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Review Article

FUNCTIONAL PROPERTIES OF *CENTELLA ASIATICA* (L.): A REVIEW

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ABSTRACT

Centella asiatica (L.) is a perennial, creeper, faintly aromatic and a valuable medicinal herb of both Old World and the New World. It is widely distributed throughout tropical and subtropical regions of World. The use of *Centella* in food and beverages has increased over the years basically due to its beneficial functional properties. Its potential antioxidant, antimicrobial, cytotoxic, neuroprotective and other activities have been widely claimed in many reports and basically is very much related to its properties and mechanism of action of the plant's bioactive constituents namely the triterpenic acid (asiatic acid madecassic acid), triterpenic saponin (madecassoside and asiaticoside), flavanoids and other phenolic compounds. The present review is an up-to-date and comprehensive literature analysis of the chemistry and various heath beneficial functional properties of the *Centella* plant.

Keywords: *Centella asiatica*, Functional properties, Bioactive constituents, Health benefits

INTRODUCTION

Centella asiatica (Linn.) Urban sys. synonym *Hydrocotyle asiatica* Linn. commonly known as Indian Pennywort, belongs to the family Apiaceae (previously known as Umbelliferae). *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 "Brain food" in India[1]. The use of *Centella* in food and beverages has increased over the years basically due to its health benefits such as antioxidant, as anti-inflammatory, wound healing, memory enhancing property and many others. The potential of *Centella* as an alternative natural antioxidant especially of plant origin and its protection against age-related changes in brain antioxidant defense system, have notably increased in recent years[2].

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), and also as an endangered species[3-5].

The plant is known as the following vernacular names: Thankuni (Bengali), Mandookaparni (Hindi), Pegaga (Malay), Kodagam (Malayalam), Gotukola (Sinhalese), Vallarai (Tamil) and Bekaparanamu (Telugu)[6].

Morphology

Centella asiatica (L.) is a prostrate, faintly aromatic, stoloniferous, perennial, creeper herb, attains height up to 15cm (6 inches). 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 and rather than clayey soil, the sandy loam (60% sand) is found to be the most fertile soil for its regeneration[7]. The leaves, 1-3 from each node of stems, long petioles, 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 approx 2 inches long, oblong, globular in shape and strongly thickened pericarp. Seeds have pedulous embryo which are laterally compressed[1].

Centella asiatica found throughout tropical and sub tropical regions of India up to an altitude of 600m. The plant is indigenous to South-East Asia, India, and Sri Lanka, parts of China, the Western South Sea Islands, Madagascar, South Africa, South East USA, Mexico, Venezuela, Columbia and Eastern South America[8].

Chemical Constituents

The scientific studies have proved a variety of biochemical components i.e. secondary metabolites have been found in *Centella asiatica*. The chemical constituents of *Centella* plant have a very important role in medicinal and nutraceutical applications and it is believed due to its biologically active components of triterpenes saponins[9]. The triterpenes of *Centella* are composed of many compounds including asiatic acid, madecassic acid, asiaticosside, madecassoside, brahmoside, brahmic acid, brahminoside, thankiniside, isothankunisode, centelloside, madasiatic acid, centic acid, and cenellicacid[10]. Among these triterpenes, the most important biologically active compounds are the asiatic acid, madecassic acid, asiaticosside, madecassoside[11]. Due to their importance, they have been used as the biomarker components for quality assessment of *Centella*[10]. However, the content of *Centella*'s triterpene components can be affected by the location and diverse environmental conditions[12].

In addition to terpenoids, it also contains high total phenolic contents which contributed by the flavonoids such as quercetin, kaempherol, catechin, rutin, apigenin and naringin and volatile oils such as caryophyllene, farnesol and elemene[13-14]. According to Zainol *et al*,[15] the highest concentration of phytochemicals was found in the leaves relative to the petioles and the roots.

Centella is also rich in vitamin C, vitamin B_1, vitamin B_2, niacin, carotene and vitamin A. The total ash contains chloride, sulphate, phosphate, iron, calcium, magnesium, sodium and potassium [8,16].

