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The therapeutic use of *Centella asiatica*

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Abstract
Centella asiatica (L.) is an effective medicinal plant for human beings. *Centella asiatica* (L.) randomly used in traditional medicine such as unani medicine, ayurvedic medicine and herbal medicine. It is a perennial, creeper, faintly aromatic and a valuable medicinal herb of all over the world. It is distributed throughout tropical and subtropical regions of World such as Bangladesh, India, China, Nepal, Madagascar, Srilanka and Indonesia etc. The requirement of *Centella asiatica* is now met from natural population, leading to their gradual depletion and thus followed by its placement in the list of threatened species as mentioned by International Union for Conservation of Nature and Natural Resources (IUCN). Much of the ancient and contemporary lore surrounding this plant with its chemistry and pharmacology related to efficacy of both herbal preparations and chemical isolates are justified on the basis of experimental evidences. This paper provides its immense importance as economic plant with medicinal value as well as brief information of its products in the market launched, showing its dependability.

Keywords: *Centella asiatica*, threatened, pharmacology, perennial and ancient

1. Introduction
Centella asiatica (Linn.) have been used as treatments for thousands of years, based on experience and folk remedies and continue to draw wide attention for their role in the treatment of mild and chronic diseases. In recent times, focus on plant research has increased all over the world and a large body of evidence has been accumulated to highlight the immense potential of medicinal plants used in various traditional systems of medicine. *Centella asiatica* L. has been used as a medicinal herb for thousands of years in Indian subcontinent, China, Srilanka, 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, hence primarily known as a "Food of brain" in Indian subcontinent. *Centella asiatica* (Linn.) Urban sys. synonym *Hydrocotyle asiatica* Linn. Commonly known as Indian Pennywort, belongs to the family Apiaceae (previously known as Umbelliferae). In Indian subcontinent the plant was earlier confused with *Bacopa monnieri* Wettst., as both plants have been sold in the market by the name "Brahmi". However, the controversy has been resolved and it is concluded that Brahmi is *B.monnieri* and mandookaparni is *Centella asiatica* (Rev Ser, (Ca-Ci), 1992). According to the reports of Export and Import Bank of India *Centella asiatica* is one of the important medicinal plants in the International market of Medicinal Plant Trade. However, the wild stock of this plant species has been markedly depleted, because of its large scale and unrestricted exploitation coupled with limited cultivation and insufficient attempts for its replacement has been made. Moreover, now it has been listed as Threatened plant species by the International Union for Conservation of Nature and Natural Resources (IUCN) (Pandey NK, Tewari KC, *et al*. 1993) [27], and also as an endangered species (Singh HG-1989, Sharma BL and Kumar A. 1998) [36, 37].

2. Vernacular Names
Bengali	:	Thankuni, Tholkuri
Hindi	:	Bemgsag, Brahma-Manduki, Gotukola, Khulakhudi, Mandookaparni.
Urdu	:	Brahmi
USA	:	Indian Pennywort, Marsh Pennywort
China	:	Fo-ti-tieng, Chi-hsueuh-ts'ao
Nepal	:	Ghod tapre
Hawaii	:	Pohe Kula
Cook Islands	:	Kapukapu
Tahiti	:	Tohetupou
Fiji	:	Totodro
Samoa, Tonga	:	Tono

(Sakshi Singh*, Asmita Gautam, Abhimanyu Sharma and Amla Batra 2010) [38].

3. Botanical Classification of *Centella asiatica*
Kingdom	:	Plantae.
Division	:	Angiospermae
Class	:	Dicotiledoneae
Order	:	Umbelliferae
Family	:	Apiaceae
Genus	:	*Centella*
Species	:	*asiatica* Linn.

