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Review article



Phytopharmacological review of Siddha medicinal herb

Centella asiatica Linn. (Vallarai)

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ABSTRACT

In recent day, plant research has increased all over the world. Plantbased drug discovery has drawn the attention of researchers, especially the one used as traditional medicines. Centella asiatica is an important medicinal herb that is widely used in the household to increase memory power, anti-oxidant, and even it was the part of green vegans. Locally in tamil, it was called as Vallarai. It is responsible for its wide therapeutic actions. The chemical constituents of Centella asiatica (Vallarai) have wide therapeutic applications in areas of antimicrobial, anti-inflammatory, anticancer, neuroprotective, antioxidant, and wound healing activities.

Apart from wound healing, the herb is recommended for the treatment of various skin conditions such as leprosy, lupus, varicose ulcers, eczema, psoriasis, diarrhoea, fever, amenorrhea, diseases of the female genitourinary tract and also for relieving anxiety and improving cognition. The present review attempts to provide comprehensive information on pharmacology, mechanisms of action, various preclinical and clinical studies and current research status of the herb etc.

Keywords: Vallarai, Centella asiatica, antioxidant, herbs Address for correspondence:

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INTRODUCTION

The plant is commonly known as Vallarai, Asiatic pennywort, Indian pennywort or Spade leaf and belongs to Umbelliferae/Apiaceae family. In India, Srilanka, China, Sri Lanka, the plant has long been used as vegetable. In Southeast Asia, it is traditionally used for the treatment of a wide variety of disorders such as skin diseases, rheumatism, inflammation, syphilis, mental illness, epilepsy, hysteria, dehydration, and diarrhea.

Centella asiatica (Vallarai) is used in Indian systems of medicine for enhancing memory and for the treatment of skin diseases and nervine disorders. In India, over 2000 years ago, it was one of the documented "miracle elixirs of life" and considering as brain booster. Herbal medicines can be used as adaptogens, these plant derived drugs either reduce stress reactions in the alarm phase and provide a certain degree of safety against long-term stress. C. asiatica (Umbelliferae) is used to treat various ailments across India which includes body aches, headaches, insanity, asthma, leprosy, ulcers, eczemas, and wound healing.

Morphological features

Centella asiatica (L.) is a prostrate, faintly aromatic, stoloniferous, perennial, creeper herb, attains height up to 15cm (6inches). Stem is glabrous, striated, rooting at the nodes. Centella asiatica flourishes extensively in shady, marshy, damp and wet places such as paddy fields, river banks forming a dense green carpet.

The leaves, 1-3 from each node of stems, long petioled, 2-6cm long and 1.5-5cm wide, orbicular-renniform, sheathing leaf base, crenate margins, glabrous on both sides. Flowers are in fascicled umbels, each umbel consisting of 3-4 white to purple or pink flowers, flowering occurs in the month of April-June. Fruits are borne throughout the growing season in apprx 2 inches long, oblong, globular in shape and strongly thickened pericarp. Seeds have pedulous embryo which are laterally compressed.

Centella asiatica found throughout tropical and sub-tropical regions of India up to an altitude of 600m. The plant has been reported to occur also at high altitudes of 1550m in Sikkim and 1200m in Mount Abu, India. The plant is indigenous to South-East Asia, India, Sri-Lanka, parts of China, the Western South Sea Islands, Madagascar, South Africa, South East USA, Mexico, Venezuela, Columbia and Eastern South America.

Chemical Constituents

The plant has long been used as folklore medicine for the treatment of a variety of diseases. Chemically been identified leading to therapeutic properties. Asiatic acid, asiaticoside, and madecassoside form the major constituents responsible for pharmacological value apart from being rich in flavonoids and terpenoids. Centelloid was term given for different constituents of secondary metabolites produced by plant which mainly comprised of pentacyclic, triterpenoid & saponins.

