REVIEW ARTICLE

Phytochemical and pharmacological review of *Mentha arvensis*

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Abstract

Mentha arvensis Linn. family Lamiaceae, it is used as a food seasoner, household remedy, and industrial purposes it is traditionally used in hypertension and in patients with ischemic heart disease. Juice of leaves is given in diarrhea and dysentery. The leaves medicinally used for stomach problems and allergy. It is also used for the treatment of liver and spleen disease, asthma and jaundice. The infusion of these leaves is used in indigestion, rheumatic pains, arthritis, and as remedy for inflamed joints. Menthol derived from its essential oil is used in pharmaceutical, perfumery, and food industries. Menthol is antiseptic, carminative, refrigerant, stimulant and diuretic in properties and is used against skin infections. It has been reported to possess diverse medicinal properties, and hence there is a need to explore its medicinal properties to support the traditional claim. This review shed a light on extensive experimental work carried on its extracts to validated classical claims.

Key words: *Mentha arvensis*, pharmacological activity, phytochemistry

INTRODUCTION

The Mother Nature has gifted a comprehensive health-care management through herbs and medicinal plants to mankind. The World Health Organization recognizes that nearly 80% of the population is depending on traditional medicine for primary health care.[1] Herbs have provided humankind with medicine from the earliest beginning of civilization. It is estimated that there are 250,000-500,000 plants on earth[2] and relatively small percentage (1-10%) of these are used as a food for human and other animal species. It is likely that even more of these are used for medicinal purpose.[3] Since immemorial times, herbals plants have been used in virtually every culture throughout the world as a source of folk medicine.[4,5] Over two millennia ago, the father of medicine Hippocrates mentioned about 400 medicinal plants and advised, "let food be your medicine and let medicine be your food."[4]

"This illustrates the need for modern medicine and science to turn its attention to plant would once again to find a new medicine that might cure cancer, AIDS, diabetes and many other disease and conditions."[6]

The word drug comes from the old Dutch word drogge meaning "to dry" as pharmacists, physicians and ancient healers often dried plants for use as a medicine. Today approximately 25% of all prescription drugs are still derived from trees, shrubs, or herbs. Some are made from plant extract; other is synthesized to mimic a natural plant compound.[1]

Herb can be leaf, flower, stem, seed, root, fruit, bark, or any other plant part used for its medicinal, food flavoring or fragment property.

In the past 150 years, chemist and pharmacists have been isolating and purifying the "active" compounds from plants in an attempt to produce reliable pharmaceutical drugs. For example, Digoxin from *Digitalis purpurea*, reserpine (Indian snakeroot) *Rauwolfia serpentina*, colchicines from *Autumn crocus*, *Colchicum autumnale*, morphine (from opium poppy) *Papaver somniaferum,* and many more.[6]

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PLANT PROFILE

It is the type species of the Japanese menthol plant mint (*Mentha arvensis* [MA] Linn. family Lamiaceae), a plant, native of Japan, is cultivated extensively in the temperate regions of Europe and western and central Asia, east to the Himalaya and eastern Siberia, it is used as a food seasoner, household remedy, and industrial purposes. It has been reported to possess diverse medicinal properties. Juice of leaves is given in diarrhea and dysentery.[7] The leaves are mostly used as salad and medicinally used for stomach problems and allergy.[8] It is also used for the treatment of liver and spleen disease, asthma and jaundice. The infusion of these leaves is used in indigestion, rheumatic pains, arthritis, and as remedy for inflamed joints. It is traditionally used in hypertension and in patients with ischemic heart disease.[9] Menthol derived from its essential oil is used in pharmaceutical, perfumery and food industries. The oil content of leaves yields 40-50% menthol, which is antiseptic, carminative, refrigerant, stimulant and diuretic in properties, and is used against skin infections. Essential oil can be diluted and used as a wash for skin irritations, itching, burns, inflammations, scabies, and ringworm or to repel mosquitoes. It is also used to relieves pain and reduces skin sensitivity.[10-12]

Vernacular Names[13]

MA has several vernacular names in different languages [Table 1].

