

Review Article

Clinical and therapeutic benefits of *Centella asiatica*

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Citation

Kulsoom Zahara, Yamin Bibi and Shaista Tabassum. Clinical and therapeutic benefits of *Centella asiatica*. Pure and Applied Biology. Vol. 3, Issue 4, 2014, pp 152-159

Abstract

Centella asiatica belongs to family Apiaceae is a traditionally important plant with wide range of therapeutic potential. Plant is traditionally used to treat a broad range of diseases such as diarrhea, hepatitis, measles, toothache, syphilis, leucorrhoea etc. Madecassic acid, asiatic acid, α -terpinene, α -copaene, β -caryophyllene are some of the important bioactive compounds responsible for its antioxidant, antimicrobial, antiulcer, antifilarial, antiviral and various other activities. Present review provides up to date information related to conventional uses, bioactivities and clinical benefits of *Centella asiatica*.

Key words: *Centella asiatica*, chemical constituents, ethnomedicinal uses, clinical uses.

1. Introduction

Centella asiatica (Linn.) Urban Sys. Synonym *Hydrocotyle asiatica* Linn., belongs to the plant family apiaceae (umbelliferae) is an important plant with wide range of traditional, medicinal and therapeutic values. This herb is found almost all over the world and is utilized as a source of food, beverages, medicine. This is a key element of numerous compound formulations used for curing gastrointestinal disorders, cutaneous problems and for revitalizing brain cells. In According to an estimate *C. asiatica* is an important plant in the International market of medicinal Plant Trade and because of its overexploitation this species has been depleted. Plant is listed as a threatened plant species by IUCN (International Union for Conservation of Nature and Natural Resources) [1].

2. Morphology Characteristics

C. asiatica (L.) is astoloniferous, perennial, prostrate herb which attain an height of up to 15cm (6 inches). Stem is glabrous; leaves are orbicular-renniform, 1.5-5cm wide and 2- 6cm long, 1-3 from each node of stems, sheathing leaf base, crenate margins, glabrous on both sides; Flowers are fascicled umbels, each umbel consisting of 3-4 white to purple flowers; fruits are oblong and globular in shape, borne right through the growing season in approx 2 inches long. Seeds have pedulous embryo, has characteristic odor, and bittersweet taste. *C. asiatica*

flourishes extensively in damp and marshy places making a dense green carpet, for its regeneration sandy loam (60% sand) is found to be the most fertile soil [2].

3. Distribution

C. asiatica is indigenous to warmer regions of both the hemispheres including India, Sri Lanka, South-East Asia, parts of China, Western South Sea Islands, Mexico, South East USA, South Africa, Columbia, Eastern South America, Venezuela and Madagascar [4].

4. Chemical Constituents

The major bioactive compounds in the plant are the madecassic acid, asiatic acid, triterpenes and their derivatives such as madecassoside, asiaticoside and triterpene ester glycosides [5]. Compounds such as α -terpinene, α -copaene, β -caryophyllene, bornyl acetate, β -elemene, β -pinene, germacrene-D, bicycloelemene and trans- β -farnesene have been isolated through GC-MS analysis [6]. Numerous polyacetylenic compounds were isolated from underground parts of *C. asiatica* among them 8-acetoxyfalcariol is the chief compound. The roots of *C. asiatica* are rich in amino acids, specially glutamic, serine, alanine, threonine, aspartic, histidine and lysine. It is also affluent in vitamin A (retinol), vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin C (ascorbic acid), vitamin B5 (niacin) and carotene [7].

5. Traditional Uses

5.1 Food and beverages

C. asiatica is commonly eaten as fresh vegetable in Indonesia and Malaysia [8]. It is used in preparation of soup or as a main vegetable. Due to slight bitterness it is cooked along with coconut, sweet potatoes and potatoes [9].

In various region of the world *C. asiatica* is used as health tonic [10]. From fresh plant drink and juice is prepared [11]. It is commonly used by Chinese and Thai people as a cooling drink and for thirst quenching purpose [12]. In India it is a constituent of a drink called “thandaayee”. In Sri Lanka leaves of *C. asiatica* are used for preparation of a porridge called “kola kenda” and a curry called “mallung” [13].

