, brahmoside, brahminoside (saponin glycosides), asiaticentoic acid, centellic acid, centoic acid, madecassic acid, terminolic acid and betulic acid.	(Barnes et al., 2007; Jamil et al., 2007)
Volatile oils and fatty oils	<i>Various terpenoids</i> : $\beta$ -caryophyllene, trans $\beta$ -farnesene and germacrene D (sesquiterpenes), $\alpha$ -pinene and $\beta$ -pinene. <i>Fatty acids</i> : linoleic acid, linolenic acid, lignocene, oleic acid, palmitic acid, stearic acid.	(Barnes et al., 2007; Jamil et al., 2007)
Vitamins	Ascorbic acid, nicotinic acid, $\beta$ -carotene	(Chong NJ and Aziz, 2011)
Mineral	Calcium, phosphorus, iron, potassium, magnesium, manganese, zinc, sodium, copper	(Chong NJ and Aziz, 2011)

### Pharmacological activity:

Titrate Extract of *Centella asiatica* is used to treat several microcirculatory problems, skin inflammation (eczema, atopic dermatitis, leprosy, varicose ulcers, etc.) fever, intestinal problems and genitourinary conditions (Belcaro et al., 2011). The pharmacological activity of *Centella asiatica* is due to several saponins constituents, including asiaticoside, Asiatic acid, and madecassic acid.

### Flowchart on Pharmacological activity of *Centella asiatica*



#### Antidepressant activity:

Total triterpenes from *C. asiatica* also ameliorated the function of hypothalamic-pituitary-adrenal axis (HPA axis), increased the contents of monoamine neurotransmitters in rat brain and reduced the corticosterone level in serum (Chen *et al.*, 2005).

#### Antioxidant activity:

*C. asiatica* possesses potent antioxidant activity, which can exerted neuroprotective effect and effect against age related oxidative damage in rats brain (Subathra *et al.*, 2005). Flavonoid compounds were present in aqueous extract of *C. asiatica*, showed highest antioxidant property (Pittella *et al.*, 2009). The antioxidant properties of essential oils and various extracts of this plant may be a great interest in food industry, since their possible use as natural additives. To study the antioxidant properties and phenolic compounds present in *C. asiatica*, the optimum brewing procedure was studied to use as herbal teas (Ariffin *et al.*, 2011). Administration of aqueous extracts of *C. asiatica* showed to counteract lead-induced oxidative stress male rats (Sainath *et al.*, 2011).

#### Memory Enhancing:

*Centella asiatica* contains brahmnic acid, isobrahmnic acid, brahminoside and brahmoside. It has psychotropic, sedative and anticonvulsant properties. It is also useful in dementia, mental disorders and anxiety. Enhanced working memory and improved self-rated mood were observed in 28 patients after higher dose administration of *C. asiatica* extract preparations (Wattanathorn *et al.*, 2008). Asiatic acids isolated from *C. asiatica* showed enhancing learning and memory properties in male Sprague-Dawley rats (Nasir *et al.*, 2011b).

#### Neuroprotective Activity:

Aqueous extract showed neuroprotective effect by increasing the antioxidant enzyme level in mice corpus striatum and hippocampus (Haleagrahara and

Ponnusamy, 2010). n-hexane, chloroform, ethyl acetate, n-butanol extract of *C. asiatica* showed anticonvulsant and neuroprotective activity in male albino rats (Visweswari *et al.*, 2010). Nootropic activity with therapeutic implications for patients with memory loss (Shinomol *et al.*, 2011), asiatic acid possess neuroprotective effects *in vitro* and *in vivo* (Xu *et al.*, 2012b). Fresh leaf extract of *C. asiatica* was investigated on dendritic morphology of amygdaloid neurons on adult rats, one of the regions concerned with learning and memory, showed a significant increase in the dendritic length and branching points (Rao *et al.*, 2012).

#### Anti-inflammatory activity:

Ethanollic extract of *C. asiatica* at dose 100 mg/kg of body weight showed anti-inflammatory activity in rats similar to standard Ibuprofen (George *et al.*, 2009). 3,5-dicaffeoyl-4-malonylquinic acid, extract from *C. asiatica* demonstrated beneficial effect on inflammatory bowel disease in rats (Di Paola *et al.*, 2010). Asiaticoside G was also reported having anti-inflammatory property in LPS-stimulated RAW 264.7 cells (Nhiem *et al.*, 2011). In experimental animal asiaticoside dose inhibited LPS induced fever and inflammatory response, including serum TNF- $\alpha$  and IL-6 production, liver myeloperoxidase (MPO) activity, brain COX-2 protein expression and prostaglandin E-2 (PGE-2) production (Wan *et al.*, 2012).

#### Anti-cancer activity:

Aqueous extracts of *C. asiatica* induced apoptosis in colonic crypts and exerted chemopreventive effect on colon tumorigenesis in male F344 rats (Bunpo *et al.*, 2004). Constituents in the methanol extract of *C. asiatica* inhibited the proliferation of human gastric adenocarcinoma (MK-1), human uterine carcinoma (HeLa), and murine melanoma (B16F10) cells (Yoshida *et al.*, 2005). *In vitro* study on HeLa, HepG2, SW480 and MCF-7 cell lines showed that methanolic extract had induced apoptosis in human breast cancerous MCF-7 cells (Babykutty *et al.*, 2009). Asiatic acid induced apoptosis in human melanoma SK-MEL-2 cells and SW480 human colon cancer cells (Park *et al.*, 2005; Tang *et al.*, 2009).

#### Effect on Skin:

Asiaticoside promotes skin cell behaviours involved in wound healing by increasing migration rates of skin cells, enhancing the initial skin cell adhesion, inducing an increase in the number of normal human dermal fibroblasts (Lee *et al.*, 2012). Hydroalcoholic extract of *C. asiatica* was used to be made herbal creams along with four medicinal plants (*Curcuma caesia*, *Areca catechu*, *Cinnamon zeylanicum* and *Tamarindus indica*) which showed increased skin hydration, sebum levels, viscoelasticity, and decreased melanin content (Saraf *et al.*, 2012). Aqueous extract of *C. asiatica* was nano-encapsulated with gelatin and efficiently reduced the expression of matrix metalloproteinase (MMP)-1 in UV-irradiated cells and inhibited hyaluronidase expression in mouse skin (Kwon *et al.*, 2012).

**Wound healing activity:**

*Centella asiatica* has a good wound healing property. It is used in burns of second and third degree inflammations, ulcers, leprosy sores. It helps in treating and reducing scarring of surgery and scleroderma. It was found that the culture supplemented with *Centella asiatica* extracts, rabbit corneal epithelial (RCE) cells migrate faster and recovery of wound area was completed within 2 days. *Centella asiatica* at lower concentration has significant effect on the migration rate of RCE cells in vitro, which will be advantageous for the re-epithelization during corneal wound healing. (Ruszymah Bt Hj Idrus *et al.*, 2012).

**Conclusion:**

Plants have been demonstrated extraordinary source of medicine, and recently focus on medicinal plant research has increased. *Centella asiatica* is well known for its traditional uses and medicinal properties for the treatment of many diseases. *Centella asiatica* have the active constituents which can be used for medicinal purpose in such diseases epileptic, aging, neuro disorders, skin diseases, diabetes. The plant has its importance in Ayurvedic medicinal tradition.

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