

Centella asiatica (Linn.) Urban óA Review

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Abstract

Centella asiatica (Linn.) Urban is valued in Indian systems of medicine for improving memory and for the treatment of nervine disorders and skin diseases. It has been used extensively as memory enhancer. The present review is an up-to-date and comprehensive literature analysis of the chemistry, pharmacology and clinical trials on Centella drug.

Keywords: *Centella asiatica*, Mandookaparni, Gotu Kola, Memory enhancer, Medicinal plant, Unani medicine.

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Introduction

Centella or Indian Pennywort, *Centella asiatica* (Linn.) Urban syn. *Hydrocotyle asiatica* Linn. belongs to the family Apiaceae. The herb is known as *Brahmi* in Unani medicine, *Mandookaparni* in Ayurvedia and *Gotu Kola* in the western world. In India, the plant was earlier confused for *Bacopa monnieri* Wettst., as both were 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 *C. asiatica*¹.

The plant is known by following vernacular names: *Manimuni* (Assam); *Brahmamanduki*, *Thankuni*, *Tholkuri* (Bengali); *Chokiora* (Bihar); *Karinga*, *Karivana* (Bombay); *Vallari* (Deccan); *Barmi*, *Moti brahmi* (Gujrati); *Bemgsag*, *Brahma-manduki*, *Khulakhudi*, *Mandookaparni* (Hindi); *Brahmisoppu*, *Urage*, *Vandelaga-illikiwigidda*, *Vondelaga* (Kanarese); *Kodagam*, *Kodangal*, *Kutakam*, *Kutakan*, *Kutannal*, *Muthal*, *Muttil*,

Muyalchevi (Malayalam); *Brahmi*, *Karinga*, *Karivana* (Marathi); *Bat-maina* (Meghalaya); *Thalkudi* (Oriya); *Bhekaparni*, *Bheki*, *Brahmamanduki*, *Darduchhada*, *Divya*, *Mahaushadhi*, *Mandukaparni*, *Mandukaparnika*, *Manduki*, *Mutthil*, *Supriya*, *Tvashti* (Sanskrit); *Hingotukola* (Sinhalese); *Babassa*, *Vallarai*, *Vallari* (Tamil); *Babassa*, *Bekaparnamu*, *Bokkudu*, *Brahmi*, *Saraswataku*, *Mandukbrammi* (Telugu); *Thankuni*, *Thunimankuni* (Tripura); *Brahmi* (Urdu)²⁻⁵.

It is a slender, tender, faintly aromatic herb, which has numerous creeping stoloniferous stems up to 2 m long. Stems are prostrate, often reddish and striated, rooting at the nodes. The leaves, 1-3 from each node of the stems, petioled, 2-6 cm long and 1.5-5 cm wide, circular-reniform rather broader than long, more or less cupped, entire shallowly crenate margins, glabrous on both sides. Flowers are in fascicled umbels, each umbel consisting of 3-4 white to purple or pink, sessile (rarely pedicelled) flowers.

Fruit 4 mm long, oval to globular in shape, like a grain of barley, hard with thickened pericarp, often crowned by the persistent petals¹⁻³.

The plant is indigenous to South-East Asia, India, Sri Lanka, parts of China, the Western South Sea Islands, Madagascar, South Africa, South-East U.S, Mexico, Venezuela, Columbia and Eastern South America. It is found in abundance on moist, sandy or clayey soils, often in large clumps forming a dense green carpet or as a weed in crop fields and other waste places throughout India up to an altitude of 600m^{1,2,6}. The plant is propagated from seeds or from stolons¹. The fresh or dried aerial parts consisting of leaves and stem are used for medicinal purpose⁶.