4. Morphology and Habitat
Centella asiatica is small creeping herb with shovel shaped leaves emerging alternately in clusters at stem nodes. This is a prostate, sparingly hairy or nearly smooth herb. The stems

root at the nodes. The leaves are rounded to reniform, 2 to 5 centimeters wide, horizontal, more or less cupped, rounded at the tip, and kidney-shaped or heart-shaped at the base, the rounded lobes often overlapping. The petioles are erect and long. The peduncles occur in pairs of three, are less than 1centimeter long, and usually bear 3 sessile flowers. The petals are dark-purple, ovate, and about 1 millimeters long. The fruit is minute, ovoid, white or green, and reticulate, each with 9 sub similar longitudinal ridges. The runners lie along the ground and the inch long leaves with their scalloped edges rise above on long reddish petioles. The insignificant greenish- to pinkish-white flowers are borne in dense umbels on separate stems in the summer. Plant is also known as gotu kola and grows abundantly in shady, moist, or marshy areas. It is distributed widely in many parts of the world,including Bangladesh, India, Sri Lanka, Madagascar, South Africa, Australia, China, and Japan (Zheng, CJ, Qin LP. 2007, Satake T., Kamiya K., An Y., Oishi Nee Taka T., Yamamoto J. 2007) [45, 33].

5. Importants Formulations

Important Unani formulations containing *Centella asiatica* are as follows:

- Qurs Penitab
- Tab.Thankuni
- Sharbat Khakshi

Important Ayurvedic formulations containing *Centella asiatica* are as follows:

- Jambadyarista
- Khudhavati Boti
- Khudhavati gutidika
- Brihat guruchyadi toil

(Bangladesh National Unani Formulary 2010, Bangladesh Ayurvedic Formulary 2010) [3].

6. Biochemical Properties

The biochemical compositions of *Centella asiatica* has been widely studied and researched.

- Triterpenoids
- Volatile oil and Fatty acids
- Alkaloids
- Glycosides
- Flavonoids
- Others
- Vitamin B, C, G and some amino acids etc.

7. Triterpenoids

Include asiatcoside, centelloside, madecossoside, thankuniside, isothankunic acid, centellose, asiatic, centellic and madecassic acids (Dutta T and Basu U.P. 1968, Singh B and Rastogi R.P. 1969) [10, 39] and brahmoside,brahminoside, brahmicacid, the structure of their genin, brahmic acid (m.p. 293°) has been established as 2,6-hydroxy, 23-hydroxy-methyl ursolic acid. Asiaticoside and madecossoside predominated in the leaves with less in roots (Aziz Z.A., Davey M.R. *et al* 2007) [2].

7.1 Volatile oil and Fatty acids

The fatty oil consists of glycerides of palmitic, stearic, lignoceric, oleic, linoleic and linolenic acids (Chopra RN, Nayar SL and Chopra IC.1956) [8].

7.2 Alkaloids

An alkaloid, hydrocotylin ($C_{22}H_{33}NO_8$) has been isolated from the dried plants (Chopra RN, Nayar SL and Chopra IC. 1956) [8].

7.3 Glycosides

Asiaticoside, madecossoside and centelloside have been isolated from the plant parts. On hydrolysis, these glycosides yield the triterpene acids, asiatic acid, madegascaric acid (Schaneberg BT, Mikell JR, Bedir E and Khan IA. 2003) [40] and centellic acid, except this Centella acid, all the above are present in free form in the plant.

7.4 Flavonoids

Flavanoids, 3-glucosylquercetin, 3-glucosylkaemferol and 7-glucosylkaemferol have been isolated from the leaves.The plant is reported to contain tannins, sugars, inorganic acids and resin,amino-acids, viz. aspartic acid, glycine, glutamic acid, α-alanine and phenylalanine(Malhotra CL, Das PK, Sastry MS and Dhalla NS.1961) [19]. The total ash contains chloride, sulphate, phosphate, iron, calcium, magnesium, sodium and potassium. The leaves are rich in vitamins such as vit.B, vit.C [15] and vit.G(Leyel, C.F., Elixiris of Life. Samuel Weiser, Inc., New York, (1970) [17, 18].