Functional Properties

Antioxidant activity

Antioxidative properties of essential oils and various extracts from many plants are of great interest in both academics and the food industry, since their possible use as natural additives has emerged from a growing trend to replace synthetic antioxidants by natural ones [17]. *Centalla asiatica* is well known to have a high antioxidant activity [18]. Antioxidant activity of *Centella asiatica* is comparable to the activity of rosemary and sage and has very good potential to be explored to as source of natural antioxidants[19]. Hashim *et al.*[20] reported that antioxidant in *Centella* (84%) is comparable to Vitamin C (88%) and grape seed extract (83%).

Wong *et al* [21] were studied the antioxidant properties of *Centella asiatica*, expressed as Trolox equivalent antioxidant capacity (TEAC), using DPPH and FRAP assays. They find out a strong correlation between TEAC values obtained for the DPPH assay and

those for the FRAP assay which implied that compounds in the extracts were capable of scavenging the DPPH free radical and reducing ferric ions. *Centella asiatica* leaves exhibited higher antioxidant activities using boiled aqueous extraction compared to aqueous extract in DPPH and FRAP assays. Total flavonoid content and total phenolic content also respond better in boiled aqueous extraction when compare to aqueous extraction[22].

Gupta and Prakash[23] find out that *Centella asiatica* cultivated in India showed good antioxidant activity which was assessed by DPPH, reducing power and ferrous ion chelating capacity methods. They also find out that *C.asiatica* is a good source of antioxidants like ascorbic acid, total and beta carotene and total phenolics. Their regression analysis showed that the relationship between antioxidant activity and antioxidant contents was highly significant. Subhasree *et al.*[24] also studied the antioxidant contents and antioxidant activity of *Centella asiatica* cultivated in India. Their results showed that *C.asiatica* had a good antioxidant activity and good source of antioxidant contents.

According to Zainol, *et al*,[13] among the different parts of *C. asiatica,* leaves showed highest antioxidant activity which also contains highest phenolic contents, when compare to other plant parts. This result suggests that phenolic compounds are the major contributors to the antioxidative activities of *C. asiatica*. On the other hand, Abdul- Hamid, *et al,*[25] reported that ethanol extract of root of *C. asiatica* exhibited the highest activity though it was not significantly different from the leaves. The antioxidative activity of different parts of *C. asiatica* may be due to the reduction of hydroperoxides, inactivation of free radicals, chelation of metal ions or combinations thereof.

Dasgupta and De[26] find out that *Centella asiatica* has strongest DPPH radical scavenging activity and highest total antioxidant capacity based on gallic acid and ascorbic acid equivalent among the eleven edible Indian green leafy vegetables studied. *Centella* is a good scavenger of hydroxyl and superoxide radical and also has good lipid peroxidation preventive property. It also has the higher total phenol content and total flavonoid content when compared to other leafy vegetables. According to Odhav *et al* [27] *Centella asiatica* leaves showed higher level of antioxidant activity among the 20 traditional leafy vegetables cultivated in South Africa. Here the antioxident activity was expressed as % scavenging capacity of the methonolic plant extracts made from the fresh leaves. The activity obtained for flavanoid rutin was taken as 100% (positive control) and other values represented were relative activity compared to rutin. Higher level of antioxidant activity was also observed by Nanasombat and Teckchuen[28] and Akula and Odhav [29] in *Centella asiatica* plants cultivated in Thailand and South Africa respectively.

Vimala, *et al.*[30] reported that *C.asiatica* leaves were found to have very high antioxidant activity in three different pathways including superoxide free radical scavenging activity (86.4%), inhibition of linoleic acid peroxidation (98.2%) and radical scavenging activity, DPPH (92.7%). Pittella *et al,*[17] were finding out that aqueous extract of *Centella asiatica* showed a high antioxidant activity by its ability to scavenge DPPH free radicals. This activity might be due to the presence of phenolic and flavonic constituents detected in the samples.

Huda-Faujan *et al*[31] studied the total phenolic content and antioxidant activity of methanolic extracts of *Centella asiatica* by reducing antioxidant power, ferric thiocyanate (FTC) and thiobarbutric acid (TBA) methods. The data of this study also suggested that *Centella asiatica* may be a potent source of antioxidant due to their high total phenolic content. Huda-Faujan *et al* [32] also obtained similar results on the antioxidant activity of *Centella asiatica* cultivated in Malaysia. Similar studies were also conducted by Jeyamalar and Suhaila [33] and Noriham *et al.*[34] about the antioxidant activity of *Centella asiatica* cultivated in Malaysia.

