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(REVIEW ARTICLE)



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Abstract

Centella asiatica is mostly used in Chinese & Ayurvedic, Unani medicine as a Memory Enhancer, Nervous system disorders, and Topical Skin Disease treatments. Triterpenoids, Saponins are important chemical constituents believed to exert these pharmacological actions. Apart from this it's also used in diarrhoea, fever, amenorrhea, reliving anxiety and cognitive effects' asiatica or Gotu kola is often confused with kola nut which does not contains any CNS stimulants like caffein and do not show any stimulant effect. For hundreds of decades before it was used in ayurvedic system of medicine, which is recorded in 'Sushruta Samhita' an ancient ayurvedic medical manuscript. It's also used by Indonesian and Javanese; Chinese ancient peoples know over 2000 years ago. This article focuses on the Phytochemistry, Traditional uses, Pharmacological effects, Toxicology of Centella asiatica.

Keywords: CA (*Centella asiatica*); Gotu kola; Indian pennywort; Asiatic pennywort; Kodavan; Mandookaparni; Herbal medicine

1. Introduction

Centella asiatica belongs to the family Apiaceae which is commonly known as Indian pennywort or Gotu kola in western countries this herbal medicine is known as Brahmi in traditional medicine system, Gotu kola in Europe and American continents, in Ayurveda its referred as Mandookaparni and in unani as Brahmi (Figure: 1). It was confused with another plant known as *Bacopa monnieri* Wettst (Figure: 3) in India because both the herbs are sold by the name 'Brahmi'. Later the issue was solved by considering that Brahmi is B. monnieri and Mandookaparni is *C. asiatica* [1. It observed growing in Pakistan, Central America, Madagascar, India, equatorial Africa, and the tropics of Oceania [2]. Due to the number of herbal properties of the plant CA and CA preparation or extracts were added in the Indian Pharmacopoeia in 19th century, which was later added in other pharmacopoeias. This herb is a dried, fragmented plant, of aerial portions of *Centella asiatica* as per Polish and European Pharmacopoeias which contains not less than 6.0 per cent of total triterpenoid derivatives expressed as asiaticoside [2,3,4]. For hundreds of decades of years, C. Asiatica plants have been used to aid the healing of tiny wounds, scratches, burns, and hypertrophic wounds, particularly in dermatological disorders and as an anti-inflammatory drug for eczema. It is employed in traditional Asian medicine as a diuretic, antibacterial, and antiviral agent for the treatment of venous insufficiency, anti-rheumatic agent, cognitive enhancement, antipyretic agent, anxiety alleviation, and anti-cancer agent [2,4,5]. *C. Asiatica* was also used to treat epilepsy, hysteria, leprosy, itching, and bug bites [5].

2. History/origin

C. asiatica (Linn), endemic to Sri Lanka, South Africa, Madagascar, and Malaysia, has been utilised as a medicinal plant by tribal tribes and societies. For approximately 2000 years, *C. asiatic* has been utilised in Chinese herbal therapy, and for 3000 years in Indian Ayurvedic medicine. In Ayurvedic medicine, mandukaparni is used to treat skin diseases,

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leprosy, stomach catarrh, elephantiasis, renal difficulties, asthma, bronchitis, and leucorrhoea, and toxic fever and leucorrhoea in Chinese herbal treatment. *C. Asiatic* is used to treat anxiety, eczema, and mental weariness in Malaysia. When it is fresh, it is also eaten as a salad. For many years, the inhabitants of the Kra Peninsula and Java Island of Indonesia have employed fresh plant extracts to cure wounds both inside and topically. Plant extracts are also used in brain tonics for mental dysfunction. These characteristics are brought about by the presence of madecassoside, madecassic acid, asiaticoside, and pentacyclic triterpenes [29].

