

MEDICINAL PROPERTIES OF CENTELLA ASIATICA (L.): A REVIEWDr. Undrala Sushen*¹, Awanija Chouhan¹, Khushnuma Ali² and Veena Ranjesh²¹Department of Organic Chemistry, Dr. Sushen Research Lab, Gokul Group of Institutes, Hyderabad, India.²Department of Pharmaceutical Chemistry, Bhojjam Narasimhulu Pharmacy College for Women, saidabad, Hyderabad.***Corresponding Author: Dr. Undrala Sushen**

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Article Received on 15/07/2017

Article Revised on 04/08/2017

Article Accepted on 25/08/2017

ABSTRACT

Centella asiatica (L.) is a perennial, creeper, faintly aromatic and a valuable medicinal herb. 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 health beneficial functional properties of the *Centella* plant.

KEYWORDS: faintly aromatic and a valuable medicinal herb.**INTRODUCTION**

Medicinal plants with therapeutic properties are used for the treatment of many infectious diseases of humans as they contain many bioactive phytochemical constituents which are of curative effects. The medicinal properties of the plants are mainly due to the presence of secondary metabolites like alkaloids, cardiac glycosides, tannins, flavonoids, saponins, reducing compounds, minerals and vitamins, Amino acids, asiatic, asiaticoside, centic, centellic, centoic and pectic acids, carotene, centellose, Protein, 3-glucosylquercetin, 3-glucosyl and 7-glucosyl-kaempferols, polyacetylenes.^[1] Reactive oxygen species which create oxidative stress cause human diseases and disorders such as heart disease, inflammation, atherosclerosis, stroke, cancer, diabetes mellitus, malaria, HIV/ AIDS, etc.^[2] Antioxidants derived from plants contain the phenolics have many biological activities such as antiinflammatory, anti-cancer and antimicrobial, It promotes memory, used mainly in the bowel complaints in children, applied both externally and internally as poultice and powder respectively in the treatment of leprosy and syphilitic ulcers^[3,4]. Plants also have the capability to safeguard the body from oxidative damage by scavenging the free radicals and inhibiting peroxidation and other radical mediated process.^[5] Due to the profitable efficiency of medicinal plants on biological activities, there is a need for isolation of newer biological compounds from plants which can serve as novel drugs. *Centella asiatica* (L.) is a tropical medicinal plant from Apiaceae family native to Southeast Asian countries such as India, Sri Lanka, China, Indonesia, and Malaysia as well as South Africa and Madagascar.^[6] *C. asiatica*, commonly known as "Gotu kola, Asiatic

pennywort, Indian pennywort, Indian water navelwort, wild violet, and tiger herb" in English, is a tropical plant, cultivated successfully due to its medical importance in some countries including Turkey, and it has a utilization in ayurvedic and Chinese traditional medicines since centuries.^[7] The leaves, which are edible, are in yellowish-green color, thin, alternate with long petioles, and quite characteristic reniform, orbicular, or oblong-elliptic shapes with seven veins.^[8] The plant grows horizontally through its green to red stolones which combine to each other and roots in underground. *C. asiatica*, wide range of biological activities desired for human health such as wound healing.^[9-11] anti-inflammatory, antipsoriatic, antiulcer, hepatoprotective, anticonvulsant.^[18] sedative.^[19] immunostimulant.^[20] cardioprotective, antidiabetic.^[23] cytotoxic and antitumor, antiviral.^[26] antibacterial.^[27] insecticidal.^[28] antifungal.^[29] antioxidant.^[30-32] and for lepra^[33] and venous deficiency treatments.^[34,35] *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.

**Classification****Kingdom:** Plantae**Subkingdom:** Tracheobionta**Division:** Magnoliophyta**Class:** Magnoliopsida**Subclass:** Rosidae**Order:** Apiales**Family:** Apiaceae**Genus:** Centella**Species:** asiatica**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-reniform, 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. *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] Medical importance in some countries including Turkey, and it has a utilization in ayurvedic and Chinese traditional medicines since centuries.^[7] The leaves, which are edible, are in yellowish-green color, thin, alternate with long petioles, and quite characteristic reniform, orbicular, or oblong-elliptic shapes with seven veins.^[8] The plant grows horizontally through its green to red stolons which combine to each other and roots in underground.

