
Herba Centellae

Definition

Herba Centellae consists of the dried aerial parts or the entire plant of *Centella asiatica* (L.) Urban. (Apiaceae) (1–5).

Synonyms

Centella coriacea Nannfd., *Hydrocotyle asiatica* L., *Hydrocotyle lunata* Lam. and *Trisanthus cochinchinensis* Lour. (1, 3, 6). Apiaceae are also known as Umbelliferae.

Selected vernacular names

Artaniyae-hindi, Asiatic pennywort, barmanimuni, barmi, bhram buti, boa-bok, bodila-ba-dinku, bokkudu, brahma manduki, brahmi ghi, brahmi-buti, brahmi, bua bok, bua-bok, centella, chhota mani-muni, chi-hsueh-ts'ao, ghi brahmi, ghod tapre, ghodtapre, ghortapre, gotu kola, gotukola, herba pegagan, herba kakikuda, hydrocotyle, hydrocotyle asiatique, idrocotile, imsen korokla, Indian pennywort, Indian water navelwort, Indischer Wassernabel, karinga, karivana, kudangal, luei gong gen, lièn tièn tháo, mandooka parni, mandukaparni, mandukparni, manimuni, marsh pepperwort, matoyahuhu, matoyahuhu, mrang-khua, mtwigahuwu, pa-na-e-khaa-doh, phác chèn, phaknok, phalwaen, rau má, saraswathiaaku, takip-kohol, thalkuri, thankuni, thol-kuri, tilkushi, titjari, tono'itahi, tsubo-kusa, tungchian, vallari, vallarei, vitovitolge, water pennywort, waternavel, yahon-yahon, yerba de chavos (3–11).

Description

A slender trailing herb, rooting at the nodes. Leaves 1.3–6.3 cm diameter, orbicular reniform, more or less cupped, entire, crenate or lobulate, glabrous; leaf stalks 2–5 cm long; peduncle about 6 mm, often 2–3 nates; pedicels nil; bracts small, embracing the flowers; inflorescence in single umbel, bearing 1–5 flowers, sessile, white or reddish; fruit small, compressed, 8 mm long, mericarps longer than broad, curved, rounded at top, 7–9-ridged, secondary ridges as prominent as the primary, reticulate between them; pericarp much thickened; seed compressed laterally (1, 4, 7).

Plant material of interest: aerial part or entire plant

General appearance

A slender herb. Stems long, prostrate, emerging from the leaf-axils of a vertical rootstock, filiform, often reddish, with long internodes and rooting at the nodes; leaves thin, long-petioled, several from the rootstock and 1–3 from each node of the stems, 1.3–6.3 cm diameter, orbicular reniform, more or less cupped, entire, crenate or lobulate, glabrous; petioles very variable in length, 7.5–15 cm long or more, channelled; stipules short, adnate to the petioles forming a sheathing base (4, 5).

Organoleptic properties

Colour, greyish green; odour, characteristic; taste, slightly bittersweet (4, 5).

Microscopic characteristics

Greyish green with stomata on both surfaces of the leaf, 30 by 28 μm , mostly rubiaceous type. Palisade cells differentiated into 2 layers of cells, 45 by 25 μm ; spongy parenchyma of about 3 layers of cells with many intercellular spaces, some with crystals of calcium oxalate; midrib region shows 2 or 3 layers of parenchymatous cells without chloroplastids; petiole shows epidermis with thickened inner walls; collenchyma of 2 or 3 layers of cells; a broad zone of parenchyma; 7 vascular bundles within parenchymatous zone, 2 in projecting arms and 5 forming the central strand; vessels 15–23 μm in diameter. Some parenchymatous cells contain crystals of calcium oxalate. Fruits, epidermis of polygonal cells, trichomes similar to the leaves, sheets of elongated parquetry layer cells, bundles of narrow annular vessels, and parenchymatous cells contain single large prisms of calcium oxalate (4).

Geographical distribution

The plant is indigenous to the warmer regions of both hemispheres, including Africa, Australia, Cambodia, Central America, China, Indonesia, the Lao People's Democratic Republic, Madagascar, the Pacific Islands, South America, Thailand, southern United States of America, and Viet Nam. It is especially abundant in the swampy areas of India, the Islamic Republic of Iran, Pakistan, and Sri Lanka up to an altitude of approximately 700 m (1, 4, 6, 8, 10, 11).

General identity tests

Macroscopic and microscopic examinations; and microchemical tests for the presence of triterpenes and reducing sugars (1, 4).