BOTANICAL DESCRIPTION

Morphological Character

MA is an erect branched herb that grows up to 60 cm in height with suckers; the stem is cylindrical and the leaves are simple and opposing type 2.5-5 cm long, shortly petiole or sessile oblong-ovate or lanceolate, obtusely or acutely serrate cuneate at the base, sparsely hairy or almost glabrous; flower lilac, arranged in verticillasters, borne on axils of leaves on upper stem.[14,15] Diacytic stomata are present on the lower surface of the leaf. Under the microscope, the leaf also shows 3-8 celled clothing trichomes with striated cuticle. Two types of glandular trichome, one with a unicellular base and small single cell head and the other with a multicellular head characteristic of the family are present. Calcium oxalate is not present.[7]

Table 1: Several vernacular names of MA in different languages

Name of language	Vernacular names
Sanskrit	Puthea
Japnese	Midorihakka
German	Minze
Hindi	Pudina, podina
English	Corn mint
Unani	Pudinah
Arabian	Putnaj
Bengali	Pudina
Nepalese	Nawaghya
Tamil	Puthina
Sinhalese	Odutalan

Active Constituent

The mint plant has been reported to possess terpenes such as α-menthol, neomenthol, isomenthol, d-menthone, isomenthone, menthofuran, menthylacetate, carvomenthone, cineol, p-cymene, aromadendrene, limonine, -phellandrene, pipertone, -pinene, carvacrol, α-pinene, α-phellandrene, -pinene, dipentene, cardinene, and -thujone in different proportions depending on the season, type of climate and the plant processing.[16,17] It also contains the flavonoids such as quercetin, menthoside, and isorhoifolin,[18] vitamin K, thymol and eugenol.[16]

Pharmacological Action

The infusion of leaves is used to treat rheumatism, indigestion, infantile troubles, vomiting in pregnancy and hysteria.[17] The leaves are acrid, thermogenic, stimulant, anodyne, deodorant, vulnerary, anti-helmenthic, sudorific, dentrific, antispasmodic, febrifuge, and contraceptive.[19] The dried plant is used as an antiseptic, carminative, stomachic, refringent, stimulant, emmenagogue, and diuretic. The tea prepared from the leaves is used as an antidote for poison.[16] Mint has been reported to be used in vitiated conditions of arthralgia, halitosis, indolent ulcers, wounds, cuts, helminthiasis, dipsia, flatulence, colic, peptic ulcer, vomiting, diarrhea, cardiac debility, cough, asthma, bronchitis, strangury, skin diseases, amenorrhea, dysmenorrheal, dental caries, hepatopathy, spleenopathy, jaundice, cephalagia, fever and general weakness.[19]

Phytochemistry

Majak and Neil Towers developed new methods for the isolation and purification of certain of the ethanol-insoluble, phenolic esters of MA. "Insoluble" conjugates of caffeic, ferulic and *p*-coumaric acids were purified and were shown to be electrophoretically and chromatographically homogeneous. Two acylated anthocyanins containing *p*-coumaric acid and caffeic acid were also obtained from acetone powders.[20] It contained the highest amount of total xanthophylls.[21] Two constituents, isolated from the suckers were identified as 3-*O*-β-sitosteryl-glucopyranosyl- (1α → 2)-fructofuranoside and sucrose.[22] Linarin (acacetin-7-O-beta-d-rutinoside) from the flower extract was isolated.[23] The volatile constituents of the essential oils of different parts (shoot stem, shoot leaf, stolon

stem, stolon leaf) of MA, grown under semi-arid tropical climatic conditions were investigated. The shoot leaf gave the highest yield of oil (0.62%), while the stems produced negligible quantities of oil (0.02%). Menthol was the major component of all the oils, with the highest percentage in shoot stem oil (78.16%) and the lowest in stolon (runner) stem oil (43.7%). β-caryophyllene oxide was present in shoot (stem and leaf) oils, while α-phellandrene and terpinolene were identified in stolon (stem and leaf) oils, which were also richer in limonene, menthone, and pulegone than the shoot oils. The underground rhizomes of cornmint plants did not yield any essential oil.[24] The occurrence of menthofuran (0.01-0.04%) was determined by means of coupled gas-liquid-thin-layer chromatography in genuine essential oils obtained from plants grown in Argentina, Brazil, Formosa, India, Japan, and South Africa.[25] Lipid class and fatty acid compositions of edible tissues of MA is carried out, the lipid contents on dry-weight basis was 6.2% and 2.0% - in the leaves and stem. Lipid classes were separated by silicic acid column chromatography and thin-layer chromatography and estimated. Among the non-polar lipids, pigments were the major components. Monogalactosyl diglycerides and digalactosyl diglycerides were the chief constituents of glycolipids. Phosphatidylcholine was the predominant phospholipid among the constituent fatty acids, determined by the gas-liquid chromatography major ones were linolenic (18:3) and palmitic (16:0) in the leaves and linoleic (18:2) and palmitic in the other tissues.[26]