8. The Ethnopharmacological Values

The plant material and its products are being used for health care since ages. Indigenous knowledge is valued and recognized as a rich natural resource in the custody of our society. But this knowledge is being lost due to non-transfer to the future generations, which is mainly due to more of stress being laid on instant medication, although it is so effective even today as it was thousands of years ago. The study of folk-lore remedies more precisely 'Ethnomedicine' or 'Ethnopharmacology' procrastinately picked up momentum since the last few decades in the context of exploring scarce plant sps. for development of phytomedicine. Some of the important traditional Socio-Economic uses of this marvellous herb *Centella asiatica* in different countries and in different ways are illustrated as;

In Bangladesh

Whole plant is utilized by Kavirajes (a community of Chalna area, Bangladesh) to treat multiple ailments like dog bite, asthma, carminative, itching, leucorrhoea, malaria, tumour and wounds (Rahmatullah Mohammad, Ferdausi Dilara *et al*. 2010) [30].

In India

Centella asiatica is valued as an ethnomedicine as well as in Ayurveda and Unani, the traditional Indian medicinal systems for thousands of years for different ailments like asthma, skin disorders, ulcers and body aches(Sahu N.P., Roy S.K. and Mahato S.B. 1989; Babu TD, Kuttan G and Padikkala J.1995) [33, 4], for improving memory, as a nervine tonic and in treatment of dropsy, elephantiasis, gastric catarrh, kidney troubles, leprosy, leucorrhoea and urethritis (Kakkar KK. 1988) [15], in maternal health care(Sidhu Kiranjot, Kaur

Ramthirath and Pannu Kunwarjeet 2006) [35], in treatment of stomach disorders and also as a vegetable(Das Sandipan, Khan ML, Rabha Abhijit and Bhattacharjya DK.2009) [9],

- Paniya women (A tribal of Wayanand district in Western Ghats) prefer to cook Muthil i.e. *Centella asiatica* L. mixed with *Trianthema portulaccastrum* L. and *Passiflora calcarata* Mast. with crabs or fish(Narayanan Ratheesh MK and Kumar Anil N.2007) [22].
- Leaf extract is taken orally to cure dysentery and improve memory power (Rajendran K., Balaji P and Basu Jothi M. 2008) [29].

In China

The traditional Chinese function include the use of this herb for dysentery and summer diarrhoea, vomiting, jaundice and scabies, Hansen's disease (leprosy), nosebleeds, tonsillitis, fractures, measles, tuberculosis, urinary difficulties, as a endocrine tonic and as an 'adaptogen', have diuretic properties(Leyel, C.F. 1985) [17].

- It was historically known as "Snow plant" for the reason of its cooling properties.
- Accounts of longevity and virility are derived from Leyel's treatment of the herb. She asserts that Chinese herbalist Chang-li-yun lived to the age of 256yrs and married 24 times, attributing this to his drunk an infusion of Centella everyday, so also known as 'miracle of elixiris'.
- In Nepal-also this herb is used traditionally in rheumatism, indigestion, leprosy, poor memory(Leonard Bruce David, L.Ac.1998),
- About 4 teaspoonfuls of leaf juice by squeezing about 50 leaves between palms is taken orally in the morning for 2-3 weeks for its alleged cooling property to body and
- Stomach (Mahato R.B. and Chaudhary R.P.2005) [20].
- Crushed leaf and root extract is applied to the affected parts to kill germs from wounds (Joshi Ananda Raj and Joshi Kunjani 2007) [14].
- Decoction of leaves is also applied to cure leprotic wound (Joshi Ananda Raj and Joshi Kunjani 2007) [14].

In Malaysia

The plant is used by Kadazandusun communities around Crocker Range, Sabah as;

- Tea of the plants are taken for hypertension, diarrhoea and urinary tract infections.
- The dried herb is used as a detoxicant, diuretic and to lower blood pressure and decrease heart rate (Ahmad B. Fasihuddin and Ismail Ghazally 2003) [1].