3. Plant Profile



Figure 1 Centella asiatica



a. Centella asiatica



Figure 2 Flowers of Centella asiatica



b. Bacopa monnieri Wettst

Figure 3 Difference between C. asiatica and Bacopa monnieri



Figure 4 Dried Centella asiatica

4. Morphology of plant

It belongs to the umbelliferous family which is small perennial herbaceous creeper which is slightly aromatic grows up to 15 cm tall found in tropical and subtropical areas of India up to 600 m above sea level. The plant has also been observed to grow at heights of up to 1200 meters in Mount Abu (Rajasthan) and 1550 meters in Sikkim. It is observed in most subtropical and tropical countries like South Africa, Pakistan, Sri Lanka, India, Madagascar, South Pacific, and Europe's east. CA is related with around 20 species grow in most tropical or humid pan-tropical regions, including paddy fields and Rocky Mountains [6,7]. It is a plant that grows in and near water and has no flavor or odor. Its leaves look like small propeller or fan shaped green in color with light pink, light purple or white flowers and fruits are oval shaped (Fig. 1 and 2) the entire plant is used as medicine [8]. It is commonly used as a blood purifier and to treat high blood pressure, improve memory, and promote longevity. CA is one of the most significant herbs in Ayurveda for stimulating nerve and brain cells. Eastern therapists have relied on CA to treat emotional disorders, such as depression, thought to be related to physical problems [9,10]. Western medicine reported that in the mid-twentieth century, CA and its ethanolic extract had promising results in the treatment of leprosy [11].

5. Vernacular names

In many parts of India and elsewhere, this plant has been referred to by a variety of vernacular names which is given in table 1 & 2.

Region/	Vernacular Name	Region/	Vernacular Name
Hindi	Bemgsag, Brahma-Manduki, Gotukola, Khulakhudi, Mandookaparni	Sanskrit	Bhekaparni, Bheki, Brahmamanduki, Darduchhada, Divya, Mahaushadhi, Mandukaprnika, Manduki, Mutthil, Supriya, Tvasthi
Malayala m	Kodagam, Kodangal, Kutakm, Kutannal, Muthal, Muttil, Muyalchevi	Kanarese	Brahmisoppu, Urage, Vandelagaillikiwigidda, Vondelaga
Telugu	Bekaparnamu, Bokkudu, Saraswataku, Mandukbrahmmi, Saraswati plant	Gujrati	Barmi, Moti Brahmi
Marathi	Karinga, Karivana	Tamil	Babassa, Vallarai
Tripura	Thankuni, Thunimankuni	Bengal	Thankuni, Tholkuri
Assam	Manimuni	Deccan	Vallarai
Bihar	Chokiora	Meghalay a	Bat-maina
Oriya	Thalkudi	Sinhalese	Hingotukola
Urdu	Brahmi		

Table 1 Vernacular names in different regions of India

Table 2 Vernacular names in different regions of Abroad

Region/Language	Vernacular Name	Region/Language	Vernacular Name	
USA	Indian Pennywort, Marsh Pennywort	China	Fo-ti-tieng, Chi- hsueuh-ts'ao	
Hawaii	Pohe Kula	Nepal	Ghod tapre	
Cook Islands	Kapukapu	Tahiti	Tohetupou	
Fiji	Totodro	Samoa, Tonga	Tono	

6. Location/Demography

India's tropical and subtropical zones, up to a height of 600 m, are home to *C. asiatica*. It may also be found in Sikkim at an elevation of 1550 m and at a height of 1200 m in Mount Abu (Rajasthan, India) (a state in northeastern India). Rather than clayey soil, sandy loam (60 percent) was shown to be the greatest option for regeneration. The Centella plant grows naturally in marshy or wet soil, quagmire, and sump, bog as well as along the borders of pools, lagoons, inundation, water streams, and sewerage of irrigated rice fields. It may also be found in wet forest, plane forests, and palmetto flats, where it can produce meadows. It may grow on land or in water. This species is pan-tropical and inhabits the United States from Delaware to southern Florida, the West Indies, Mexico, Latin America, Australia, Sri Lanka, and the Philippines [57,58]. (figure: 5).