The commercial Centella drug is frequently adulterated with *B. monnieri*¹ and other herbs or plants with semi-lunar or orbicular leaves like *Merremia emarginata* Hallier f. (syn. *Ipomoea reniformis* Choisy, *Evolvulus emarginatus* Burm. f.), *Hydrocotyle javanica* Thunb. and *H. rotundifolia* Roxb.⁷. Recently a large scale adulteration of the herb with *Malva rotundifolia* Linn. has been observed. The Chinese herb *Fo-ti tieng*, which means elixir for long life, is obtained from a closely allied plant and is sometimes, supplied as *Gotu Kola*. A variety of *Centella* known as



Centella asiatica



Bacopa mannieri

asiatic^{1,12}, thankunic^{1,12,18,19} and isothankunic^{1,12}. These acids except the last two are also present in free form in the plant besides isobrahmic¹ and betulic acids¹. Oxyasiaticoside¹⁵,

Thankuni, found in East India is cooked and eaten as spinach and is also sold as a genuine herb but is considered inferior⁸.

There has been plenty of research work on this plant as evidenced by the literature review presented in this paper.

Chemical composition

C. asiatica is reported to contain following type of compounds:

Triterpene acids

The plant contains following triterpene acids: asiatic^{1,6,9}, madecassic (madegascaric acid-6-hydroxy asiatic acid)^{1,6,10}, terminolic^{1,6,11}, centic¹, centellic¹, centoic acid¹, indocentoic acid¹, isobrahmic^{1,12,13}, betulic^{1,13}, brahmic^{9,13} (2 α , 3 β , 6 β , 23-tetrahydroxy-urs-12-en-28-oic acid)¹² and madasiatic acid (2 α , 3 β , 6 β -trihydroxyurs-12-en-oic acid)¹⁴.

Volatile and Fatty oil

The plant contains volatile and a fatty oil^{6,15}. The fatty oil consists of

glycerides of palmitic, stearic, lignoceric, oleic, linoleic and linolenic acids¹.

Alkaloids

An alkaloid, hydrocotylin (C₂₂H₃₃NO₈), has been isolated from the dried plant^{1,15}.

Glycosides

Asiaticoside A, asiaticoside B, asiaticoside^{1,6,9,11,15,17,18}, madecassoside^{1,11,12,17,18} and centelloside¹ have been isolated from the plant. On hydrolysis, these glycosides yield the triterpene acids, asiatic acid^{1,11,18}, madegascaric acid (madecassic acid^{1,11,12,18}) and centellic acid¹. These acids except the last one are also present in free form in the plant. Samples of the Indian plants collected from different places showed the presence of the following glycosides: indocentelloside¹, brahmoside^{1,9,12}, brahminoside^{1,9,12}, thankuniside^{1,12,18,19} and iso thankuniside^{1,9,18}. The corresponding triterpene acids obtained on hydrolysis of the glycosides are: indocentoic¹, brahmic¹,

glycoside D¹ and glycoside E¹ have also been reported. The variation in the chemical composition of Indian samples of the plant is attributed to geographical conditions¹.

Flavonoids

Flavonoids, 3-glucosylquercetin, 3-glucosylkaempferol and 7-glucosylkaempferol have been isolated from the leaves^{1,17}.

Others

The plant is reported to contain, mesoinositol^{1,9} oligosaccharide centellose^{1,9}, kaempferol¹, quercetin¹, stigmasterol^{1,9}, sitosterol^{1,15}, campesterol¹, polyacetylenes^{1,14}, carotenoids¹, vitamin B¹ and vitamin C^{1,15}. A bitter principle, vellarine^{1,15} pectic acid^{1,15}, tannins²⁰, sugars²⁰, inorganic acids²⁰ and resin^{1,15} are also present. The plant also contains amino acids, viz. aspartic acid, glycine, glutamic acid, α -alanine and phenylalanine. The total ash contains chloride, sulphate, phosphate, iron, calcium, magnesium, sodium and potassium²¹.

An alcoholic extract of the herb gave an essential oil possessing the strong odour of the herb, a fatty oil¹, tannin^{1, 15} and a resinous substance^{1, 15}. The major terpenoidal constituent identified in the ether extract of the herb are β -caryophyllene, trans- β -farnesene, germacrene-D and an unidentified terpenic acetate¹.