The total extract contains plant sterols, flavonoids, tannins (20-25%), essential acid (0.1% with beta-chariophylen, trans-beta-pharnesen and germachrene D), phytosterols (campesterol, sitosterol, stigmasterol), mucilages, resins, free aminoacids (alanine, serine, aminobutyrate, aspartate, glutamate, lysine and treonine), madecassoside, asiaticoside, madecassic acid, and asiatic acid.

PHARMACOLOGICAL REVIEW

Antioxidant Property

C. asiatica extract and powder was evaluated for reduction in oxidative stress in Sprague-Dawley rats. Results showed a decrease in the generation of ROS and oxidative stress in the rats. It was also noted that there was a significant decrease in SOD level. Essential oil of C. asiatica extracted through steam distillation showed to be excellent antioxidant for food containing lipids. Its activity was quite comparable with the synthetic antioxidant butyl hydroxyl anisole (BHA).

Polyphenol, flavonoid, β -carotene, tannin, Vitamin C, and DPPH compounds are readily found in C. asiatica contributing to significantly higher antioxidant activity in the herb. Crude methanolic extract on continuous supplementation for 14 days resulted in increase in level of antioxidant enzymes and ascorbic acid level reduced in lymphoma-bearing mice

Cognitive Function

Water extract of C. asiatica was observed to enhance synaptic differentiation and dendritic arborization with reference to $A\beta$ which causes cognitive improvement. In a study, Vallarai extract supplemented for weeks was in defined concentration results showed to be effective in the treatment of cognitive function impairment after stroke impairment of cell proliferation, spatial working memory caused by treatment with valproic acid. Water extract helped to improve cognitive function by activation of antioxidant response gene and mitochondrial biogenesis, normalized calcium homeostasis.

Hepatoprotective Activity

Hepatoprotective activity of plant extract was checked against Ccl4-induced liver injury, and the extract showed hepatoprotective activity most probably due to the presence of asiaticoside (14.5%) in the extract. The functional group of asiatic acid showed hepatoprotective effects against GaIN-induced hepatotoxicity (66.4% protection at 50 µM) and moderate hepatoprotective activities against CCl4-induced hepatotoxicity (20.7% protection at 50 µM). Asiatic acid protects liver injury by onset of Smad7-dependent inhibition of TGF-beta/Smad-assisted fibrogenesis. Conventionally, used plants to get rid of liver dysfunction might, therefore, could be potential source for new hepatoprotective compounds for development as pharmaceutical entities

Antidiabetic Activity

Anti-diabetic properties of leaves extract of C. asiatica was evaluated in Effect of ethanol extract was tested in streptozotocin (50 mg/kg)induced Wistar rats. In a study, lower inhibitory activities of a-amylase of C. asiatica extract and rutin were observed when compared to acarbose and an anti-diabetic drug. Extract of C. asiatica led to reducing blood glucose level in dose-dependent manner by 29.4%, 32.8%, 33.6%, and 35.7%, respectively, at doses of 50, 100, 200, and 400 mg per kg body weight. In alloxan-induced rats, reduction in blood glucose level was observed at a dose level of 50 mg/kg bwt of C. asiatica juice. The effect of intestinal disaccharides and alpha amylase was inhibited, and lowered glucose absorption was observed when supplemented with plant extract. Long-term administration of plant extract reversed the blood glucose level to normal in obese diabetic rat.

Neuroprotective Activity

Neuroprotective potential of modern medicine constituents of the plant includes asiatic acid, madecassic acid, and brahmaside as well as flavonoids madecassoside and madesiatic acid. C. asiatica was explored for neuroprotective effect on cell death and cognitive irregulation in aluminumtreated rat. Significant improvement in memory performance, oxidative defense was observed on chronic administration of CA.