Figure 5 Location/demography of Centella asiatica

7. Phytochemical Constituents

Table 3 Phytochemical Constituents of Centella asiatica

C	entella asiatica is reported to have following types of chemi	ical compounds:
Main groups	Constituents	References
Carbohydrates	Glucose, mesoinositol, centellose, pectin, arabinogalactan	(Chong NJ and Aziz, 2011)
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),
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)
Vitamins	Ascorbic acid, nicotinic acid, β-carotene	(Chong NJ and Aziz, 2011)
Minerals	Calcium, phosphorus, iron, potassium, magnesium, manganese, zinc, sodium, copper	(Chong NJ and Aziz, 2011)
Volatile oils and fatty oils	Various terpenoids: β-caryophyllene, – and germacrene D (sesquiterpenes), α-pinene and β-pinene. Fatty acids: linoleic acid, linolenic acid, lignocene, oleic acid, palmitic acid, stearic acid.	(Barnes et al., 2007; Jamil et al., 2007)
Phenols	Flavanoids: Kaempferol, kaempferol 3 o β d glucuronide, castilliferol, quercetin, quercetin-3 o β d glucuronide, castillicetin, apigenin, rutin, luteolin, naringin. Phenylpropanoids: 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,	(Bhandari et al., 2007; Zheng and Qin, 2007: Chong NJ and Aziz, 2011) (Chong NJ and Aziz, 2011)
	Tannin: Tannin, phlobatannin	(Chong NJ and Aziz, 2011)
$HO \qquad \qquad$	HO +	CH CH CH CH CH CH CH CH CH CH CH CH CH C







8. Pharmacological Action

Figure 6 Pharmacological Action of Centella asiatica

8.1. Antioxidant

On lymphoma bearing mice, a raw methanolic extract of *Centella asiatica* had antioxidant action [12]. It demonstrated to be a powerful antioxidant with considerable neuroprotective properties. Effective in shielding the rat brain from age-related oxidative damage. Simultaneous administration of the medication dramatically reduces arsenic induced oxidative levels in the liver, kidneys or brain. As a result, it's possible that coadministration CA of despite having no chelating action, centella shields animals against the oxidative damage brought on by arsenic [13]. It demonstrated considerable neuroprotective effects and was effective in preventing age-related oxidative damage to the rat brain [18].

8.2. Wound Healing

Madecassol, a plant extract comprising Asiatic acid, asiaticoside and madecassic acid hastens cicatrisation and wound grafting [6]. *C. asiatica*'s asiaticoside increases angiogenesis and collagen formation, which helps to heal wounds. The asiaticoside accelerates wound healing be increasing the capacity for stretching of newly produced skin. It also suppresses the inflammatory response, which can cause hypertrophy in abrasions by increasing capillary permeability. Additionally, Asiatic acid and madecassic acid have shown an increase in peptidic hydroxyproline indicating enhanced collagen production remodeling in wounds [14,15]. A preclinical investigation revealed that several ointment, cream, and gel formulations of an aqueous CAE administered to rats' open sores three times each day for enhanced cellular proliferation (after 24 days) Increased collagen production at the injury site, as demonstrated via an increase in Tensile and collagen content strengths [16].

When compared to the untreated control wounds, the investigators discovered that the CAE-treated wounds epithelialized more quickly and contracted at a higher rate. With the gel product, healing was more pronounced. It is thought to have an impact on keratinization, which helps to thicken skin in infected regions [17].

8.3. Memory enhancing

The herb's aqueous extract improved acquisition and reminiscence while decreasing levels of norepinephrine, dopamine, and 5-HT and their metabolites in the brain [19]. Aqueous extract of the plant demonstrated cognitive enhancing and antioxidant properties in rats with Streptozotocin-induced cognitive impairment and oxidative stress

[20]. Aqueous extract reduced Pentylenetetrazole-induced seizures and improved the learning loss caused by PTZ kindling, indicating its potential as an antiepileptic medication with the added benefit of preventing cognitive damage [21]. Brahmoside, isobrahmic acid, brahmic acid, and brahminoside, which contains anticonvulsant, psychotropic, and sedative activities, make up the chemical makeup of *C. asiatica*. It helps with mental illnesses, dementia, and anxiety. As a result, children with learning disabilities who take the complete herb have an improvement in their attention, memory, and awareness [22].