Ursane- and oleanane-type triterpene oligoglycosides, centellasaponins B, C and D, were isolated from the aerial parts of the plant together with madecassoside, asiaticoside B, and scelleoside A. The chemical structures of centellasaponins B, C, and D were determined to be madecassic acid 28-O- β -D-glucopyranosyl(1 \rightarrow 6)- β -D-glucopyranoside, madasiatic acid 28-O- α -L-rhamnopyranosyl(1 \rightarrow 4)- β -D-glucopyranosyl(1 \rightarrow 6)- β -D-glucopyranoside, and 3 β , 6 β , 23-trihydroxyolean-12-en-28-oic acid 28-O- α -L-rhamnopyranosyl(1 \rightarrow 4)- β -D-glucopyranosyl(1 \rightarrow 6)- β -D-glucopyranoside, respectively²².

Isolation of ursolic acid lactone, ursolic acid, pomolic acid, 2 α , 3 α -dihydroxyurs-12-en-28-oic acid, 3-epimaslinic acid, asiatic acid, corosolic acid and rosmarinic acid from methanolic extract of *C. asiatica* have been reported²³.

Analysis of leaves gave the following values: moisture, 87.2; protein, 1.7; fat, 0.7; carbohydrates, 4.8; crude fibre, 3.4; and ash, 2.3 g/100g; calcium, 176.0; phosphorus, 72.0; iron, 12.0; vitamin C, 42.0; and niacin, 0.8 mg/100g; carotene, 2400 μ g/100g; and energy, 32.0 Kcal/100g. An ethanolic extract (80%) of the plant showed the presence of a number of free amino acids¹.

Medicinal uses

The plant is cooling, alterative, soporific, cardiotoxic, nervine tonic, sedative to nerves, stomachic, carminative, improves appetite, antileprotic, antiseptic, diuretic, exhilarant, demulcent, de-obstrant, tonic to vital organs (liver, kidneys, brain), tonic to nerves and memory and febrifuge. It is used in diseases of skin, nerves and blood and taken as tonic for accelerating nervous activity and for improving youth, longevity and memory. It is given for the treatment of mental illness, insomnia, hysteria, insanity, epilepsy, etc. The leaves are said to be useful in the treatment of ulcerations, chronic and callous, scrofulous and syphilitic with gummatous infiltration in chronic and obstinate eczema, psoriasis, leprosy, tuberculosis, leucoderma, cardiac debility, hoarseness, asthma, bronchitis, hiccup, abdominal disorders, headache, strangury, spermatorrhoea and fever. The leaves are also useful in abdominal disorders due to dysentery in children. Its efficacy has been valued as a stimulant to healthy mucous secretion in infantile diarrhoea and ozena. It stimulates fast growth of skin and nails^{1-4, 6, 16, 20, 24-27}.

In Chinese medicine the herb is used for dysentery and summer diarrhoea, vomiting, jaundice, urinary calculi, epistaxis and scabies⁶.

In Homoeopathic medicine it is used for skin diseases associated with itching and swelling. It is used in inflammation and ulceration of uterus, eczema, elephantiasis, ascariasis and in granular cervicitis^{6, 9}.

Precautions and adverse reactions

The drug sometimes causes allergic contact dermatitis²⁸⁻³³ but the

sensitizing capacity is considered to be low^{28, 32, 33}. In large doses the plant acts as narcotic, producing cephalgia, vertigo and sometimes coma^{1, 8}. Studies on the compound asiaticoside showed that it is not very toxic. At higher concentration it affected the epidermis by keratinization. The herb caused 20% mortality at a dose of 10 g/kg³⁴.

Pharmacological studies

Several research workers have reported different biological activities of *C. asiatica* in various *in vitro* and *in vivo* test models. These have been described in detail in following headings.