Phytochemical Content of Centella Asiatica**Triterpenoids**

Include asiaticoside, centelloside, madecossoside, thankuniside, isothankunic acid, centellose, asiatic, centellic and madecassic acids^[6,7] and brahmoside, brahminoside, brahmic acid, the structure of their genin, brahmic acid (m.p. 293°) has been established as 2,6-hydroxy, 23-hydroxymethyl ursolic acid. Asiaticoside and madecossoside predominated in the leaves with less in roots.^[8]

Volatile and Fatty Acids

The fatty oil consists of glycerides of palmitic, stearic, lignoceric, oleic, linoleic and linolenic acids.^[9]

Alkaloids

An alkaloid, hydrocotylin (C₂₂ H₃₃ NO₈) has been isolated from the dried plants.^[9]

Glycosides

Asiaticoside, madecossoside and centelloside have been isolated from the plant parts. On hydrolysis, these glycosides yield the triterpene acids, asiatic acid, madegascaric acid.^[10-12] and centellic acid.

Flavanoid

Flavanoids, 3-glucosylquercetin, 3- glucosylkaemferol and 7-glucosylkaemferol have been isolated from the leaves.^[11] The plant is reported to contain tannins, sugars, inorganic acids^[13] and resin^[13] amino-acids, viz. aspartic acid, glycine, glutamic acid, α -alanine and phenylalanine.^[14] The total ash contains chloride, sulphate, phosphate, iron, calcium, magnesium, sodium and potassium. The leaves are rich in vitamins such as vit.A, vit.C and vit.E.^[16]

Pharmacological Uses of Centella Asiatica**Antioxidant Capacity**

Antioxidant is used by aerobic organism to protect the cells from oxidative damage by oxidants during oxygen metabolism. The main antioxidant agents such as superoxidase dismutase (SOD), catalase, glutathione peroxidase (GSH-Px), glutathione, ascorbic acid and tocopherol are important to protect the cells due to their ability in eliminating free radicals such as reactive oxygen species (ROS).^[17] The consumption of *Centella* is useful for the antioxidant effect as it offer an effective and safe way of increasing body immune system against free radicals.^[18]

Neuroprotection Effect

Centella extract has been used in Ayurvedic medicine as a nerve tonic. The micronutrients in the extract is reported to be responsible in retarding brain aging and assist in renewal of neural tissue, hence it is effective in enhance memory and revitalize the brain as well as increase attention span and concentration.^[19] In Ayurvedic medicine and traditional Chinese medicine, *Centella* has been used for centuries to control anxiety, helps in relaxation and mental calmness.^[20] Studies in

human and animal models have reported that *Centella* possesses anxiolytic activity potential.

Safety

Centella has been widely used in pharmaceutical industries and has shown good efficacy, performance and safety.^[20] With a very low toxicity, the fresh *Centella* plants have been used in salads, vegetable and drink as juice. It has been used for traditional Indian Ayurvedic and Chinese medicines for decades. In Chinese medicine, *Centella asiatica* is used for treatment of vomiting, epistaxis, urinary calculi, scabies and jaundice. In homeopathic medicine, it is used for treating ascariasis, elephantiasis and in granular cervicites.^[21] Clinical tests have formulated several benefits of *C. asiatica* extracts in terms of wound healing, burns and in skin diseases in gastrointestinal disorders and in treatment of leprosy, lupus, scleroderma, eczema, vein diseases and for treatment of psoriasis. It gives protection against diseases by enhancing immunity of the body.^[22]

Wound Healing

Madecassol, an extract of this plant containing madecassic acid, asiatic acid and Asiaticoside accelerates cicatrization and grafting of wounds.^[23] Asiaticoside promotes fibroblasts proliferation and extracellular matrix synthesis in wound healing.^[24]

Cytotoxic and Antitumour

Oral administration of the crude extract of *C. asiatica* and its partially purified fractions induced apoptosis in solid and Ehrlich Ascites tumour and increased the life span of these tumours bearing mice. Asiatic acid was found to have anticancer effect on skin cancer.^[25]

Memory Enhancing

Aqueous extract of the herb showed significant effects on learning and memory and decreased the levels of norepinephrine, dopamine and 5-HT and their metabolites in the brain.^[25] *Centella asiatica* contains brahmic acid, isobrahmic acid, brahminoside and brahmoside. It has psychotropic, sedative and anticonvulsant properties. It is also useful in dementia, mental disorders and anxiety.

