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Review Article

Peppermint, (Mentha × piperita): Role in Management of Diseases through Modulating Various Biological Activities

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ABSTRACT

Peppermint, (Mentha ×piperita), aromatic perennial herb of the mint family (Lamiaceae). It is a natural hybrid of *Mentha spicata* and *Mentha aquatica* and is found wild with its parent species in central as well as southern Europe. It holds various types of ingredients including menthol, menthone and cineol. Menthol, which is extracted from peppermint, play an important role in the inhibition of various types of pathogenesis. Peppermint oil also acts as a mild carminative agent and used for disorder of the large intestines that causes stomach pain. Moreover, experimental studies have confirmed its role in health management through anti-oxidant, anti-inflammatory, anti-inflammatory, anti-diabetic, neuroprotection and hepatoprotective effects. its topical application shows relief from cold, muscle pain, and headache. The health promoting role of Peppermint has gained a noteworthy scientific attention, but the exact mechanism of its action still remains not clear. The current review mainly emphases on the pharmalogical effects of peppermint in the inhibition of pathogenesis. The purpose of this review is to provide an overview of peppermint in the management of various types of diseases.

Key words: Peppermint, Mentha ×piperita, Antioxidant, Anti-microbial, Pathogenesis.

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INTRODUCTION

Mentha piperita L., a medicinally significant plant belongs to the Family Lamiaceae[1,2] and is a hybrid of *Mentha aquatica* and *Mentha spicata* L. and usually known as peppermint. Though *M. piperita* is a native genus of the Mediterranean region, it has been spread worlwide for use in fragrance, flavor, and pharmaceutical applications.[3] The peppermint plant holds over 40 distinct chemical compounds (including menthol, menthone, and menthyl acetate) and its consumption safety was proven in toxicological investigations.[4] The differences in essential oil composition among the members of this genus offer a diversity of strains with high contents of menthone, menthol, carvone, linalool, or other valued terpenoid components synthesized by the mevalonic acid pathway.[5] Peppermint and their ingredients has proven role in the inhibition of various types of pathogenesis. Moreover, mint plants role in diseases cure has been noticed long ago, dating to ancient Egypt, Greece, and Rome where they were commonly used as stomach soothers.[6] Its role as analgesic attributed due to its main ingredients such as Limonene, Carvone, and Menthol.[7,8] Also, menthol in peppermint soothe the pain in return. Furthermore, menthol is in effect in soothing the pain via increasing the stimulation threshold of cells and decreasing synoptic stimulations as well as transmits.[9] Its role in disease prevention has been noted as antiviral,[10] antibacterial,[11] antifungal,[12] as well as analgesic[13] activity. The current review mainly emphases on the pharmalogical effects of peppermint in the inhibition of pathogenesis. The purpose of this review is to provide an overview of peppermint in the management of various types of diseases.

PHARMALOGICAL ACTIVITIES OF *MENTHA PIPERITA* (PEPPERMINT)

Antioxidant activity

A study result demonstrated that peppermint essential oil was found to be an effective alternative treatment of irritable bowel syndrome in humans, of which the result is measured to be arbitrated via its antioxidant as well as anti-inflammatory activities.[14] The oil and *Mentha piperita* extracts also showed important antioxidant activity and the oil showed about half effectiveness when compared to the standard BHT. These finding revealed the strong antibacterial and antioxidant activities of peppermint oil.[15] Antioxidant as well as antibacterial activities and the composition of *Mentha spicata* extracts were measured. The methanolic extract revealed a higher content of total phenolic compounds and stronger antioxidant activity, whereas only the essential oil exhibited antibacterial activity.[16]