Ullah *et al* [35] studied the *n*-hexane, carbon tetrachloride and chloroform soluble fractions of methanol extract of the plant *Centella asiatica* against antioxidant activity. All the fractions showed moderate to potent antioxidant activity, of which the chloroform and aqueous soluble fraction demonstrated the strongest antioxidant activity. Oxygen radical absorbance capacity (ORAC) value of methanolic extract of *Centella asiatica* was higher than the aqueous methanolic and ethyl acetate extracts of the same plant[36]. Tan *et al*, [37] find out the solid-to-solvent ratio of 1:15 was the optimum condition for extraction of phenolic compounds (TPC and TFC) of *C. asiatica* by using ethanol as a solvent among the different solid-to-solvent ratio like 1:5, 1:10, 1:15 and 1:20. This ratio also exhibited higher antioxidant capacities (ABTS and DPPH radical scavenging capacities) when compared to other ratios. Higher level of antioxidant activity was observed in ethanolic extract of *Centella* leaves when compared to aqueous extract [38].

Gnanapragasam, *et al* [39] were find out the protective effect of *Centella asiatica* on antioxidant tissue defense system against adriamycin induced cardiomyopathy in rats. Co-administration of C*entella* protects animals from arsenic induced oxidative stress but exhibits no chelating property [40]. Hussain *et al,*[41] evaluated the effect of *Centella asiatica* extract and powder in reducing oxidative stress in Spraque Dawley rats. Results of their studies revealed that *C. asiatica* extract and powder reduced the H_2O_2-induced oxidative stress by decreasing lipid peroxidation via alteration of the antioxidant defence system of the rats. Veerandra Kumar and Gupta [42] find out that the aqueous extract of whole plant of *C. asiatica* have two pronounced effects on Male Wister rats, i.e. improving the learning and memory and, the antioxidant property by decreasing the lipid peroxidation and augmenting the endogenous antioxidant enzymes in brain. The findings by Gupta *et al* [43] suggest the potential of aqueous extract of *C. asiatica* as adjuvant to antiepileptic drugs with an added advantage of preventing cognitive impairment. Similar research findings were also obtained by Shinomol and Muralidara [44].

Oral treatment of crude methanol extract of *C.asiatica* on lymphoma-bearing mice significantly increased the antioxidant enzymes, like superoxide dismutase (SOD), catalase and glutathione peroxidase (GSHPx) [45].

Shukla, *et al.*[46] investigated the role of asiaticoside as antioxidant properties in wound healing activity. Asiaticoside derived from *Centella* has been attributed to increase the antioxidant levels at an initial stage of healing. Yusuf, *et al.*[47] also observed the antioxidative activities of carotenoid and ascorbate peroxidase in herb *Centella*. *C.asiatica* exhibited optimum antioxidant activity at neutral pH and the activity remained stable up to 50^0C. The antioxidative activities of *Centella* extracts increased when concentration was increased from 1000 to 5000ppm [25]. Subban *et al* [48] isolated two new flavonoids named castilliferol 1 and castillicetin 2 from the whole plant of *Centella asiatica*. These isolates exhibited good antioxidant activity with DPPH radical solution.

According to Chanwitheesuk *et al*[49] *Centella asiatica* contains higher levels of natural antioxidants compounds like vitamin E, vitamin C, total carotenes, total xanthophylls, tannins and total phenolics and good antioxidant index among the 43 edible plants cultivated in Thailand.

Antibacterial activity

Various microorganisms are known to cause food spoilage and food born diseases in human beings. About 200 diseases are caused by contaminated water, milk and other foods. The most frequently identified causal organisms are *Cornebacterium diptheriae*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeroginosa* [50].

Many plants were found to contain compounds, which are used as natural medicines to treat common bacterial infections. Medicinal plants are regularly used in various system of medicine because of minimal side effect and cost effectiveness. The potential for developing antimicrobials from higher plants appears rewarding as it may lead to the development of phytomedicine against microbes. *Centella asiatica* is one of the important plant shows antibacterial activity against wide variety of bacteria [51].

Diarrhea is a major public health problem in developing countries. Multiple drug resistance among enteropathogens in various geographic regions presents a major threat in the control of diarrhea. Mamtha *et al,*[52] was observed broad spectrum activity of

Centella asiatica against a wide range of enteric pathogens. They used viable cell count method to study whether the observed inhibition was bactericidal or bacteriostatic in action. In case of *Vibrio cholerae, Shigella* species and *Staphylococcus aureus,* the alcoholic extract of plant showed bactericidal action within 2 hours.