5.2 Ethnomedicinal uses

C. asiatica is an ethnomedicinally important plant, used all over the world for the treatment of cholera, jaundice, diarrhea, hepatitis, syphilis, measles, toothache, leukorrhoea, smallpox, haematemesis, toothache, asthma, urethritis, renal stones, rheumatism, varices, neuralgia, anorexia, leprosy and skin diseases as an analgesic, antipyretic and anti-inflammatory.

6. Bioactivities

6.1 Antioxidant activity

According to Zainol *et al.*, [20] the leaves of *C. asiatica* showed highest antioxidant activity they also found that leaves contain highest phenolic content as compare to other parts of *C. asiatica* which propose that phenolic compounds are the chief contributors to the antioxidative activities. Leaves are reported to have high antioxidant potential in three different pathways include inhibition of linoleic acid peroxidation (98.2%), superoxide free radical scavenging activity (86.4%) and radical scavenging activity, DPPH (92.7%) [21].

Conversely, Abdul- Hamid *et al.*, [14] stated that ethanol extract of *C. asiatica* root demonstrated the maximum activity although it was not considerably dissimilar from the leaves.

Another study proved that *C. asiatica* has strongest DPPH radical scavenging activity based on ascorbic acid and gallic acid equivalent amongst the eleven edible green leafy vegetables [22]. In another study conducted on 20 traditional leafy vegetables cultivated in South Africa *C. asiatica* is proved to have highest antioxidant activity [23]. Higher antioxidant activity of *C. asiatica* was also observed by Akula and Odhav [24], Pittella *et al.*, [25] and Nanasombat and Teckchuen [26].

6.2 Antibacterial activity

Through viable cell count method Mamtha *et al.*, [27] observed that the alcoholic extract of plant showed bactericidal action within 2 hours against *Shigella*

species, *Staphylococcus aureus* and *Vibrio cholera*. In another study the carbon tetrachloride, *n*-hexane, chloroform soluble fractions of methanol extract from *C. asiatica* showed antibacterial activity against 8 gram negative bacteria i.e. *Shigella dysenteriae*, *Escherichia coli*, *Salmonella paratyphi*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Shigella boydii*, *Vibrio mimicus* and *Vibrio parahemolyticus* and 5 gram negative strains of bacteria i.e. *Bacillus megaterium*, *Bacillus cereus*, *Staphylococcus aureus*, *Bacillus subtilis* and *Sarcinalutea* [28]. Diethyl ether, hexane, dichloromethane, ethyl acetate, and methanol extracts of *C. asiatica* showed inhibition of *K. aerogenes*, *P. vulgaris*, *B. subtilis* and *S. aureus* species. But no activity was observed against *Pseudomonas aerogenes* and *Escherichia coli* [29].

In another study conducted against 10 isolates of pathogenic fish bacteria i.e. *Escherichia coli*, *Escherichia coli*, *Edwardsiella tarda*, *Staphylococcus aureus* *Citrobacter freundii*, *Streptococcus agalatae*, *Aeromonas hydrophila*, *Vibrio alginolyticus*, *V. vulnificus*, *V. parahaemolyticus* and *Streptococcus aginosus*, *C. asiatica* did not show any inhibition of these tested strains [29].

6.3 Antifungal activity

Petroleum ether and Ethanolic extracts of *C. asiatica* showed considerable activity against different strains of fungi like *Candida albicans*, *Aspergillus flavus* and *Aspergillus niger* [30, 49]. In another study the Chloroform, Hexane, carbon tetrachloride and aqueous soluble fractions of methanolic showed inhibition of *Saccharomyces cerevisiae*, *Aspergillus niger* and *Candida albicans* [28].

Using agar well diffusion method Bobbarala *et al.*, [31] observed the antifungal potential of 49 plant species against *Aspergillus niger* and proved that the methanolic extracts of 43 plants including *C. asiatica* demonstrated varying degrees of inhibition activity.

6.4 Antiviral activity

A study conducted on proved that the crude aqueous extract of *Mangifera indica* and *C. asiatica* confirm anti-herpes simplex virus activities [32].

6.5 Antifilarial activity

Sarkar *et al.*, [33] conducted an investigation on dogs infected with *Dirofilaria immitis* and reported that the mixture of *Acacia auriculiformis* and *C. asiatica* extracts showed considerable reduction in filarial counts.