The plant is known to utilize neuroprotective effects by attenuating the changes in an animal model such as pathological neurobehavioral and neurochemical properties. Phosphoinositides-assisted cytodynamics and synaptic function show the neuroprotective effects of asiaticoside in the rat which includes mode of ROT-infused hemiparkinsonism

Antibacterial Activity

In vitro antibacterial activity of the plant extract against Staphylococcus aureus ATCC 25923 and methicillin resistance S. aureus (wild type) showed a zone of inhibition of 5 mm and 7 mm respectively. In a study, it was observed that essential oil extract showed antibacterial properties against Gram-positive (Bacillus subtilis and S. aureus) and Gram-negative (Escherichia coli, Pseudomonas aeruginosa, and Shigella sonnei) with MIC values ranging from 1.25 to 0.039 mg/ml. Bacillus cereus and Listeria monocytogenes 10403S were selected to study the antibacterial activity in C. asiatica under both normal and osmatic stress condition. At 95% ethanolic extract, antibacterial activity was enhanced twice under osmotic stress condition. The MIC of C. asiatica was observed to be 16 µl/ml against B. cereus while 8 µl/ml for L. monocytogenes.

Anticancer Activity

The effect of C. asiatica juice was checked on human HepG2 cell line using MTT assay, and it showed cytotoxic effects on tumor cells in a dosedependent manner. At a concentration above 0.1% of juice, a higher amount of DNA damage and apoptotic cell death was observed on human HepG2 cell line.

Asiatic acid was evaluated for antiproliferative effect in lung cancer cells using MTT assay. Oral administration of AA inhibited weight and tumor volume significantly in lung cancer xenograft model. In another study, asiatic acid showed induced apoptosis and decreased viability in human melanoma SK-MEL-2 cells in a dose-dependent manner. Asiatic acid derived from C. asiatica showed antiproliferative effects on RPMI 8226 cells. It decreased the expression levels of focal adhesion kinase (FAK), and the probable mechanism of AA may be related to the inhibition of signal transduction mediated by FAK. Induction of apoptosis was observed in A-549 cell line due to presence of asiatic acid which helped in regulation of miR-1290, BCL2 protein level, and cell cycle regulation

Antidepressant activity

Compared to diazepam C. asiatica possesses antianxiety effect but has no effect on behavioral despair. Total triterpenes and imipramine from C. asiatica were evaluated for antidepressant activity using forced swimming test, the result showed a reduction in stillness duration and regulated amino acid levels. In another study, decrease in corticosterone level in serum and enhanced 5-HT, NE, DA and their metabolites 5-HIAA and MHPG in rat brain were observed. Standardized extract showed a reversal of physiological and behavioral changes following OBX-induced depression in rats

Wound Healing Activity

An increase in DNA, protein, and collagen content of granulation tissues was observed on supplementation of extract of C. asiatica resulting in collagen synthesis and cellular proliferation at wound site. The extract of C. asiatica considerably enhanced the wound breach power in incision model when compared to controls (p<0.001), wound contraction rate was noticeably enhanced as compared to control wounds (p<0.001), and wounds epithelized faster when treated with an extract of CA. Rats treated with extract showed a better tensile strength of wound after 7 days of wound infliction when compared with control

Diuretic Activity

The method of Lipschitzet al. employed for the assessment of diuretic activity by using metabolic cage. The animals randomly divided into four groups- Group 1 (Normal), Group 2 (Standardfurosemide10 mg/kg, p.o.), Group 3 (aqueous extract 250 mg/kg, p.o.) and Group 4 (aqueous extract 500 mg/kg, p.o.) The diuretic effect was assessed by measuring total urine volume and the concentration of sodium, potassium and chloride ions in the urine. The extract significantly increased urine volume and electrolyte concentration in urine when compared with normal group. Conclusion: That aqueous extract of dried leaves of Centella asiatica showed potential diuretic effect and can be used as a diuretic agent.

CONCLUSION

The therapeutic potential of this plant in terms of its efficacy and versatility is such that further detailed research appears crucial. The growing number of herbal preparations in the market, including CA, raised the possibility of complications related to improper use of these products, or the lack of medical supervision along with the likelihood of interactions with the drugs and herbs on simultaneous use. Several of the recent cases reported to the special Nutritionals adverse event monitoring System indicated the importance of providing patient counselling on the use of herbal preparations.

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