In Fiji

For treating Childhood tidal fevers, eye problems, fractures, swollen joints, rib pain and unwanted pregnancy.

In Madagascar

This herb traditionally utilized in leprosy, tuberculosis etc. (Bontemps J., Gazette Medicale Madagascariensis, Vol 5, 1942, Boiteau P., Dureuil M. and Ratsimamanga R.R. 1949) [6].

In Brazil

For elephantiasis and leprosy etc.

Economically the whole plant especially the leaves are used for the preparation of hair oil. Leaves are also used to prepare chutney, hasuvale, tambali and toddy.

9. Pharmacological Uses

Several research workers have reported different biological activities of *Centella asiatica*. These have been given under following headings;

9.1 Memory Enhancing

Aqueous extract of the herb showed significant effects on learning and memory and decreased the levels of norepinephrine, dopamine and 5-HT and their metabolites in the brain (Nalini K, Aroor AR, Karanth Ks and Rao A.1992) [23]. *Centella asiatica* contains brahmicacid, isobrahmic acid, brahminoside and brahmoside. It has psychotropic, sedative and anti-convulsant properties. It is also useful in dementia, mental disorders and anxiety. Thus, Mentat a polyherbal formulation where all the herbs act in synergistic manner produces improvement of memory, attention and concentration in children with learning disability(Upadhyay S.K., Saha Abhijeet, Bhatia B.D., and Kulkarni Kala Suhas 2002)

9.2 Mental-retardation

Centella asiatica tablets administered orally to mentally retarded children showed significant increase in general ability and behaviour patterns (Rao Appa MVR, Srinivasan K and Rao KT.1973) [31].

9.3 Cytotoxic and Antitumour

Oral administration of the crude extract of *Centella asiatica* and its partially purified fractions induced apoptosis in solid and Ehrlich Ascites tumour and increased the life span of these tumours bearing mice(Babu TD and Paddikkala J.1994) [7]. Asiatic acid was found to have anticancer effect on skin cancer (Park BC, Bosire KO, Lee ES, Lee YS and Kim JA. 2005) [26].

9.4 Alzheimer's Disease

In various studies testing cognitive improvements of rats and standard shuttle box, step-through paradigm, elevated plus maze and passive avoidance tests, *Centella asiatica* improved learning and memory(Soumyanath A, Zhong Y, Henson E, Wadsworth T, Bishop J, *et al*. 2012) [41]. When aqueous extracts of *Centella asiatica* at doses of 100-300 mg/kg per day were distributed to newborn mice from 15 days old to 30 days old, learning and spatial memory were improved without influencing motor functioning skills(Soumyanath A, Zhong Y, Henson E, Wadsworth T, Bishop J, *et al*. 2012) [41]. Researchers reported that doses of *Centella asiatica* influenced the cell nerves of the pyramidal cells in the prefrontal cortex, the hippocampus, and other areas, in newborn and adult mice and rats [46]. Researchers suggest that results from these studies presents aqueous extract of *Centella asiatica* as lowering the degenerative impairments of memory, learning and aging in relation to Alzheimer's disease(Soumyanath A, Zhong Y, Henson E, Wadsworth T, Bishop J, *et al*. 2012) [41]. Researchers tested the effect of aqueous extract *Centella asiatica* on behavioral loss in the

Tg2576 transgenic mouse, most commonly used for Alzheimer's disease testing. To test characteristics similar to Alzheimer's disease, the mutant human amyloid precursor protein (APP) was injected in each mouse. APP produces cortical β-amyloid (Aβ) plaques similar to Alzheimer's disease pathology [46]. Fifteen Tg2576 mice and twenty wild-type twenty-month-old female mice organized according to genotype. Half of each genotype group was given *Centella asiatica* in drinking water (2 mg/mL) and water bottles were changed every other day. Spatial memory impairment in Tg2576 mice progressed with *Centella asiatica* treatment. The progression was correlated with the appearance of Aβ plaques. Although few studies have been performed on humans, Soumyanath *et al*. found that *Centella asiatica* improved the mental capabilities of 30 mentally retarded children. Thirty children between the ages of 7-18 were administered 500 mg of the dried herb/daily for three months. It was found that *Centella asiatica* improved mental capabilities(Soumyanath A, Zhong Y, Henson E, Wadsworth T, Bishop J, *et al*. 2012) [41].