Gastric ulcer healing

Asiaticoside prevented development of cold induced gastric ulcers in rats¹⁴. Asiaticoside administered orally to rats, significantly reduced the formation of stress-induced ulcers³⁵. Extract of the plant inhibited significantly gastric ulceration induced by cold and restraint stress in Charles-Foster rats. The dose dependent reduction of gastric ulceration was associated with a dose dependent increase of the GABA level in the brain³⁶. Ethanolic extract of *Tinospora cordifolia* (Willd.) Miers ex Hook. f. & Thoms. and centella at dose of 100 mg/kg daily showed marked protective action against stress induced ulceration due to the adaptogenic property of the mixture³⁷. *C. asiatica* prevented ethanol induced gastric mucosal lesions by strengthening the mucosal barrier and reducing the damaging effects of free radicals³⁸. Fresh juice of the plant showed significant protection against the experimental ulcer models and the ulcer protective effect may be due to

strengthening of the mucosal defensive factors³⁹. Water extract and asiaticoside showed healing effects on acetic acid induced gastric ulcers in rats⁴⁰.

Wound healing

Madecassol, an extract of this plant containing madecassic acid, asiatic acid and asiaticoside accelerates cicatrization and grafting of wounds¹. Total triterpenoid fraction extracted from *C. asiatica* increased the percentage of collagen in cell layer fibronectin and thus may help in promoting wound healing⁴¹. Herb extract, madecassic acid, asiatic acid and asiaticoside are effective locally on wounds in rats¹⁰. Asiaticoside facilitates wound healing through an increase in peptidic hydroxyproline content, tensile strength, collagen synthesis, angiogenesis and epithelialization, as shown in animal models⁴²⁻⁴⁴. Asiatic acid and madecassic acid have also demonstrated an increase in peptidic hydroxyproline showing an increased remodeling of collagen synthesis in wounds^{42, 45}. Oral and topical administration of an alcoholic extract increased cellular proliferation and collagen synthesis at the wound site, as evidenced by increase in DNA, protein and collagen content of granulation tissues on rat dermal wounds. Quicker and better maturation and cross linking of collagen was observed in the extract-treated rats, as indicated by the high stability of acid-soluble collagen and increase in aldehyde content and tensile strength. The extract treated wounds were found to epithelialise faster and the rate of wound contraction was higher, as compared to control wounds. The results show that the herb produced different actions on the various phases of wound repair⁴⁶. Formulations

(ointment, cream and gel) of aqueous extract of *C. asiatica*, when applied topically on the open wounds in rats increased cellular proliferation and collagen synthesis at the wound site, as evidenced by increase in collagen content and tensile strength. The treated wounds epithelialised faster and the rate of wound contraction was higher as compared to control wounds. The process of healing was better with gel formulation when compared to ointment and cream⁴⁷. Asiaticosides enhanced induction of antioxidant levels at an initial stage of healing which may be an important contributory factor in its healing properties⁴⁸. Asiaticoside exhibits significant wound healing activity in normal as well as delayed healing models and is the main active constituent of *C. asiatica*⁴⁴. Titrated extract which is a reconstituted mixture of three triterpenes extracted from the plant, asiatic acid, madecassic acid and asiaticoside stimulate collagen synthesis, glycosaminoglycan synthesis and extracellular matrix accumulation in rat experimental wounds. Asiatic acid and asiaticoside were more active than madecassic acid⁴⁵. Thus, the plant appears to be effective in the treatment of wound healing disturbances⁴⁹. Asiaticoside, promotes fibroblast proliferation and extracellular matrix synthesis in wound healing^{50, 51}.

Cytotoxic and antitumour

Oral administration of the crude extract of *C. asiatica* and its partially purified fractions retarded the development of solid and ascites tumours and increased the life span of these tumour bearing mice. Cytotoxic and anti-

tumour effects involve direct action on DNA synthesis⁵². A partially purified fraction of methanol extract of the herb inhibited the growth of tumour cells with no toxic effect against lymphocytes⁵³. Studies involving *C. asiatica* induced apoptosis in Ehrlich Ascites tumour cells⁵⁴ and in chemotherapeutic drug induced toxicity showed anti-cancer effect of the drug and there was a reduction in myelosuppression⁵⁵. Water extract has a chemopreventive effect on colon tumorigenesis⁵⁶. *C. asiatica* modulates nitric oxide and tumour necrosis factor- α in mouse macrophages⁵⁷. Asiaticoside possesses good wound healing activities because of its stimulative effect on collagen synthesis. It might be useful in cancer chemotherapy as it induces apoptosis and enhances anti-tumour activity of vincristine in cancer cells⁵⁸. Asiatic acid was found to have anticancer effect on skin cancer⁵⁹.

