Review Article

Review on Centella Asiatica: A Wonder Drug

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ABSTRACT

Centella asiatica, Family: Umbelliferae, also popularly known as Brahmi, is an herb used since ancient times as a memory enhancer. It is considered to be a controversial drug and many reports claim *Bacopa monnieri* as Brahmi and *Centella asiatica* as Mandukaparni, the name so derived in Sanskrit since the leaf resembles the feet of a frog. The present review aims at enlisting the work done so far on this wonder drug.

Keywords: Centella asiatica, Brahmi, Asiaticoside.

INTRODUCTION

Source

It comprises of the whole plant of *Centella asiatica* (Linn.) Urban. Family: Umbelliferae.

Synonyms

Sanskrit: Manduki, Mandukaparni
English: Indian Pennywort
Hindi: Brahma Manduki, Brahmi
Kannada: Ondelaga, Brahmi soppu
Malayalam: Kodangal
Marathi: Karivana
Telugu: Saraswati Aku, Vauari

TAXONOMY

Kingdom: Plantae
Division: Tracheophyta
Subdivision: Spermatophytina
Class: Magnoliopsida
Order: Apiales
Family: Apiaceae
Genus: Centella
Species: *Centella asiatica*

CHEMICAL CONSTITUENTS

Essential oil

Centella asiatica contains a green, strongly odoriferous essential oil. (Anonymous, 1950). GC analysis of the steam distillate of the plant material, established the presence of camphor, cineole and n-dodecane (Castellani et al, 1981). While a GC-MS analysis of ether extract of the plant indicated the chief component of the essential oil as a still-unidentified terpene acetate [36% of total oil], (Asakawa et al., 1982). Larger amounts of trans-β farnesene, germacrene and β-caryophyllene were also detected. The presence of p-cymol, α-pinene, methanol and allyl mustard oil in the plant was also reported (Salgues et al, 1969).

Triterpenoid compounds

The triterpenoid compounds apparently represent the chief pharmacologically active material in *Centella asiatica*. Although the saponin-like sugar esters of the triterpenoid acids are scarcely active hemolytically, they are frequently referred to as saponins and occur as a mixture of similar compounds that can be separated with great difficulty. Duplicate names and contradictory findings in the chemical literature for triterpenoid compounds of *Centella asiatica* have also been reported (Hegnauer et al, 1966). The situation is made difficult by the fact that source of *Centella asiatica* from India, Sri Lanka, and Madagascar apparently do not contain the same constituents.

Although the full historical sequence of investigation of triterpenoid compounds would not appear useful for this review, several important works have detailed the extraction and isolation of the triterpenoids (Karrer et al, 1985. Kartnig et al, 1987. Lythgoe et al, 1949, Rahandraha et al, 1963). The first report of a new heteroside, asiaticoside in *Centella asiatica* was published by Bontems in 1941. Boiteau, Boiteau et al. and Bhattacharya and Lythgoe initially undertook clarification of the structure with later investigations by Polonsky who studied structural aspects of asiaticoside and Asiatic acid. Asiaticoside has been identified as an ester of Asiatic acid with 2 molecules of glucose and 1 molecule of rhamnose attached.

Derivatives of asiaticoside have been synthesized (Boiteau et al, 1963) and asiaticoside has been isolated from *Centella asiatica* with the use of cationite (Pasich et al, 1968).

The constituents of *Centella asiatica* and structures for centoic acid and centellic acid have been reported (Bhattacharyya et al,

1956). Madecassic acid was isolated from *Centella asiatica* growing in Madagascar.

The presence of Asiatic acid, thankunic acid, isothankunic acid, brahmic acid, isobrahmic acid, and sugar-containing derivatives of the acids were also reported (Drude et al, 1898, Dutta et al, 1968, Dutta & Basu et al, 1968). The structure of madasiatic acid isolated from *Centella asiatica* was also reported (Pinhas et al, 1969). Brahmic acid, isobrahmic acid and associated saponins were also isolated and reported (Rastogi et al, 1960). The structural clarification of asiaticoside and madecassoside by means of mass and nuclear magnetic resonance (NMR) was also done (Luo et al, 1980 & Luo and Chin et al, 1981). The relative amounts of Asiatic acid, asiaticoside, and other constituents in *Centella asiatica* have been quantified and reported (Singh & Rastogi et al, 1969).