9.5 Immunomodulating

Pectin isolated from *Centella asiatica* showed immunostimulating activities (Wang Xs, Dong Q, Zuo JP and Frong JN. 2003) [42] and triterpenoid Saponins (Plohmann B, Bader G, Streich S, Hiller K and Franz G. 1994) [25] and methanol extracts showed preliminary immunomodulatory effect(Jayathirtha MG and Mishra SH. 2004) [13].

9.6 Anxiolytic Properties

Centella asiatica has a historic reputation for reducing anxiety(Wijeweera P, Arnason J, Koszycki D, Merali Z 2006) [44]. Tested *Centella asiatica* on anxiety levels in rats during the elevated plus maze, open field test, social interaction test, locomotor activity, Vogel test and novel environment test and found that anxiolytic activity may be cause of triterpene heavy components in extracts of *Centella asiatica*. Although other active compounds may contribute to important plant activity effected by, or linked with asiaticoside, asiaticoside is the most active and most dominant triterpene (Wijeweera P, Arnason J, Koszycki D, Merali Z 2006) [44].

9.7 Antioxidant Activity

Oxidative stress inflicts physical function in age. Antioxidants curb age-related physical and cognitive declines and also contribute to a positive influence in psychological capacity (Mato L, Wattanathorn J, Muchimapura S, Tongun T, Piyawatkul N, *et al*. 2009) [21]. To determine the positive influence and antioxidant functions of *Centella asiatica* tested the positive influence and antioxidant functions of *Centella asiatica* on physical ability, physical satisfaction and emotional wellness and outlook in healthy elderly volunteers(Mato L, Wattanathorn J, Muchimapura S, Tongun T, Piyawatkul N, *et al*. 2009) [21]. Defined health as a "dynamic state of well-being characterized by a physical, mental and social potential affected by "health" (Mato L, Wattanathorn J, Muchimapura S, Tongun T, Piyawatkul N, *et al*. 2009) [21]. *Centella asiatica* was a candidate herbal remedy for improved physicality in healthy elderly because of its antioxidant compounds determined *Centella asiatica* as an herbal remedy candidate for improved physicality in healthy elderly because of its antioxidant compounds. The improvement of physical health and quality of life influenced by *Centella asiatica* was tested on elderly volunteers for two months. Volunteers participated in various strength tests under the controlled administration of *Centella asiatica* (doses of 500 and 750 mg/daily). Strength tests determined the improved strength of the leg, specifically the thigh, ankle, foot and hip. After two months of tests and doses of *Centella asiatica* found that leg, thigh, ankle, foot and hip strength increased, determining that *Centella asiatica* can improve quality of life and physical capacities.

9.8 Wound Healing

Madecassol, an extract of this plant containing madecassic acid, asiatic acid and Asiaticoside accelerates cicatrisation and grafting of wounds. Asiaticoside promotes fibroblasts proliferation and extracellular matrix synthesis in wound healing(Srivastava R, Shukla YN and Kumar S.1997) [42].

9.9 Cardioprotective

The alcoholic extract of the whole plant showed strong cardioprotective activity in limiting ischemia-reperfusion induced myocardial infraction in rats (Pragada RR, Veeravalli KK, Chowdary KP and Routhn KP. 2004) [24].