Purity tests

Microbiology

The test for *Salmonella* spp. in Herba Centellae products should be negative. The maximum acceptable limits of other microorganisms are as follows (12–14). For preparation of decoction: aerobic bacteria—not more than 10^7 /g; fungi—not more than 10^5 /g; *Escherichia coli*—not more than 10^2 /g. Preparations for internal use: aerobic bacteria—not more than 10^5 /g or ml; fungi—not more than 10^4 /g or ml; enterobacteria and certain Gram-negative bacteria—not more than 10^5 /g or ml; *Escherichia coli*—0/g or ml.

Foreign organic matter

Not more than 2% (4).

Total ash

Not more than 19% (2, 3).

Acid-insoluble ash

Not less than 6% (2).

Water-soluble extractive

Not less than 6% (2, 3).

Alcohol-soluble extractive

Not less than 9.5% (2, 3).

Pesticide residues

To be established in accordance with national requirements. Normally, the maximum residue limit of aldrin and dieldrin in Herba Centellae is not more than 0.05 mg/kg (14). For other pesticides, see WHO guidelines on quality control methods for medicinal plants (12) and guidelines for predicting dietary intake of pesticide residues (15).

Heavy metals

Recommended lead and cadmium levels are not more than 10 and 0.3 mg/kg, respectively, in the final dosage form of the plant material (12).

Radioactive residues

For analysis of strontium-90, iodine-131, caesium-134, caesium-137, and plutonium-239, see WHO guidelines on quality control methods for medicinal plants (12).

Other purity tests

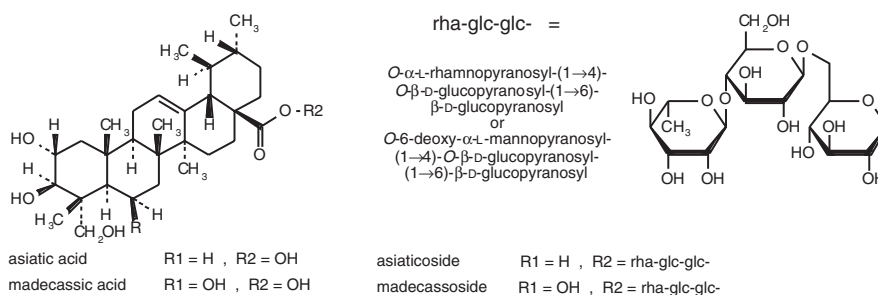
Chemical tests, and tests for drug interactions and moisture to be established by national authorities.

Chemical assays

Contains not less than 2% triterpene ester glycosides (asiaticoside and madecassoside) (10). Determination of asiaticoside and related triterpene ester glycosides by thin-layer chromatography (16) and spectroscopic analysis (17).

Major chemical constituents

The major principles in Herba Centellae are the triterpenes asiatic acid and madecassic acid, and their derived triterpene ester glycosides, asiaticoside and madecassoside (8, 10, 11).



Dosage forms

Dried drug for infusion (18); galenic preparations for oral administration (10). Powder or extract (liquid or ointment) for topical application (1, 4). Package in well-closed, light-resistant containers.

Medicinal uses

Uses supported by clinical data

Treatment of wounds, burns, and ulcerous skin ailments, and prevention of keloid and hypertrophic scars (10, 18–21). Extracts of the plant have been employed to treat second- and third-degree burns (19). Extracts have been used topically to accelerate healing, particularly in cases of chronic postsurgical and post-trauma wounds (19). Extracts have been administered orally to treat stress-induced stomach and duodenal ulcers (10).

Uses described in pharmacopoeias and in traditional systems of medicine

Herba Centellae is reported to be used in the treatment of leprosy ulcers and venous disorders (5, 6, 8, 10, 22).

Studies suggest that extracts of *Centella asiatica* cause regression of inflammatory infiltration of the liver in cirrhosis patients (10, 23). Further experimentation is needed to confirm these findings.

Uses described in folk medicine, not supported by experimental or clinical data

Therapy of albinism, anaemia, asthma, bronchitis, cellulite, cholera, measles, constipation, dermatitis, diarrhoea, dizziness, dysentery, dysmenorrhoea, dysuria, epistaxis, epilepsy, haematemesis, haemorrhoids, hepatitis, hypertension, jaundice, leukorrhoea, nephritis, nervous disorders, neuralgia, rheumatism, smallpox, syphilis, toothache, urethritis, and varices; and as an antipyretic, analgesic, anti-inflammatory, and "brain tonic" agent (4, 5, 7). Poultices have been used to treat contusions, closed fractures, sprains, and furunculosis (7).