Brahmic acid has been demonstrated to be identical with madecassic acid and isobrahmic acid has been observed to be a mixture of Asiatic acid and madecassic acid (Rao & Seshadri et al, 1969). The concentration of triterpenoid compounds in *Centella asiatica* plant differs depending upon the source of the plant material (castellani et al, 1981). Although the free and esterified forms of Asiatic acid are present in comparable amounts, madecassic acid is predominantly observed in the free form in *Centella asiatica*.

Madasiatic acid, a compound that resembles madecassic acid except for a methyl group in place of a hydroxymethyl group has also been reported (Pinhas et al, 1969).

Other compounds

The occurrence of glucose in *Centella asiatica* has been reported (Wali & Katti et al, 1937). In an analyses of plant tissue, the presence of kaempferol, quercetin, the glycosides of these 2 flavonols, and an unidentified third flavonoid has also been reported (Rao & Seshadri et al, 1969). Polyphenols (Castillo et al, 1980) and tannins (Chopra et al, 1969, Chopra & Nayar et al, 1956, Malhotra et al, 1961, Wali et al, 1937) have also been reported in *Centella asiatica* and the plant is known to contain wax, carotenoids, and chlorophyll (Rao & Seshadri et al, 1969).

The presence of a bitter substance vellarin and a resin in the leaves and roots has been reported (Anonymous, 1950). The presence of alkaloids in the plant tissue has not been positively established. The isolation of an alkaloid named hydrocotyline with the empirical formula $C_{22}H_{33}NO_8$ from *Centella asiatica* has been reported (Basu & Lamsal et al, 1947). Aspartic acid, glycine, glutamic acid,alanine and phenyalanine have been isolated from the dried plant (Malhotra et al, 1961). Castellani et al have noted the presence of lysine, glutamic acid, phenyalanine, alanine, aspartic acid, and serine in plant tissue by using two-dimensional thin-layer chromatography and gas chromatography.

The presence of polyacetylinic compounds in *Centella asiatica* have been reported (Bohlmann & Zdero et al, 1975). 14 polyacetylenes were isolated from underground parts of *Centella asiatica* (Schulte et al, 1973).

Pharmacology

The pharmacological activity of *Centella asiatica* is thought to be due to several saponin constituents, including asiaticoside, Asiatic acid, and madecassic acid. (Kartnig T et al, 1988). *In vitro*, each of these compounds stimulated the production of human collagen I, a protein involved in wound healing. (Bonte F et al, 1994). Stimulation of collagen synthesis in foreskin fibroblast monolayer cultures by an extract of herba centellae has also been reported (Maquart FX et al, 1990).

Asiaticoside accelerated the healing of superficial post surgical wounds and ulcers by accelerating cicatricial action. (Morisset R et al, 1987). Asiaticoside stimulates the epidermis by activating the cells of the malphighian layer in porcine skin, and by keratinization *in vitro*. (May et al, 1968). Topical application of asiaticoside promoted wound healing in rats and significantly increased the tensile strength of newly formed skin (Morisset R et al, 1987 & Rosen et al, 1972)

Extracts of *Centella asiatica*, and in particular its major triterpene glycoside, asiaticoside, are valuable in the treatment of hypertrophic scars and keloids (Morisset R et al, 1987). Asiaticoside has been reported to decrease fibrosis in wounds, thus preventing new scar formation (Morisset R et al, 1987). The mechanism of action seems to be two fold, by increasing the synthesis of collagen and acid mucopolysaccharides, and by inhibiting the inflammatory phase of hypertrophic scars and keloids. It has further been proposed that Asiatic acid interferes with scar formation by increasing the activity of myofibroblasts and immature collagen (Morisset R et al, 1987).

Extracts of *Herba centellae* effectively treated stress-induced stomach and duodenal ulcers in humans (Kartnig T et al, 1988 & Shin et al, 1982). Oral administration of *Centella asiatica* extract to rats produced a dose-dependent reduction in stress-induced gastric ulceration,

and the antiulcer activity was similar to that of famotidine (Chaterjee et al, 1992). The mechanism of action appears to be associated with a central nervous system-depressant activity of *Centella asiatica*, owing to an increase in the concentration of GABA in the brain. (Chaterjee et al, 1992).