6.6 Antitumour activity

With no toxic effects on lymphocytes the methanol extract of *C. asiatica* is proved to inhibit the growth of tumor cells and its aqueous extract has a chemo protective effect on colon tumorigenesis [34]. Due to stimulative effect on collagen synthesis asiatic acid isolated from *C. asiatica* possesses good wound healing activities. It could be valuable in



Figure 1: *Centella asiatica* (a) Plant body (b) Leaf

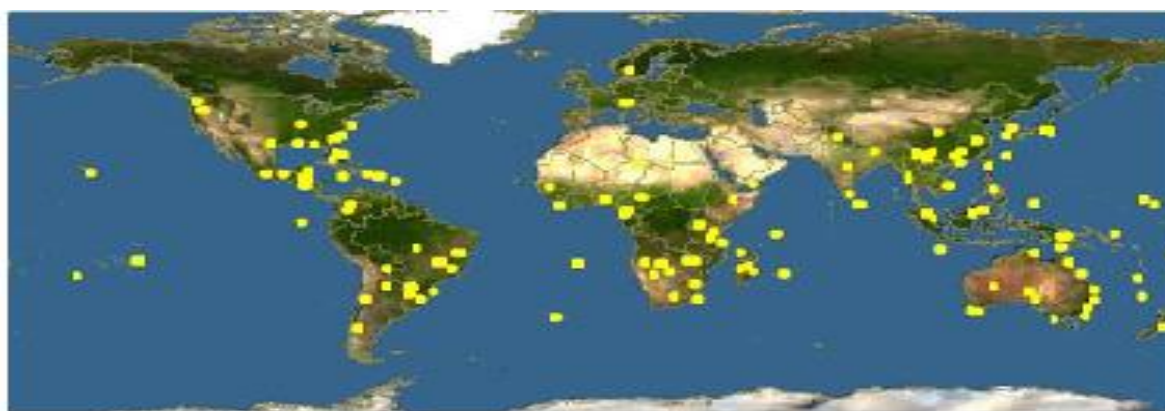


Figure 2: Distribution of *Centella asiatica*

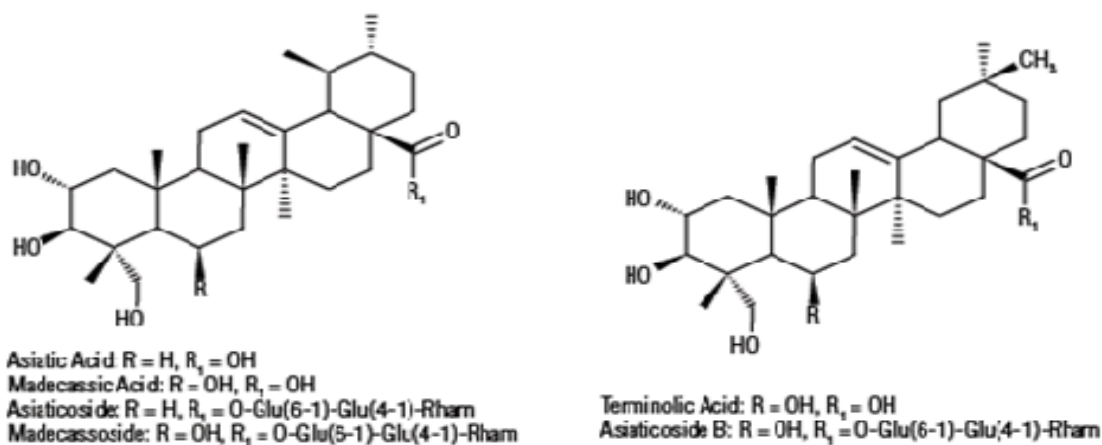


Figure 3: Chemical structure of some important bioactive compounds of *Centella asiatica*

Table-1, Vernacular names of *Centella asiatica* [2].

Region/Language	Vernacular Name
China	Fo-ti-tieng, Chi-hsueh-ts'ao
USA	Indian Pennywort, Marsh Pennywort
Hawaii	Pohe Kula
Nepal	Ghodtapre
Urdu	Brahmi
Malay	Pegaga
Malayalam	Kodagam
Hindi	Mandookaparni
Bengali	Thankuni

Table-2, Systematic classification (Taxonomy) of *Centella asiatica* [3]

Classification	Name
Kingdom	Eukaryota
Subkingdom	Embryophyta
Division	Spermatophyta
Subdivision	Angiospermae
Class	Dicotyledoneae
Subclass	Rosidae
Superorder	Aralianae
Order	Araliales (Umbelliflorae)
Family	Apiaceae or Umbelliferae
Subfamily	Hydrocotyle
Genus	Centella
Species	Centellaasiatica