Memory enhancing

Aqueous extract of the herb showed significant effect on learning and memory and significantly decreased the levels of norepinephrine, dopamine and 5-HT and their metabolites in the brain⁶⁰. Syrup prepared from *Centella* and *Bacopa* showed significant effect on learning ability of albino mice⁶¹. Aqueous extract of the plant showed cognitive-enhancing and antioxidant properties in Streptozotocin induced cognitive impairment and oxidative stress in rats^{62, 63}. Aqueous extract decreased the Pentylene-tetrazole-kindled seizures and showed improvement in the learning deficit induced by PTZ kindling suggesting its potential to antiepileptic drugs with an added advantage of preventing cognitive impairment⁶⁴. Treatment during postnatal

developmental stage with *C. asiatica* aqueous extract influenced the neuronal morphology and promoted the higher brain function of juvenile and young adult mice⁶⁵.

Neuroprotective

Asiatic acid exerted significant neuroprotective effects on cultured cortical cells by potentiation of the cellular oxidative defense mechanism. Therefore, it may prove efficacious in protecting neurons from the oxidative damage caused by exposure to excess glutamate⁶⁶. The plant accelerates nerve regeneration upon oral administration and contains multiple active fractions increasing neurite elongation *in vitro* suggesting that components in centella may be useful for accelerating repair of damaged neurons⁶⁷.

Cardioprotective

C. asiatica showed cardioprotective effect on antioxidant tissue defense system during Adriamycin induced cardiac damage in rats⁶⁸. The alcoholic extract of the whole plant showed strong cardioprotective activity in limiting ischemia-reperfusion induced myocardial infarction in rats⁶⁹.

Hepatoprotective

C. asiatica possesses *in vitro* anti-hepatoma activity⁷⁰. Total glucosides of the plant has significant preventive and therapeutic effect on dimethylnitrosamine induced liver fibrosis in rats⁷¹.

Antioxidant

Crude methanol extract of *C. asiatica* showed antioxidant activity on lymphoma-bearing mice⁷². Antioxidant

activity of the plant is comparable to the activities of rosemary and sage and has very good potential to be explored as source of natural antioxidants⁷³. As a potent antioxidant it exerted significant neuroprotective effect and proved efficacious in protecting rat brain against age related oxidative damage⁷⁴. Simultaneous supplementation of the drug significantly protects against arsenic-induced oxidative stress but does not influence the arsenic concentration in liver, kidney and brain. It can thus be suggested that co-administration of centella protects animals from arsenic-induced oxidative stress but exhibits no chelating property⁷⁵.

Immunomodulating

Triterpenoid saponins of centella showed immunomodulatory effect⁷⁶. Oral administration of *Brahma Rasayana*, containing centella, significantly increased white blood cell count, bone marrow cellularity, natural killer cells and antibody dependant cellular activity in mice exposed to gamma radiations. It reduced radiation induced peroxidation in the liver⁷⁷. Pectin isolated from *C. asiatica* showed immunostimulating activities⁷⁸ and methanol extracts showed preliminary immunomodulatory activities⁷⁹. Centella and *Rhinacanthus nasutus* (Linn.) Kurz revealed immunomodulating activity with regard to both non-specific cellular and humoral immune responses suggesting that they may have chemopreventive or anticancer potential⁸⁰.

Anabolic effect

Centella prevented mortality due to gross protein deficiency in albino rats

fed on a low protein diet. It increased the blood protein nitrogen and prevented fatty acid infiltration of liver. The increase in haemoglobin content was quite high and statistically significant. It decreased the mean level of blood urea⁸.

Radioprotective

Madecassol from the plant reduced acute radiation dermatitis in rats by anti-inflammatory activity⁸¹. *C. asiatica* could be useful in preventing radiation induced behavioural changes during clinical radiotherapy⁸². The plant extract showed radioprotective properties⁸³ and pretreatment with it prior to gamma ray irradiation was found to be effective against radiation induced damage in the mouse liver⁸⁴.