Ullah *et al,*[35] was observed the *n*-hexane, carbon tetrachloride, chloroform soluble fractions of methanol extract from the plant *Centella asiatica* showed antibacterial activity against 5 gram positive bacteria (*Bacillus cereus, Bacillus megaterium, Bacillus subtilis, Staphylococcus aureus and Sarcina lutea)* and 8 gram negative bacteria (*Escherichia coli, Pseudomonas aeruginosa, Salmonella paratyphi, Salmonella typhi, Shigella boydii, Shigella dysenteriae, Vibrio mimicus and Vibrio parahemolyticus).*

Wei *et al,*[53] was observed that methanol extract of *C. asiatica* whole plant showed inhibition zone against *V. alginolyticus*, *V. vulnificus* and *Streptococcus* sp while inhibition zone was found in *C. freundii* and all *Vibrio* sp. except *V. vulnificus* against aqueous extracted *C. asiatica* whole plant.

Taemchuay *et al,*[54] was find out that crude extract of *Centella asiatica*, particularly extracted with water, had a promising antibacterial effect against *Staphylococcus aureus.* Water extracts of *Centella* leaves cultivated in Similipal biosphere reserve in Orissa, India showed antibacterial activity against *Staphylococcus aureus, Pseudomonas aeruginosa*, *Escherichia coli*, *Bacillus subtilis, Shigella flexneri* and *Candida kruesi* [55].

Methanolic extract of *Centella* was showed antibacterial activity against 3 Vibrio species named *V. harveyi, V. alginolyticus and V. parahaemolyticus.* But acetone, chloroform and hexane cxtracts was not showed antibacterial activity against these species[56].

Hexane, dichloromethane, ethyl acetate, diethyl ether and methanol extracts of *Centella asiatica* showed antibacterial activity against *B. subtilis*, *K. aerogenes*, *P.* v*ulgaris* and *S. aureus* species. But they did not show antibacterial activity against *Escherichia coli* and *Pseudomonas aerogenes* [57]. Similarly Srivastava *et al,*[58] and Zaidan *et al* [59] was also observed the antibacterial activity of *Centella* plant extracts by using diffusion method. Methanolic extract of *C. asiatica* showed antibacterial activities to gram positive *S. aureus* and Methicillin Resistant *S. aureus* (MRSA). But it did not show antibacterial activities to gram negative bacteria like *E. coli* and *K. pneumonia*[59].

Ethanolic extract of *Centella asiatica* shows significantly higher rate of sensitivity against various bacteria strains like *Staphylococcus aureus, Escherichia coli, Bacillus subtilis,* and *Propionibacterium vulgaris*, while petroleum ether extract shows moderately sensitivity and water extract showed that least sensitivity against these strains[51]. Crude extracts of *Centella asiatica* showed antibacterial activity against agne inducing bacteria like *Propionibacterium acnes* and *Staphylococcus epidermidis*[60].

Panthi and Chaudhary[61] was observed that methanolic extracts of *Centella asiatica* collected from Nepal showed antibacterial activity against one gram positive bacteria *Staphylococcus aureus* and three gram-negative *bacteria* like *Escherichia coli, Pseudomonas aeruginosa* and *Shigella boydii*. But another similar study in Nepal by Mahato and Chaudhary[62] was not observed antibacterial activity in methanolic extracts of *Centella asiatica* against bacteria like *Bacillus subtilis, Staphylococus aureus, Escherichia coli* and *Pseudomonas aeruginosa*.

Extracts of *C.asiatica* did not showed antibacterial activity against ten isolates of pathogenic fish bacteria including *Aeromonas hydrophila*, *Citrobacter freundii*, *Edwardsiella tarda*, *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus agalatiae*, *Streptococcus aginosus*, *Vibrio alginolyticus*, *V. parahaemolyticus* and *V. vulnificus* [63]. Ethanolic and ethyl acetate extracts of *C.asiatica* plant leaves cultivated in Thailand did not showed antibacterial activity against some gram positive and negative bacteria like *Staphylococcus aureus, Listeria innocua, Bacillus subtilis, Lactobacillus plantarum, Lactococcus lactis, Proteus mirabilis, Pseudomonas aeruginosa, Echerichia coli and Salmonella* anatum[64]. Water extract of *Centella* did not show antimicrobial activity against *E.coli*, *Staphyloccoccus aureus* and *Klebsiella pneumonia*[38].