Antibacterial Activity

Various microorganisms are known to cause food spoilage and food borne diseases in human beings. About 200 diseases are caused by contaminated water, milk and other foods. The most frequently identified causal organisms are *Cornibacterium diphtheriae*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*.^[26]

Centella asiatica is one of the important plants that shows antibacterial activity against a wide variety of bacteria. 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.*,^[27]

was observed broad spectrum activity of *Centella asiatica* against a wide range of enteric pathogens. In case of *Vibrio cholerae*, *Shigella* species and *Staphylococcus aureus*, the alcoholic extract of plant showed bactericidal action within 2 hours. Ullah *et al.*,^[28] 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.*,^[29] was observed that methanol extract of *Centella asiatica* whole plant showed inhibition zone against *V. alginolyticus*, *V. vulnificus* and *Streptococcus* sp while inhibition zone was found in *Centella freundii* and all *Vibrio* sp. except *V. vulnificus* against aqueous extracted *Centella asiatica* whole plant. Taemchuay *et al.*,^[30] was found 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*.^[30] Methanolic extract of *Centella* was shown antibacterial activity against 3 *Vibrio* species named *V. harveyi*, *V. alginolyticus* and *V. parahaemolyticus*.

Cardioprotective

The alcoholic extract of the whole plant showed strong cardioprotective activity in limiting ischemia-reperfusion induced myocardial infarction in rats.^[31]

Radioprotective

Centella asiatica could be useful in preventing radiation induced behavioral changes during clinical radiotherapy.^[32]

Antidepressant

The total triterpenes had antidepressant activity and caused significant reduction of the corticosterone level in serum.^[33]

Immunomodulating

Pectin isolated from *Centella asiatica* showed immunostimulating activities and triterpenoid saponins and methanol extracts showed preliminary immunomodulatory effect.^[34]

Antiprotozoal

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

Mental-Retardation

Centella asiatica tablets administered orally to mentally retarded children showed significant increase in general ability and behaviour patterns.^[35]

Antitubercular and Antileprotic

Asiaticoside is useful in the treatment of leprosy and certain types of tuberculosis. Clinical trials conducted on normal adults showed that the drug increased the level of RBC, blood sugar, serum cholesterol and total protein. It has a calming effect on the body and supports the central nervous system.^[36]

Immunomodulatory

C. asiatica, contains triterpenoid, saponins in it possesses immunomodulatory activity.^[37]

Venous Insufficiency

The triterpenoid saponins present in *C. asiatica* strengthen weakened veins by improving wall alterations in chronic venous hypertension and thereby protecting venous endothelium. It also plays important role in stabilizing connective tissue growth by stimulating the production of hyaluronidase and chondroitin sulfate and also imparts balancing effect on connective tissue.^[38]

Antifungal Activity

Ethanol 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 compared to water extracts.^[39] 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*.^[40] 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.^[40] Methanol, chloroform and acetone extracts of *Centella asiatica* showed significant inhibitory effect on growth and sporulation of *Colletotrichum gloeosporioides*.^[41] Alcoholic extracts of *Centella asiatica* did not show antimicrobial activity against yeasts like *Pichia anomala* and *Saccharomyces cerevisiae* and molds like *Aspergillus niger* and *Penicillium pinophilum*.

Autoimmune

Madecassol, component isolated from *Centella asiatica* found to be efficacious in the treatment of chronic or subchronic systemic scleroderma and advanced focal scleroderma.^[42]

Anticancer

Preclinical studies have shown that methanolic extract of *Centella asiatica* causes inhibition in breast cancer cells by inducing apoptosis in different cancer cell lines HeLa, HepG2 and SW48 and MCF-7.

Antidiabetic

Clinical studies have revealed that the two glycosides present in *Centella asiatica* (L.) viz. bhramoside and brahminoside exert sedative and hypoglycemic effect.^[42]

Antiviral Activity

Crude water extracts of combinations each of *Centella* and *Mangifera indica* showed anti-herpes simplex virus activities.^[42]

Antiprotozoal Activity

Alcoholic extract of entire plant showed antiprotozoal activity against *Entamoeba histolytica*.^[42]

Antifilarial Activity

A mixture of ethanolic extracts of *Centella asiatica* and *Acacia auriculiformis* resulted in a considerable decrease in filarial counts in dogs naturally infected with *Dirofilaria immitis*.^[43]

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.^[44] 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. Results of the studies conducted by Abdulla *et al.*, also revealed protection of gastric mucosa and inhibition of leucocytes infiltration of gastric wall in rats pretreated with *Centella asiatica* extract.^[45]