8.4. Gastric ulcer healing

In rats, Asiaticoside inhibited the formation of cold-induced stomach ulcers [23]. Oral administration of Asiaticoside to rats dramatically reduced the formation of stress-induced ulcers [24]. A plant extract significantly reduced stomach ulcers brought by cold and restraint stress in Charles-Foster rats. The reduction in stomach ulcers was coupled with a dose-dependent increase in GABA levels in the brain [25]. *C. asiatica* reduced ethanol-induced stomach mucosal lesions by reducing and enhancing the mucosal barrier free radical damage [26]. The plant's fresh juice provided significant protection against experimental ulcer models, and the ulcer-protective effect could be attributed to the enhancement of mucosal defense elements. In rats, water extract and asiaticoside both showed healing benefits on acetic acid-induced stomach ulcers [27].

8.5. Cytotoxic and antitumor

The lifespan of mice with tumours was increased by oral administration of *C. asiatica* crude extract and its partly purified fractions, which also inhibited the growth of solid and ascites tumours. Action on DNA synthesis directly causes cytotoxic and antitumor effects [28]. A partially purified component of the herb's methanol extract reduced tumour cell proliferation while having no harmful effect on lymphocytes. *C. asiatica* produced apoptosis in Ehrlich Ascites tumour cells and in chemotherapeutic drug induced toxicity demonstrated that the medication had an anti-cancer impact and reduced myelosuppression. *C. asiatica* regulates nitric oxide and tumour necrosis factor- in murine macrophages. Asiaticoside promotes wound healing by stimulating collagen production. It may be effective in cancer chemotherapy since it promotes apoptosis and increases the antitumor activity of vincristine in cancer cells. Asiatic acid was discovered to have an anticancer effect on skin cancer [29].

8.6. Neuroprotective

By enhancing the neuroprotective effects of glutamate, asiatic acid significantly reduced the oxidative defense mechanism in cells. Consequently, it might be effective in defending neurons from oxidative stress damage brought on by excessive exposure glutamate [30]. The plant's ability to speed up nerve regeneration after oral administration and the presence of several active fractions that increase neurite elongation in vitro raise the possibility that centella components might speed up the repair of injured neurons [31].

8.7. Cardioprotective

When rats' hearts were damaged by adriamycin, *C. asiatica* had a cardioprotective effect on the body's antioxidant tissue defense mechanism [32]. The whole plant's alcoholic extract demonstrated strong cardioprotective efficacy in reducing rats' ischemia-reperfusion-induced myocardial infarction [33].

8.8. Antidepressant properties

Total triterpenes from CA were found to have antidepressant effects on the immobility period in forced swimming mice and the content of amino acids in mouse brain tissue. In the research, imipramine and total CA triterpenes decreased immobility time and improved amino acid level imbalances, confirming CA's antidepressant effect [34]. The same scientists measured the concentration of corticosterone in mouse brains to look into the potential antidepressant effects of total triterpenes of CA [35].

8.9. Hepatoprotective

In vitro anti-hepatoma action is present in *C. asiatica* [36]. Rats' liver fibrosis caused by dimethylnitrosamine can be significantly reduced and treated by the plant's total glucosides [37].

8.10. Immunomodulating

Centella's triterpenoid saponins exhibited immunomodulatory properties. Oral administration of Brahma Rasayana, which contains centella, significantly increased white blood cell count, bone marrow cellularity, natural killer cells, and antibody-dependent cellular activity in mice exposed to gamma radiation. It decreased liver peroxidation brought on

by radiation [38]. Pectin from *C. asiatica* has immunostimulating properties [39]. and methanol extracts demonstrated early immunomodulatory effects [40].

8.11. Anabolic effect

A low-protein diet was offered to albino rats, centella decreased mortality brought on by gross protein shortage. It raised blood protein nitrogen levels and stopped fatty acids from entering the liver. The rise in haemoglobin content was statistically significant and fairly high. It reduced the average blood urea level [41].

8.12. Radioprotective

The plant's madecassol, which has anti-inflammatory properties, decreased rats' acute radiation dermatitis [42]. During clinical irradiation, *C. asiatica* may be helpful in reducing radiation-induced behavioural abnormalities [43]. Plant extract exhibited radioprotective qualities [44]. and pretreatment with it before gamma radiation exposure was discovered to be successful in preventing radiation-induced damage in the mouse liver [45].