Antifungal activity

Ethanolic and petroleum ether extracts of *Centella asiatica* plant shows significantly higher rate of antifungal activity against various fungal strains like *Aspergillus niger, Aspergillus flavus* and *Candida albicans* when compare to water extracts[51]. Hexane, carbon tetrachloride, chloroform and aqueous soluble fractions of methanolic extract showed antimicrobial activity against various yeast and mold strains like *Aspergillus niger, Saccharomyces cerevisiae* and *Candida albicans*[35]

Methanolic extract of *Centella asiatica* showed significant inhibitory effect on spore germination against various fungal strains like *Alternaria, Cercospora, Curvularia, Drechslera* and *Fusarium.* The inhibitory effect on spore germination of the above fungus strains was increased proportionately with the increase in the concentration of methanolic extracts of the leaves [65-66].

Bobbarala *et al* [67] examined the antifungal activity of forty nine plants including *Centella* against *Aspergillus niger* fungi using agar well diffusion method. Among the 49 plants studied the methanolic extracts of 43 plants including *Centella* exhibited varying degrees of inhibition activity against the above fungi. Methanol, chloroform and acetone extracts of *Centella asiatica* showed significant inhibitory effect on growth and sporulation of *Colletotrichum gloeosporioides* [68].

Alcoholic extracts of *C.asiatica* did not showed antimicrobial activity against yeasts like *Pichia anomala* and *Saccharomyces cerevisiae and* molds like *Aspergillus niger* and *Penicillium pinophilum* [64].

Antiviral activity

Crude water extracts of combinations each of *Centella* and *Mangifera indica* showed anti-herpes simplex virus activities [69].

Antiprotozoal activity

Alcoholic extract of entire plant showed antiprotozoal activity against *Entamoeba histolytica* [70].

Antifilarial activity

A mixture of ethonolic extracts of *Centella asiatica* and *Acacia auriculiformis* resulted in a considerable decrease in filarial counts in dogs naturally infected with *Dirofilaria immitis*[71].

Antiulcer activity

Asiaticoside prevented development of cold induced gastric ulcers in rats. Asiaticoside administered orally to rats, significantly reduced the formation of stress induced ulcers. 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 brain [72]. 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 factors [73]. Results of the studies conducted by Abdulla *et al*,[74] also revealed protection of gastric mucosa and inhibition of leucocytes infiltration of gastric wall in rats pretreated with *C. asiatica* extract.

Antidiabetic activity

Ethanolic and methanolic extracts of *C. asiatica* had shown significant protection and lowered the blood glucose levels to normal in glucose tolerance test carried out in the alloxan induced diabetic rats [75]. Nganlasom *et al,*[76] were treated the wounds of the diabetic induced Male Spraque-Dawley rats with *Centella* plant extract. They found the wounds of the plant extract treated wounds epithilialised faster when compared to control.

Anti-inflammatory activity

Extract of *Centella* exerted anti-inflammatory effects by reduction of acute radiation reaction in rats. *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 healing [77]. Crude extract of *Centella asiatica* showed anti inflammatory activity in rats by prostaglandin E*2*-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 [78].

Cytotoxic and antitumour activity

A partially purified fraction of methanol extract of *C. asiatica* inhibited the growth of tumour cells with no toxic effects on lymphocytes. Water extract has a chemo preventive effect on colon tumourigenesis [79]. Asiatic acid was found to have anticancer effect on skin cancer[80]. Asiaticosides 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 antitumour activity of vincristine in cancer cells[8]. The *n*-hexane, carbon tetrachloride, chloroform and aqueous soluble fractions of methanol extract of *C. asiatica* showed significant cytotoxic activities in the brine shrimp lethality bioassay[35].

Neuroprotective activity

The consumption of *Centella* was useful to protect the cells from oxidative damage, to destroy excess free radicals and keep the oxidative stress state in balance. As a potent antioxidant *Centella* exerted significant neuroprotective effect and proved efficacious in protecting rat brain against age related oxidative damage[2]. Asiatic acid exerted significant neuroprotective effect 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 excessive glutamate[81]. 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 neurons [82].