Antidiabetic activity

Ethanol and methanolic extracts of *Centella 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. Nganlasom *et al.*, were treated the wounds of the diabetic induced Male Sprague-Dawley rats with *Centella* plant extract.^[44] They found the wounds of the plant extract treated wounds epithelialised faster when compared to control.^[45]

Anti-inflammatory activity

Extract of *Centella* exerted anti-inflammatory effects by reduction of acute radiation reaction in rats. *Centella 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.^[45] Crude extract of *Centella asiatica* showed anti-inflammatory activity in rats by prostaglandin E2-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.^[46]

Cytotoxic and antitumour Activity

A partially purified fraction of methanol extract of *Centella asiatica* inhibited the growth of tumour cells with no toxic effects on lymphocytes. Water extract has a chemo preventive effect on colon tumourigenesis. Asiatic acid was found to have anticancer effect on skin cancer. Asiaticosides possesses good wound healing activities because of its stimulative effect on collagen synthesis.^[46] It might be useful in cancer chemotherapy as it induces apoptosis and enhances antitumour activity of vincristine in cancer cells. The *n*-hexane, carbon tetrachloride, chloroform and aqueous soluble fractions of methanol extract of *Centella asiatica* showed significant cytotoxic activities in the brine shrimp lethality bioassay.^[47]

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. Asiatic acid exerted significant neuroprotective effect on cultured cortical cells by potentiation of the cellular oxidative defense mechanism.^[44] Therefore it may prove efficacious in protecting neurons from the oxidative damage caused by exposure to excessive glutamate.^[42] 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. 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.^[45] 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.^[44] 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.^[43]

Cardioprotective Activity

Centella asiatica showed cardioprotective effect on antioxidant tissue defense system during Adriamycin induced cardiac damage in rats.^[43] The alcoholic extract of *Centella asiatica* whole plant was evaluated by Pragada *et al.*, 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.^[45]

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.^[46] Asiaticoside, a saponin component isolated from *Centella asiatica*, has been shown to induce type I collagen synthesis in human dermal fibroblast cells.

Radioprotective activity

Centella asiatica could be useful in preventing radiation induced behavioural changes during clinical radiotherapy.^[45] 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.^[45]

Immunomodulatory Effect

Triterpenoid saponins of *Centella* showed immunomodulatory effect. Pectin isolated from *Centella asiatica* showed immunostimulating activities and methanol extracts showed preliminary immunomodulatory activities.^[46] Ethanol extract of *Centella asiatica* stimulates cell-mediated immune system by increasing neutrophil phagocytic function.^[44]

Memory Enhancing Activity

Aqueous extract of *Centella 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.^[45] Aqueous extract of the plant showed cognitive enhancing and antioxidant properties in Stereptoizotocin induced cognitive impairment and oxidative stress in rats.^[45] Treatment during postnatal developmental stage with *Centella asiatica* aqueous extract influenced the neuronal morphology and promoted the higher brain function of juvenile and young adult mice.

Wound Healing Effect

Total triterpenoid fraction extracted from *Centella asiatica* increased the percentage of collagen in cell layer fibrnectin and thus may help in promoting wound healing. Asiatic acid and medacassic acid from *Centella asistica* have demonstrated an increase in peptidic hydroxyproline showing an increased remodeling of collagen synthesis in wounds.^[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 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.^[49] The extract treated wounds were found to epithelialise faster and the rate of wound contraction was higher, as compared to control wounds. Asiaticosides enhanced induction of antioxidant levels at an initial stage of healing which may be an important contributory factor in its healing properties. Asiaticoside exhibits significant wound healing activity in normal as well as delayed healing models and is the main active constituent of *Centella 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.^[50]

CONCLUSION

In recent years, ethno-botanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. The therapeutic potential of these plants in terms of its efficacy and versatility is such that further detailed research appears crucial. The elaboration of a wide variety of phytochemicals have significant pharmacological activity, and the large scale harvesting for other utilities render the plant of potential importance. *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. 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 the plant is popularly used as a natural product, *Centella asiatica* can be a potential herbal plant in many healthcare applications.

ACKNOWLEDGEMENT

The Authors and the research group are very much thankful for financial support from Himanshu Educational Society, I.S.Sadan, and Hyderabad. The authors are specially thankful to Mr. Swamy Rajan Garu, Mrs. Kowsalya (Ayurvedic medicine specialists) and Mrs. S. Subbalakshmi Garu (Principal Padmavathi Degree and P.G College) for spending their valuable time and advising the group with suggestions and preparative methods.

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