Pharmacology

Experimental pharmacology

The pharmacological activity of *Centella asiatica* is thought to be due to several saponin constituents, including asiaticoside, asiatic acid, and madecassic acid (10). *In vitro*, each of these compounds stimulated the production of human collagen I, a protein involved in wound healing (24). Stimulation of collagen synthesis in foreskin fibroblast monolayer cultures by an extract from Herba Centellae has also been reported (25). Asiaticoside accelerated the healing of superficial postsurgical wounds and ulcers by accelerating cicatricial action (21). Asiaticoside stimulates the epidermis by activating the cells of the malpighian layer in porcine skin, and by keratinization *in vitro* (26). Topical application of asiaticoside promoted wound healing in rats and significantly increased the tensile strength of newly formed skin (21, 27).

Extracts of *C. asiatica*, and in particular its major triterpene ester glycoside, asiaticoside, are valuable in the treatment of hypertrophic scars and keloids (21). Asiaticoside has been reported to decrease fibrosis in wounds, thus preventing new scar formation (21). The mechanism of action appears to be twofold: by increasing the synthesis of collagen and acidic mucopolysaccharides, and by inhibiting the inflammatory phase of hypertrophic scars and keloids. It has further been proposed that asiaticoside interferes with scar formation by increasing the activity of myofibroblasts and immature collagen (21).

Extract of Herba Centellae effectively treated stress-induced stomach and duodenal ulcers in humans (10, 28). Oral administration of *C. asiatica* extract to rats produced a dose-dependent reduction in stress-induced gastric ulceration, and the antiulcer activity was similar to that of famotidine (29). The mechanism of action appears to be associated with a central nervous system-depressant activity of *C. asiatica*, owing to an increase in the concentration of GABA (γ -aminobutyric acid) in the brain (29).

A 70% ethanol extract of the drug administered intraperitoneally to mice produced anticonvulsant activity (30).

Clinical pharmacology

In clinical trials, an extract of *C. asiatica* in a 1% salve or 2% powder accelerated healing of wounds (31). A formulation containing asiaticoside as the main ingredient healed 64% of soiled wounds and chronic or recurrent atony that was resistant to usual treatment (21). In an open clinical study, treatment of 20 patients with soiled wounds and chronic or recurrent atony with a galenical formulation containing 89.5% *C. asiatica* healed 64% and produced improvement in another 16% of the lesions studied (20). Local application of an extract of the drug to second- and third-degree burns expedited healing, prevented the shrinking and swelling caused by infection, and further inhibited hypertrophic scar formation (11).

Twenty-two patients with chronic infected skin ulcers were treated with a cream containing a 1% extract of *C. asiatica* (32). After 3 weeks of treatment, 17 of the patients were completely healed and the ulcer size in the remaining 5 patients was decreased (32). Another trial using the same cream preparation demonstrated similar results (33). A standardized extract of Herba Centellae was reported to treat ulcus cruris (indolent leg ulcers) effectively in clinical trials (34, 35). In a double-blind study, no significant effect on healing was observed in patients with ulcus cruris after oral treatment with asiaticoside (36).

Oral administration of *C. asiatica* or asiaticoside and potassium chloride capsules was reported to be as effective as dapsone therapy in patients with leprosy (37). In a controlled study of 90 patients with perforated leg lesions owing to leprosy, application of a salve of the plant produced significantly better results than a placebo (11, 22, 38).

Clinical trials of the drug have demonstrated its antiulcer activity after oral administration (28, 39, 40). Fifteen patients with peptic or duodenal ulcer were treated with a titrated extract of Herba Centellae (60.0 mg/person). Approximately 93% of the patients exhibited a definite improvement in subjective symptoms and 73% of the ulcers were healed as measured by endoscopic and radiological observations (28).

Clinical studies of Herba Centellae in the treatment of various venous disorders has demonstrated a positive therapeutic effect (11). In patients suffering from venous insufficiency who were treated with a titrated extract of the drug, venous distension and oedema improved significantly, as compared with controls (41).

Contraindications

Allergy to plants of the Apiaceae family.

Warnings

No information available.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility

Asiaticoside has been implicated as a possible skin carcinogen in rodents after repeated topical application (42). Further experimentation is needed to substantiate this claim.

Other precautions

No information was available concerning drug interactions, drug and laboratory test interactions, teratogenic or non-teratogenic effects on pregnancy, nursing mothers, or paediatric use.

Adverse reactions

Allergic contact dermatitis has been associated with topical application of *C. asiatica* (21, 43, 44). However, further testing revealed that these reactions may be due to other ingredients in the preparations (45).

Posology

Oral dose: 0.33–0.68 g or by oral infusion of a similar amount three times daily (4–6).

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