Vascular/Venous tone effects

Total triterpenic fraction of centella is effective in improving venous wall alterations in chronic venous hypertension and in protecting the venous endothelium. Total triterpenic fraction is active on connective tissue modulation, improves the synthesis of collagen and other tissue proteins by modulating the action of fibroblasts in the vein wall, and stimulates collagen remodeling in and around the venous wall. This is due to the modulating action of total triterpenic fraction on fibroblasts as shown by experiments on the growth of human embryonal fibroblasts⁸⁵.

Ethanol extracts *in vitro* had a remarkable enhancement of fibroblast cell attachment and tissue plasminogen activator⁸⁶. Varicose veins are associated with increased uronic acid and lysosomal enzymes involved with mucopolysaccharide (β -glucuronidase,

β -N-acetylglucosaminidase) metabolism. Total triterpenic fraction decreases uronic acid, β -glucuronidase, β -N-acetylglucosaminidase and arylsulfatase in the connective tissue and vascular wall⁸⁷.

Antidepressant

The total triterpenes had antidepressant activity in forced swimming mice and ameliorated the imbalance of amino acid levels⁸⁸. The triterpenes showed antidepressant effect and caused significant reduction of the corticosterone level in serum and increase in the contents of monoamine neurotransmitters in rat brain⁸⁹.

Antipsoriatic

Aqueous extracts inhibited keratinocyte replication and its anti-psoriatic activity is worthy of further investigation. The effect produced may, however, be due to its two constituent triterpenoid glycosides madecassoside and asiaticoside⁹⁰.

Antitubercular and Antileprotic

Asiaticoside has been shown to be useful in the treatment of leprosy^{1, 4} and certain types of tuberculosis¹.

Antifilarial

A mixture of ethanol extracts of *C. asiatica* and *Acacia auriculiformis* A. Cunn. ex Benth. resulted in a considerable decrease in filarial count in dogs naturally infected with *Dirofilaria immitis*⁹¹.

Slimming

Slimming liposomes containing two micro-circulation activators, i.e., esculoside and *C. asiatica* extracts

showed a dramatic increase in the cyclic adenosine monophosphate content in human adipocytes with a subsequent rise in the nonesterified fatty acids content of human adipocyte incubation medium *in vitro* tests and could provide an actual potent slimming effect on human volunteers *in vivo* studies⁹².

Antiviral

Crude water extracts of combinations of each of centella, *Maclura cochinchinensis* Lour. and *Mangifera indica* Linn. showed anti-herpes simplex virus activities⁹³.

Antifertility

A crude extract of the plant and the glycoside isothankuniside and its derivative methyl-5-hydroxy-3, 6-diketo-23 (or 24)-nor-urs-12-ene-28-oate exhibited antifertility activity in female mice^{1, 10}.

Tranquilizing and Sedative

Saponins exhibited sedative action in rats and mice¹⁴. It has weak sedative but cardiodepressant and hypotensive action¹⁸. The alcoholic extract produced a tranquilizing effect in rats⁹⁴ and the glycosidal fraction showed a sedative effect²¹. Brahmoside possessed sedative action in rats equivalent to that of a minor tranquilizer⁹⁵. Experimental studies on the psychotropic effects in rats showed a significant barbiturate hypnosis potentiation effect, besides producing significant alterations in the neurochemistry of the brain. The histamine and catecholamine contents in the brains of the treated group increased significantly⁹⁶. Alcoholic extract of the herb prolonged the hypnotic effect of

sodium phenobarbitone in rats and decreased the acetylcholine and histamine content of the whole brain while catecholamine was increased. Its effect on the central nervous system resembled that of Chlorpromazine and Reserpine. It also had an anti-amphetamine activity and produced hypothermia, reduced the motor activity and was a potential neuroleptic³⁴. Barbiturate hypnosis potentiation effect was observed in different fractions⁹⁷ and a depressant property was detected in this herb⁹⁸. Methanol and ethyl acetate extracts of Gotu Kola as well as pure asiaticoside, imparted anxiolytic activity in elevated plus maze⁹⁹.