9.10 Anti-inflammatory activity

Extract of Centella exerted anti-inflammatory effects by reduction of acute radiation reaction in rats. *Centella asiatica* water extract and its active constituent asiaticoside have an anti-inflammatory property that is brought about by inhibition of NO synthesis and thus facilitate ulcer healing (Guo,JS, Cheng, CL and Koo 2004) [11]. Crude extract of *Centella asiatica* showed anti inflammatory activity in rats by prostaglandinE2-induced paw edema. Bioactive terpene acids such as asiatic acid and madecassic acid may be present in the crude extract that may account for the anti inflammatory activities(Somchit, MN. Sulaiman,MR Zuraini,A Samsuddin L, Somchit, N. Israf DA., Moin S 2004) [32].

10. Safety and Dosages

While using suggested doses of *Centella asiatica* extract will not cause serious side effects, using large amounts of *Centella asiatica* for topical use of *Centella asiatica* may cause skin allergies and burning sensations, headache, upset stomach, nausea, dizziness and drowsiness. Fresh *Centella asiatica* may cause a skin rash (Gohil K, Patel J, Gajjar A 2010) [12]. Taking very large amounts of *Centella asiatica* can be the source of headaches and unconsciousness. Taking *Centella asiatica* for a long period of time may make it difficult for women to become pregnant and may cause spontaneous abortion for pregnant women (Gohil K, Patel J, Gajjar A 2010) [12]. Individuals taking sleep aides should not consume *Centella asiatica* in high doses as it is a sedative(Gohil K, Patel J, Gajjar A 2010) [12].

11. Commercial Products

List of some Products launched in the market, containing *Centella asiatica*; Table 1.

Table 1: Some Products launched in the market, containing *Centella asiatica*.

Name of the Product	Company	Applications
Centurin	Hamdard Laboratories (Waqf) Bangladesh	Improves cognitive function,boost up memory,antiaging,boosts up immune system,remove free radicals and effective in dementia,alzheimer's diseases, Senile sickness,nervous debility,all kinds of skin diseases.
Mandukaparni	The Himalaya Drug Company, Bangalore [India]	Improves mental abilities, vascular support, blood circulation and psoriasis.
Mentat	The Himalaya Drug Company, Bangalore [India]	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 Himalaya Drug Company, Bangalore [India]	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.
Abana (Heart Care)	The Himalaya Drug Company, Bangalore [India]	Abana regulates serum lipids by lowering the cholesterol, triglycerides, low- density lipoprotein (LDL) and very low density lipoprotein (VLDL) levels and restores the cardioprotective high density lipoprotein (HDL) level. It also reduces platelet aggregation.
Menosan	The Himalaya Drug Company, Bangalore [India]	Menosan possesses phytoestrogens, which act through estrogen receptor dependent mechanism. Menosan helpsb in alleviating symptoms of menopausal syndrome.
Nourishing Skin Cream	The Himalaya Drug Company, Bangalore [India]	Provides all day moisturizing, nourishment and protection to skin from pollution and dry weather.
SNP Control Cream	SD Biotechnologies co., Ltd. [Korea]	*Centella asiatica* extract and Allantoin, improves drying and delays skin aging.
Weight Loss Tea	Pairs of Horses Biotechnology Co. Ltd. [China]	C. asiatica, Wolfberry fruit, Chrysanthemum, Pinellia, Salvia, for sliming.

12. Future Directions

As medicinal therapies increase, more studies must be conducted to better understand the pharmacological compounds and chemical reactions of *Centella asiatica* and how it can advance remedial therapies. Clinical and preclinical studies will advance research on herbal remedies and provide greater opportunity for therapeutic uses.

13. Conclusion

Although the results from this review are quite promising for the use of *Centella asiatica* as a multi-purpose medicinal agent, several limitations currently exist in the current literature. While *Centella asiatica* has been used successfully in Unani and Ayurvedic medicine for centuries, more clinical trials should be conducted to support its therapeutic use. It is also important to recognize that *Centella asiatica* may be effective not only in isolation, but may actually have a potentiating effect when given in combination with other herbs or drugs.

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