Central administration of colchicine produces marked destruction of hippocampal granule cells and septohippocampal pathways resulting in loss of cholinergic neurons and decreased activities of acetylcholinesterase and choline acetyltransferase Centella was able to ameliorate the colchicine induced decrease in AChE activity in rats. Thereby prevents colchicine-induced cognitive impairment and associated oxidative stress. Oxidative stress appears to be an early event involved in the pathogenesis of Alzheimer's disease [83].

It has been reported that *Centella asiatica* has neuroprotective effect on cognition and hippocampal neurons. During early postnatal development and preventing cognitive deficits, the dendritic arborization of hippocampal neurons is promoted. Prenatal stress is known to adversely affect the learning and memory abilities. Postnatal treatment of *Centella asiatica* fresh leaves extracts will protect the hippocampal neurons against prenatal stress and also enhanced learning and memory abilities in rats [84].

Cardioprotective activity

Centella asiatica showed cardioprotective effect on antioxidant tissue defense system during Adriamycin induced cardiac damage in rats [39]. The alcoholic extract of *Centella asiatica* whole plant was evaluated by Pragada *et al.*[85] for cardioprotective activity against ischemia-reperfusion induced myocardial infarction in rats and their results strongly suggests the cardioprotective activity of the plant in limiting ischemia-reperfusion induced myocardial injury.

Skin protective activity

Skin aging appears to be principally related to a decrease in the levels of type I collagen, the primary component of the skin dermis. Asiaticoside, a saponin component isolated from Centella asiatica, has been shown to induce type I collagen synthesis in human dermal fibroblast cells [86].

Radioprotective activity

Centella asiatica could be useful in preventing radiation induced behavioural changes during clinical radiotherapy. The plant extract showed radioprotective properties and pretreatment with it prior to gamma ray irradiation was found to be effective against radiation induced damage in the mouse liver [87].

Immunomodulatory effect

Triterpenoid saponins of *Centella* showed immunomodulatory effect [8]. Pectin isolated from *Centella asiatica* showed immunostimulating activities [88] and methanol extracts showed preliminary immunomodulatory activities [89]. Ethanol extract of *Centella asiatica* stimulates cell-mediated immune system by increasing neutrophil phagocytic function [90].

Memory enhancing activity

Aqueous extract of *C. asiatica* showed significant effect on learning and memory enhancing and significantly decreased the levels of norepineprine, dopamine and 5-HT and their metabolites in the brain. Aqueous extract of the plant showed cognitive enhancing and antioxidant properties in Stereptozotocin induced cognitive impairment and oxidative stress in rats [42]. 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 mice [91].

Wound healing effect

Total triterpenoid fraction extracted from *C.asiatica* increased the percentage of collagen in cell layer fibrnectin and thus may help in promoting wound healing [92]. Asiatic acid and medacassic acid from *C. asistica* have demonstrated an increase in peptidic hydroxyproline showing an increased remodeling of collagen synthesis in wounds [93]. 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 of 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 the 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 [94].

Asiaticosides enhanced induction of antioxidant levels at an initial stage of healing which may be an important contributory factor in its healing properties [46]. Asiaticoside exhibits significant wound healing activity in normal as well as delayed healing models and is the main active constituent of C. asiatica. Asiatic acid and asiaticoside were more active than madacassic acid. Thus the plant appears to be effective in the treatment of wound healing disturbances [95].

CONCLUSION

Centella asiatica has been in use since time immemorial to treat wide range of indications. It has been subjected to quite extensive phytochemical, experimental and clinical investigations. The dynamic nature of indigenous knowledge has led to its survival through centuries. The use of this knowledge is necessary as it is not only socially desirable but is economically affordable, sustainable and involves minimum risks and procedures [96-97]. Many research studies have demonstrated its different functional properties like antioxidant activity, antibacterial, antifungal and antiviral activities, antiulcer activity, antidiabetic activity, anti-inflammatory activity, cytotoxic activity, cardio, neuro and skin protective activities, radioprotective activity, immunomodulatory effect, memory enhancing activity and wound healing effect. With a very low toxicity as attested by its long popular use as a natural product, *Centella* can be a potential herbal plant in many healthcare applications [98-99].

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