PHARMACOLOGICAL PROPERTIES

Antibacterial Activities

The effects of the essential oils on the proliferation of *Helicobacter pylori*, *Salmonella enteritidis*, *Escherichia coli* O157:H7, methicillin-resistant *Staphylococcus aureus,* and methicillin sensitive *S. aureus* were examined. The essential oils inhibited the proliferation of each strain in liquid culture in a dose-dependent manner. In addition, they exhibited bactericidal activity in phosphate-buffered saline. The antibacterial activities varied among the bacterial species tested but were almost the same against antibiotic-resistant and antibiotic-sensitive strains of *H. pylori* and *S. aureus*.[27] By using disc diffusion assay, the antimicrobial activity of essential oil sample extracted from MA var. *piperacens* cultivated in Thailand was evaluated against zoonotic enteropathogens including *Salmonella* spp., *E. coli* O157, *Campylobacter jejuni,* and *Clostridium perfringens* which are important for broiler export. The essential oil of, MA var. *piperacens*, showed promising antibacterial activity against the bacteria tested.[28]

Antioxidant Activities

It has been reported that cineole, an important constituent of mint extract, mitigated the ethanol-induced gastric mucosal damage in rats and studies have shown that this activity has been due to the antioxidant, lipoxygenase inhibitory and capacity to restore the non-protein sulfhydryl to the normal levels by the test compound. Cineole, eugenol, and thymol, which are present in mint are reported to be a good antioxidant and inhibit lipid peroxidation.[29-32] The flavonoids like quercetin, which is present in the mint have been reported to scavenge OH and superoxide free radicals and also inhibit the lipid peroxidation.[33,34] The eugenol, terpenes, and flavonoids that are present in mint extract are good antioxidants and modulators of the xenobiotic enzymes, especially the Phase-2 enzymes like glutathione-s-transferase, and glutathione.[35] It was investigated using a β-carotene bleaching method, in Thailand, The results showed that the highest amount of total xanthophylls were responsible for the antioxidant activity in the plant.[21] Plant was tested for their possible regulatory effect on nitric oxide (NO) levels using sodium nitroprusside as a NO donor *in vitro*. Chloroform extract shows maximum activity than aqueous. Both evaluated extracts exhibited a dose-dependent NO scavenging activity. This results suggest that these spices might be potent and novel therapeutic agents for scavenging of NO and the regulation of pathological conditions caused by excessive generation of NO and its oxidation product, peroxynitrite.[36] Water-soluble extracts, the varieties MA var. Japanensis (MA var. piperascens Holmes ex Christ) were screened for potential anti-oxidative properties. These properties included iron (III) reduction, iron (II) chelation, 1,1-diphenyl-2-picrylhydrazyl radical scavenging, and the ability to inhibit iron (III)-ascorbate-catalyzed hydroxyl radical-mediated brain phospholipid peroxidation. Total phenol content and qualitative and quantitative compositional analyses of each extract were also made. The extracts demonstrated varying degrees of efficacy in each assay.[37]

Antifertility Activities

Antifertility investigation of the petroleum ether extract of the leaves of MA in male albino mice has been carried out. In male albino mice at the doses 10 and 20 mg/day/mouse for 20, 40 and 60 days, when administered orally, showed a dose and duration dependent reduction in the number of offspring of the treated male mated with normal females. Negative fertility was observed in both dose regimens after 60 days of the treatment. The body weight and libido of the treated animals remain unaffected. However, a significant decrease in the weight of the testis, epididymis, cauda epididymal sperm count, motility, viability, and normal morphology of the spermatozoa was observed. The levels of serum protein, bilirubin, glutamic oxaloacetic transaminase, glutamic pyruvic transaminase and acid phosphatase, blood urea and hematological indices were unaltered throughout the course of the investigation. All the altered parameters were reversible following withdrawal of treatment. The results suggest that the petroleum ether extract of the leaves of MA possess reversible antifertility property in male mice.[38] Assessment of reversible contraceptive efficacy of methanol extract of

MA leaves in male albino mice was studied. An aqueous solution of the extract (10 mg/day/mouse) when administered orally to male mice of proven fertility for 20, 40 and 60 days caused inhibition of fertility while maintaining their normal sexual behavior. With the increase in treatment duration, there occurred a corresponding decrease in the mean weight of testis and accessory organs of reproduction. Sperm concentration, motility, and viability in the cauda epididymis were also decreased. Spermatozoa with coiled tails also appeared in the epididymal smear. However, all the induced effects returned to normalcy within 30 days following withdrawal of 60 days treatment. Oral administration of the extract also did not affect the body weight of the mice and their blood cells count, packed cell volume, hemoglobin, and blood/serum biochemistry.[39] 50% ethanolic extract of leaves has been found to reduce the fructose synthesis in seminal vesicles; as a result of which the viability of spermatozoa seems to be altered. Fertility testing revealed sterile mating till 30 days of last treatment.[40] Postcoital antifertility effect of MA has been carried out an uterotonic fraction of MA (UM-fraction) in rats. Subcutaneous administration of the UM-fraction to rats pregnant from day 1 to day 10 caused a significant interruption in pregnancy. The effect was pronounced during the post-implantation period. At the effective dose, the UM-fraction did not exhibit significant estrogenic or anti-gonadotropic activities. However, it enhanced the estrogenic effect of estradiol when administered concurrently.[41]