Antiprotozoal

Alcoholic extract of the entire plant showed antiprotozoal activity against *Entamoeba histolytica*¹⁰⁰.

Antispasmodic

An alcoholic extract of the plant showed anti-spasmodic activity on acetylcholine induced contractions of rat ileum, which is attributed to the glycosides^{1, 10}.

Anti-inflammatory

Madecassoside and madecassic acid, both showed anti-inflammatory activity^{1, 10}. Extract of centella exerted anti-inflammatory effects by reduction of acute radiation reaction in rats⁸¹. A polyherbal Ayurvedic preparation *Brahmi Rasayana*, containing centella as well as other herbs showed anti-inflammatory activity¹⁰¹. *C. 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 healing¹⁰².

Effect on skin

Alcoholic extract containing asiatic acid and asiaticoside was used as a cream to improve skin texture and regenerate skin of old people. Alcoholic extract of the herb with other ingredients is useful in pruritis and other skin disorders¹⁰.

Clinical trials

Mental retardation

Centella tablets administered orally to mentally retarded children for 12 weeks showed very significant increase in general ability and behaviour pattern^{12, 103}.

Venous hypertension

The effect of an extract of centella with capillary filtration and ankle edema was evaluated in patients with venous hypertension. Capillary filtration rate and ankle edema both significantly improved in a dose-dependent manner in the extract-treatment group. The subjective symptoms (swelling, sensation, restless lower extremity, pain and cramps and tiredness) were significantly improved in the extract-treatment group with no change in the placebo treatment group¹⁰⁴. A study involving combined after treatment with total triterpenic fraction and the possibility of using the vacuum suction chamber device showed improvement of the microcirculation and capillary permeability in patients with venous hypertension¹⁰⁵. In a placebo-controlled, randomized trial, total triterpenic fraction of centella, was effective in improving the microcirculation in venous hypertension and microangiopathy and venous

microangiopathy was improved by this treatment¹⁰⁶. Total triterpenic fraction displayed a significant activity in the treatment of venous hypertension using a combined microcirculatory model¹⁰⁷. In a double-blind study in patients with chronic venous hypertensive microangiopathy the efficacy of oral total triterpenic fraction administered for 60 days was tested. The results confirm the efficacy of total triterpenic fraction in venous hypertensive microangiopathy. Furthermore, the effects of this fraction appear to be dose-related¹⁰⁸.

Striae gravidarum

Compared to placebo, treatment with a cream containing centella extract, α -tocopherol and collagen-elastin hydrolysates was associated with less women developing stretch marks. Cream appears to help prevent the development of stretch marks in pregnancy, but only for women who had previously suffered stretch marks in pregnancy¹⁰⁹.

Hepatic disorder

Titrated extract of centella caused improvement in chronic hepatic disorders¹¹⁰.

Anxiolytic activity

A polyherbal preparation containing centella was quite effective in insomnia¹¹¹. A mixture of centella, liquorice and *Nardostachys* in the ratio of 1:2:2 was more active in psychomotor performance, compared with a well known tranquilizer, Diazepam, and a placebo. The drug was effective in controlling somatic and psychic anxiety, preferably in old age¹¹². *Ksheerbala tailam*—a mixture of herbs was

suspended in milk and oil emulsion and dropped on the forehead was effective in enhancing perceptual discrimination and psychomotor performance¹¹³. A double-blind, placebo-controlled study on the effects of centella in healthy subjects suggests that it has anxiolytic activity in humans as revealed by the acoustic startle response. It remains to be seen whether this herb has therapeutic efficacy in the treatment of anxiety syndromes¹¹⁴.

Anti-inflammatory and Wound healing

Preliminary study revealed positive clinical effects of an innovative preparation from the two herbal extracts centella and pomegranate (*Punica granatum* Linn.) in the form of biodegradable chips as a subgingival adjunct to scaling and root planing. Local delivery of extracts from centella and pomegranate plus scaling and root planing significantly reduced the clinical signs of chronic periodontitis, promoted tissue healing and modulated host responses¹¹⁵.