Table-3, Chemical constituents

Main Groups	Constituents
Flavone derivatives	Quercetin glycoside, Kaempferol, glycoside and in free form Astragalin
Sesquiterpenes	Trans-farnesene, Ermacrene D, Caryophyllene, Elemene and bicycloelemene
Triterpenic acid sugar esters	Asiaticoside (major component), Asiaticoside A, Asiaticoside B, Asiaticoside A (Madecassoside) and B, Braminoside, Brahmoside, Brahminoside, Thankuniside, Isothankuniside
Triterpenic steroids	Stigmasterol, Sitosterol
Triterpenic acids	Asiatic acid, 6-hydroxy asiatic acid, Madecassic acid, Madasiatic acid, Betulinic acid, Thankunic acid, Isothankunic acid
Essential oil	Terpene acetate, Germacrene, Caryophyllene, p-Cymol, Pinene

Table-4, The Ethno-pharmacological uses of *Centella asiatica*

Country	Diseases	Used part	Mode of utilization	References
Malaysia	mental fatigue diarrhoea urinary tract infections, hypertension,	Leaves and Whole plant	Decoction	[14]
Central africa	Wounds and sores are treated topically.	Whole plant	Poultice and Decoction	[15]
Nepal	rheumatism, indigestion, leprosy, poor memory, cooling property to body and stomach, kill germs from wounds, cure leprotic wound	Whole plant	leaf juice, Crushed leaf and root extract, Decoction of leaves	[4]
Madagascar	leprosy	Leaves		[16]
Java and the Malay Peninsula	Brain tonic	Whole plant	Fresh extract	[5]
Thailand	tonic	leaves	Tea and juice	[17]
Bangladesh	jaundice, mental illness, dysentery, diarrhea	whole	Infusion and decoction	[18]
Bansoa	Varicocele [widening of the veins along the cord that holds up a man's testicles (spermatic cord)].	whole	Dried and powdered whole plant is swallowed with water.	[19]

Table-5, Products containing *Centella asiatica* [2].

Country	Product Name	Application	
Korea	SNP Control Cream	<i>Centella asiatica</i> extract and Allantoin, improves drying and delays skin aging.	
	Eye Treatment Serum	<i>Centella asiatica</i> extract, fucoidan sea algae ingredient pacify the skin moistly provides high purity.	
	Diamond Shiny Pearl BB	<i>Centella asiatica</i> and Portulaca oleracea extract, makes the skin viable by calming irritation.	
	Organic Baby Skin Care	Centella asiatica and Portulaca extracts, it soothes and calms the irritated skin and restores the purified and clean skin	
	India	Mandukaparni	Improves mental abilities, vascular support, blood circulation and psoriasis
		Mentat	Improves mental functions by a modulation of the cholinergic and GABAergic neurotransmission. It improves mental quotient, memory span, concentration ability and stress threshold, beneficial in insomnia and corrects speech defects. It exhibits significant anti-parkinsonian activity.
		Gertiforte	The antistress, adaptogenic properties of Gertiforte retard degenerative changes and accelerate cellular regeneration. It enhances body immunity, delays aging, it assists cardiovascular functioning by improving circulation and reducing raised lipid levels also improves appetite.
	Menosan	Menosan possesses phytoestrogens, which act through estrogen receptor dependent mechanism. Menosan helps in alleviating symptoms of menopausal syndrome	
	Nourishing Skin Cream	Provides all day moisturizing, nourishment and protection to skin from pollution and dry weather.	
China Sundari	Weight Loss Tea Gotu Kola and Germanium Moisturizer	<i>C. asiatica</i> , Wolfberry fruit, Chrysanthemum, Pinellia, Salvia, for sliming. Gotu kola (<i>Centella asiatica</i>) firms and lifts skin while Germanium extract balances sebum productions to produce faster results leaving a soft, dewy finish.	

cancer chemotherapy as it stimulate apoptosis and boost antitumor activity of vincristine [4].