Effect on Anaphylactic Reactions and Tumor Necrosis Factor (TNF)-alpha Production

The effect of aqueous extract of MA L. var. piperascens Malinv. (MAAE) on immunologic and non-immunologic stimulation-mediated anaphylactic reactions were studied. MAAE (0.001-1 g/kg) dose-dependently inhibited passive cutaneous anaphylaxis when intraperitoneally, intravenously, and orally administered. MAAE (0.001-1 mg/ml) dose-dependently inhibited the histamine release from rat peritoneal mast cells (RPMC) activated by compound 48/80 or anti-DNP immunoglobulin E (IgE). Moreover, MAAE (0.1 mg/ml) had a significant inhibitory effect on anti-DNP IgE-mediated TNF-alpha production. These results indicate that MAAE inhibits immunologic and non-immunologic stimulation-mediated anaphylactic reactions and TNF-alpha production from RPMC.[42]

Radioprotective Activity

The radioprotective effect of various doses (0, 2.5, 5, 10, 20, 40 and 80 mg/kg body weight) of chloroform extract of mint (MA) was studied in mice exposed to 10 Gy gamma radiations. The 10 mg/kg of mint extract was found to afford best protection as evidenced by the highest number of survivors in this group at 30 days postirradiation, the mice treated with 10 mg/kg body weight mint extract or oil were exposed to 6, 7, 8, 9 and 10 Gy of gamma radiation and observed for the induction of radiation sickness and mortality up to 30 days post-irradiation. The mint extract pre-treatment was found to reduce the severity of symptoms of radiation sickness and mortality at all exposure doses and a significant increase in the animal survival was observed when compared with the oil + irradiation group. The mint extract treatment protected the mice against the gastrointestinal death as well as bone marrow deaths. The dose reduction factor was found to be 1.2.[9]

Cardiovascular Disease

Three polarity based fraction from the crude extract of MA were investigated their effects on arachidonic acid metabolism. This crude extract inhibited arachidonic acid metabolite thromboxane B2-a stable analogue of thromboxane-A2, made via cyclooxygenase pathway and lipoxygenase product 1 and 12-hydroxyeicosatetraenoic acid made via lipoxygenase pathway. MA might possess antiplatelet activity as thromboxane-B2 is one of the strongest proponents of platelet aggregation. MA was found to inhibit human platelet aggregation induced by arachidonic acid as well as by adenosine diphosphate but platelet activating factor was unaffected by MA. It indicates that inhibition of platelet aggregation may be important mechanism for observed beneficial effects of herb in patients with ischemic heart disease. It was also effective in enhancing glutathione peroxidase activity.[43]

Anti-allergic and Anti-inflammatory Activity

Anti-inflammatory activity and anti-allergic (histamine production by mast cells) of ethanolic and aqueous extracts (leaves, stem and roots) of MA were determined by histamine-induced paw edema in mice and histamine release inhibition test, respectively. MA (specifically, leaves) are rich source of secondary phytoconstituents, which impart their therapeutic effects against allergic and inflammatory diseases. Results for anti-allergic revealed that ethanolic extracts of leaf and root possessed marked inhibitory activity expressed as percentage inhibition, that is, 57% and 53%, respectively. Anti-inflammatory potential exhibited by ethanolic extracts of plant parts is leaf = 68.30 > root = 48.80 > stem = 10.70% and compared with percentage inhibitory potential of standard drug, diclofenac sodium which caused 77.87% edema inhibition.[44]

CONCLUSION

Herbs have been used by humankind in the form of medicine since their origin. Modern medicine showed several side effects at the cost of its fast relief. This medicine has several shortcoming as per as treatment toward AIDS, cancer, diabetes, etc. Hence, world is seeing with new hope toward folk medicine. MA was one of the important herbs of folk

medicine and culinary source. Several researchers have claimed that MA herb would be potential tool to cure many diseases or can be used as an adjuvant therapy. Since that is consumed by many people in the form of juice so by this way one can prevent from many diseases. On basis of its phytochemical studies, it has been found that it contains different types of flavonoids, polyphenols, essential oil that may be responsible for its antioxidant and inflammatory activities. If any herb claimed to be anti-inflammatory or antioxidant then, it may have radioprotective activity. It has been validated for the same. Now there is need to isolate active drug and formulate so that it might help to control adverse effect associated with modern drugs.

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