Vascular diseases

A randomized, double blind, placebo controlled study evaluated the efficacy of a titrated extract of centella in treating chronic venous insufficiency. The asiaticoid mixture, administered as 60 mg daily and 120 mg daily for two months, led to significant improvement in subjective (heaviness in legs, pain on standing up, edema) and objective (plethysmographic measurements of vein tone) parameters compared to placebo¹¹⁶. Total triterpenic fraction of *C. asiatica* by modulating collagen production in a period of 12 months increased the echogenicity of echolucent plaques at the

femoral bifurcation. These observations indicate a positive action of total triterpenic fraction on the stabilization of hypoechoic, low-density femoral plaques¹¹⁷. Total triterpenic fraction of centella improved signs and symptoms observed in patients with venous hypertension by improving capillary filtration rate and ankle edema. Dose ranging showed that 180 mg/day is more effective in improving symptoms and capillary filtration rate¹¹⁸. Total triterpenic fraction of centella is useful in diabetic microangiopathy by improving microcirculation and decreasing capillary permeability. Also total triterpenic fraction protects against the deterioration of microcirculation due to diabetic microangiopathy¹¹⁹. In a placebo-controlled randomized study in patients with diabetic microangiopathy and edema, the treatment with total triterpenic fraction of centella caused decrease in capillary filtration and edema along with symptomatic improvement. The action on edema is beneficial for the evolution of neuropathy and the effects of total triterpenic fraction on capillary filtration and edema are important in early stages of microangiopathy to avoid progression to clinical stages¹²⁰. In a placebo-controlled, randomized trial, treatment with total triterpenic fraction was effective in modulating collagen production over 12 months, by producing an increase in echogenicity in echolucent carotid plaques. These observations suggest a positive action of total triterpenic fraction on the stabilization of hypoechoic, low-density carotid plaques¹²¹. In a comparative clinical study, combination of α -tocopherol, rutin, Melilotus and centella showed significant improvement

of the clinical symptomatology in chronic venous insufficiency¹²². *C. asiatica* triterpenic fraction reduces the number of circulating endothelial cells in subjects with post phlebotic syndrome¹²³. Titrated extract of centella improved symptoms of heaviness in the lower limbs and edema in the patient of venous insufficiency of the lower limbs¹¹⁶. In patients prone to edema and microcirculation disturbances during long flights, total triterpenic fraction prevented edema and microcirculation alterations. These results are very interesting and indicate an option for patients prone to edema and microcirculation disturbances during long flights¹²⁴.

Others

In 93% cases of duodenal and gastric ulcer, the herb exhibited definite improvement¹²⁵. Clinical trials conducted on normal adults showed that the drug increased the mean level of RBC, blood sugar, serum cholesterol, vital capacity and total protein. The increase in the haemoglobin percentage was quite high. The drug also decreased the mean blood urea level and a moderate decrease in serum phosphate^{126, 127}.

Conclusion

C. asiatica has been in use since times immemorial to treat wide range of indications. It has been subjected to quite extensive phytochemical, experimental and clinical investigations. Its active constituents include pentacyclic triterpene derivatives. Experimental studies have demonstrated its gastric ulcer and wound healing and cytotoxic activity, neuro-protective, cardioprotective, radioprotective and hepatoprotective

effects, antioxidant and immunomodulating activity, anti-inflammatory, tranquilizing, anti-anxiety, anti-stress as well as effects on improving mental functions such as concentration and memory. It has a calming effect on the body and supports the central nervous system and therefore, is an ideal balancing tonic that helps to increase concentration while soothing and relaxing overactive nervous system.

Clinical studies have shown its positive effects in the treatment of venous insufficiency and *striae gravidarum*. *C. asiatica* appears to be effective in strengthening vascular system and connective tissue and in treating venous and arterial problems. The scientific studies have proved the claims of Indian system of medicine. However, further detailed clinical research appears worthwhile to explore the full therapeutic potential of this plant in order to establish it as a standard drug.

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