7. Pharmacological Uses

7.1 Antiulcer activity

Results of the studies conducted by Chatterjee et al., [35] showed that the fresh juice of *C. asiatica* significantly protects the experimental ulcer models and this effect is might be due to intensification of the mucosal defensive factors. After daily oral intake of fresh juice of *C. asiatica* at the dose level of 60 mg/kg a diminutive clinical test concerning fifteen patients confirmed its antiulcer activity. Around 93% of the patients displayed a clear-cut improvement in subjective symptoms and among them 73% of the ulcers are reported to be healed as measured by radiological and endoscopic observations [36].

Asiatic side isolated from *C. asiatica* is reported to reduce the formation of stress induced ulcers when administered orally to rats. Plant extract considerably inhibit gastric ulceration caused by cold and restraint stress in Charles-Foster rats [35].

7.2 Antidiabetic activity

In glucose tolerance test carried out in the alloxan induced diabetic rats the methanolic and Ethanolic extracts of *C. asiatica* had revealed considerable protection and reduce the blood glucose levels to normal [37]. In another study *C. asiatica* showed faster healing of wounds indidiabetic induced Male Sprague-Dawley rats faster than the control [38].

7.3 Cardioprotective activity

Through Adriamycin stimulated cardiac damage in rats *C. asiatica* showed effective cardioprotective activity on antioxidant [39]. In another study on ischemia-reperfusion induced myocardial infarction in rats' *C. asiatica* showed a significant cardioprotective activity [40].

7.4 Radioprotective activity

Sharma et al., [41] conducted a survey on and revealed that *C. asiatica* could be used in clinical radiotherapy because it is useful in preventing radiation stimulated behavioral changes. The extract has radio protective properties and when tested on mouse liver, pretreatment with it prior to gamma ray irradiation was effective against radiation induced damage.

7.7 Antimutagenic effects

Through cytogenetic assay aqueous extracts of *C. asiatica* was studied for *in vivo* detection of micronuclei in bone marrow cells and chromosomal aberration of mice. On the genetic damage induced by chromium (potassium dichromate) and cyclophosphamide the modulating effects were investigated and it was proved that the *C. asiatica* has a fair antimutagenic nature [42].

7.8 Skin protective activity

Skin aging become visible due to decrease in the levels of type I collagen, Asiaticoside isolated from *C. asiatica* showed synthesis of type I collagen in human dermal fibroblast cells [43].

7.9 Sliming effect

C. asiatica Extract showed amazing amplification in the cyclic adenosine mono phosphate content in human adipocytes with a successive increase in non-esterified fatty acids content [44].

7.10 Immuno-modulating effects of *C. asiatica*

Methanolic extract of *C. asiatica* is reported to have immuno-stimulating potential and demonstrate preliminary immunomodulatory effects [45]. In an experiment conducted on chronic renal failure rats and it was proved that *C. asiatica* injections in these rats has considerable healing results [46].

7.11 Memory enhancing

Aqueous extract of *C. asiatica* is proved to have significant effects on memory and learning. It also decreases dopamine, norepinephrine5-HT and their metabolites in the brain. Brahmic acid, brahminoside, isobrahmic acid and brahmoside isolated from the plant are responsible for its sedative, anti convulsant and psychotropic properties and are useful in anxiety and mental disorders. Mentat an herbal formulation containing *C. asiatica* improve memory and concentration in children [47].

7.12 Commercial Products

Various products containing *C. asiatica* are launched in international market such as creams, baby lotions, slimming tea, tonics etc. due to its immense clinical and therapeutic benefit. Some of the products and their applications are shown in Table 5.

7.12 Precautions and safety

In recommended doses no toxic effect of *C. asiatica* is observed yet. Side effects are exceptional however at very high dose of herb possible side effects will include burning sensations (with external use), skin allergy, nausea, headache, dizziness, stomach upset, and extreme drowsiness. The fresh plant may have a low potential for skin irritation. Subcutaneous injections may result in cause pain at the injection site, discoloration and can also cause allergic reactions. It is also reported that by causing spontaneous abortion chronic treatment may prevent women from becoming pregnant [48].

8. Conclusion

A critical investigation of literature for this review exposed that *Centella asiatica* is a valuable plant traditionally utilized to treat wide range of diseases and proved to having immense medicinal and therapeutic benefits. Phytochemicals such as asiatic acid, Madecassic acid, Madasiatic acid, Betulinic acid and Thankunic acid isolated from this plant are utilized in various commercial products such as skin

care, anti-aging, slimming teas etc. However, further studies should be conducted in order to explore unexploited potential of this plant.

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