8.13. Effects on Venous Insufficiency

C. asiatica is thought to aid in connective tissue maintenance by strengthening weakened veins. It can also aid in the therapy of scleroderma by soothing connective tissue development and decreasing its formation by stimulating the formation of chondroitin sulphate and hyaluronidase. *C. asiatica* acts on the connective tissue vascular wall, causing venous insufficiency and hypertensive microangiopathy. It also reduces capillary filtration rate by fine-tuning microcirculatory parameters [46].

8.14. Antiviral

Crude water extracts of centella, Maclura cochinchinensis Lour., and Mangifera indica Linn. each demonstrated antiherpes simplex virus activity [47].

8.15. Antifertility

A crude plant extract, as well as the glycoside isothankuniside and its derivative methyl 6-diketo-3, -5-hydroxy-3 (or 24) -nor-urs-12-ene-28-oate inhibited fertility in female mice [48].

8.16. Antiprotozoal

An alcoholic extract of the whole plant was shown to be antiprotozoal against Entamoeba histolytica [49].

8.17. Antipsoriatic

Aqueous extracts decreased keratinocyte multiplication, and their antipsoriatic efficacy warrants further study. However, the action may be attributed to its two component triterpenoid glycosides madecassoside and asiaticoside [50].

8.18. Antitubercular and Antileprotic

Asiaticoside has been demonstrated to help cure leprosy and certain kinds of TB [51].

8.19. Antifilarial

A combination of ethanol extracts of *Centella asiatica* and *Acacia auriculiformis* A. Cunn. ex Benth. resulted in a significant reduction in filarial count in dogs naturally infected with *Dirofilaria immitis* [52].

8.20. Slimming

Slimming liposomes containing two microcirculation activators, esculoside and *C. asiatica* extracts, showed a dramatic increase in the cyclic adenosine monophosphate content in human adipocytes in vitro tests, with a subsequent rise in the nonesterified fatty acids content of human adipocyte incubation medium, and could provide an actual potent slimming effect on human volunteers in vivo studies [53].

8.21. Antispasmodic

The glycosides in the plant were shown to have anti-spasmodic efficacy on acetylcholine-induced spasms of the rat ileum in an alcoholic extract of the plant [54].

8.22. Effect on skin

A lotion containing asiatic acid and asiaticoside was used to enhance skin texture and renew the skin of elderly persons. Pruritis and other skin problems benefit from an alcoholic extract of the plant combined with additional substances [54].

8.23. Antiepileptic Properties

Asian *C. asiatica* increases gamma aminobutyric acid levels in the brain, which has historically been utilized as an anticonvulsant and anxiolytic. The steroid extracts from the plant are used to cure leprosy. It also inhibits the production of spontaneous motor activity, lipid peroxidation products, hypothermia, diazepam withdrawal-induced hyperactivity, and pentobarbitone resting instant. Pentylenetetrazol-induced convulsions are completely blocked by the extract (200 mg/kg body weight). These findings point to its potential as a central nervous system depressant, as well as antioxidant and anticonvulsant properties [55].

8.24. Antidiabetic Activity

To test the anti-diabetic properties of *C. asiatica*, methanolic and ethanolic extracts were produced and tested on alloxan-induced diabetic rats. Blood glucose levels were dramatically lowered by alcoholic extracts [56].

8.25. Side effects and toxicity

When administered to the skin, *C.asiatica* is safe for pregnant women.

People with liver illness should avoid using *C.asiatica* since it worsens liver damage. Also, discontinue use of this plant two weeks before surge.

9. Conclusion

Plants have been shown to be an incredible source of medicine, and interest in medicinal plant research has lately surged. *Centella asiatica* is widely recognised for its traditional applications and therapeutic capabilities in the treatment of a variety of ailments. *Centella asiatica* has active ingredients that can be utilised to treat ailments such as epilepsy, ageing, neuro disorders, skin problems, and diabetes. The herb is significant in the Ayurvedic medical practice.

Compliance with ethical standards

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Authors Contribution

All the authors have equally contributed to conceiving this paper and participated in its revisions. All authors read and approved the final manuscript.

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