The antiulcerogenic activity of the fresh juice of *Centella asiatica* was studied against ethanol, aspirin, cold restraint stress and pyloric ligation induced gastric ulcers in rats. When given orally at doses of 200 and 600 mg/kg twice daily for 5 days, the drug showed significant protection against all the above experimental ulcer models. This effect was thought to be due to the strengthening of mucosal defensive factors. Oral administration of *Centella asiatica* extract (0.05,0.25, and 0.5 g/kg) before ethanol administration significantly inhibited gastric lesion formation (by 58-82%) and decreased mucosal myeloperoxidase (MPO) activity in a dose dependant manner. It prevented gastric mucosal barrier and reducing the damaging effects of free radicals. (Cheng Cl et al, 1969).

Spasmolytic activity was demonstrated when tested *In vitro* on isolated pig ileum (Singh et al, 1969).

An alcoholic extract showed stimulatory effect on the reticuloendothelial system (RES) in mice and an *in vitro* study of the aqueous extract demonstrated a positive effect on both the classic and alternative pathways of complement activation (Di Carlo et al, 1964 & Labadie et al, 1989).

An injection of 0.5 ml of a 4% solution of hydroxyasiaticoside was given in guinea pigs, inoculated 15 days previously with tubercular lesions in the liver, lungs, nerve ganglions and spleen and decreased the volume of the spleen over that of untreated control animals, thereby displaying antitubercular activity.(Boiteau P et al, 1949).

The alcoholic extract, when given orally to rats and mice treated with phenobarbitone, significantly prolonged sleeping time. In the maximum electroshock-induced convulsion test in rats, it significantly reduced the duration of individual convulsions. In a behavioral test reduced the duration of the immobility phase, indicating sedative, antidepressive and analgesic actions. (Sakina et al, 1990).

Asiaticoside at a concentration of 10 mg/ml showed antibacterial activity against *Pseudomonas pyocyaneus* and *Trichoderma mentagrophytes* (Tschesche W et al, 1965)

The alcoholic extract showed antiviral activity against Herpes simplex type II virus (Zheng et al, 1989).

Asiaticoside is reported to be active against Mycobacterium tuberculosis, Bacillus leprae and *Entamoeba histolytica* (Oliver-Bever et al 1986).

A new triterpenoid glycoside 3-O-[α-L-arabinopyranosyl] 2α,3β, 6β, 23α-tetrahydroxyurs-12-ene-28-oic acid exhibited dose-dependant growth inhibitory activity against larvae of *Spilarctia oblique* (Shukla YN et al, 2000).

The usage of Asiaticoside in tablet, ointment and powdered form was found to be efficacious in the treatment of chronic or sub chronic systemic scleroderma with limited skin involvement, and in progressive and/or advanced focal scleroderma. (Guseva et al, 1998).

Researchers at the Amala Cancer Research Centre in Kerala, India, tested both a crude extract of *Centella asiatica* (CE) and its partially purified fractions (AF) for their antitumor activity.AF significantly inhibited the proliferation of the transformed cell lines in Ehrlich ascites tumor cells and Dalton's lymphoma ascites tumor cells with no toxic effects on normal human lymphocytes. AF was also found to inhibit the development of mouse lung fibroblast. Oral administration of both CE and AF retarded the development of solid and ascites tumors, and increased the life span of tumor bearing mice. (Babu et al, 1995). Fresh juice is reported to have moderate cytotoxic action in human ascites tumor cells (Lin et al, 1972).

A three week treatment of triterpene fraction of *Centella asiatica* in clients with postphlebetic syndrome significantly reduced the number of circulating endothelial cells, as compared to normal subjects. The use of an oral extract of *C. asiatica* in a randomized controlled trial of 87 clients with chronic venous hypertensive microangiopathy was found efficacious, without side-effects. (Montecchio et al, 1991).

A clinical trial of an extract of *Centella asiatica* found that it was efficacious in the treatment of venous insufficiency, reducing ankle, edema and foot swelling, and improving capillary filtration rate and microcirculatory parameters (Cesarone et al, 1992, 1994).

Table 1: Quantities of Terpenoid Compounds in *Centella asiatica*[*]

SUBSTANCE	WEIGHT (mg/g)	MIXTURE (%)
Asiaticoside	9.21	37.6
Asiatic acid	7.02	28.5
Madecassoside	0.051	1.8
Madecassic acid	7.89	32.1

*From data of Castellani et al.

Fig.1: Centella asiatica leaf

Fig. 2: Centella asiatica plant

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