Anti-inflammatory activity

A study was made to evaluate the effectiveness of menthol on acetic acid induced acute colitis in rats. Result demonstrated that menthol reduced significantly the colonic levels of interleukin 1β (IL-1β), tumor necrosis factor-α (TNF-α), myeloperoxidase (MPO), interleukin 6 (IL-6) activity in inflamed colons. Therefore, the findings of the study provide proof that menthol may be beneficial in patients suffering from acute ulcerative colitis.[17] The role of L-menthol and mint oil as an anti-inflammatory drug, preclinical *in vitro*-investigations were performed L-menthol significantly suppressed the production of each of the inflammation mediators by monocytes *in vitro*. Whereas mint oil had an effect

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on PGE subset2 production: lower concentrations of 10 superset-10 to 10 superset-8 g/ml increased PGE subset2 up to 6-fold compared to baseline but concentrations of 10 superset-7 g/ml suppressed PGE subset2 production by approximately 50%. These results obtained with human monocytes suggest preferable anti-inflammatory effects of L-menthol compared to mint oil at therapeutically relevant concentrations supplied in enteric coated capsules.[18]

Neuroprotective effect

The potential central nervous system (CNS) activities of traditional medicinal plants, four species and one hybrid of the genus Mentha (M. aquatica, M. longifolia, M. pulegium, M. suaveolens and M. x piperita) were selected. Mentha x piperita and Mentha aquatica produced significant protection of the PC12 cells against oxidative stress. All the plants exhibited antioxidant and MAO-A inhibitory activity, M. x piperita being the most active. M. aquatica showed the highest affinity to the GABA(A)-receptor assay. Finally, fining exhibited that mints might have effect on the CNS.[19] The highest (100 µL) dose of essential oil improved performance on the cognitively demanding Rapid Visual Information Processing task. Peppermint (*Mentha piperita*) essential oil with high levels of menthol/menthone and characteristic *in vitro* cholinergic inhibitory, calcium regulatory and $GABA_A$/nicotinic receptor binding properties, beneficially modulated performance on demanding cognitive tasks and attenuated the increase in mental fatigue associated with extended cognitive task performance in healthy adults.[20]

Anti-diabetic effect

The antidiabetic effect of Mentha spicata plant in the experimental diabetic state was evaluated. In normal rats, both a single and repeated administration of the extract had not shown a significant reduction in blood glucose levels. However, repeated oral administration of M. spicata aqueous extract showed a significant blood glucose lowering effect in STZ diabetic rats. The blood glucose lowering activity of A.P.A.E was comparable to glibenclamide treatment at the dose used.[21] Another finding reported that the effect of peppermint leaf juice on glucose tolerance level was studied in non-diabetic and streptozotocin (STZ) diabetic induced rats. Peppermint leaf juice at dose of 100 g/L exhibited meaningfully reduced glucose, LDL-c, cholesterol as well as triglycerides levels and significant rise in HDL-c.[22] The effect of Menthe piperita on serum lipid levels of albino rats was investigated. The results of the study revealed that Mentha piperita had significant beneficial effects against fructose-induced hyperlipidemia and showed good antioxidant activity. The aqueous extract of the plant produced a significant decrease in elevated levels of glucose, triglycerides, cholesterol, low density lipoprotein, very low density lipoprotein, and atherogenic index and also increased the high density lipoprotein cholesterol levels and HDL-ratio without affecting serum insulin levels in fructose-fed rats.[23]

Hepatoprotective effect

The protective effect of peppermint (*Mentha piperita*) and parsley (*Petroselinum crispum*) leaves oils against hepatotoxicity induced by carbon tetrachloride (CCl_4) in experimental rats was evaluate. Hepatotoxicity by CCl_4 resulted in significant elevation of total cholesterol, low density lipoprotein (LDL-C), serum triglycerides, very low density lipoprotein (VLDL-C) and decreasing in serum high density lipoprotein (HDL-C). Administration of 0.5 ml of each peppermint, parsley and their mixture oils attenuated the adverse effects and biochemical alterations caused by CCl_4 especially, at 0.5 ml of peppermint oil. Peppermint, parsley and their mixture oils have strong radical scavenging activity and antioxidant activity specially, at 0.5 ml of peppermint oil that reversed these negative changes by significant increase in the activity of SOD, GSH and decreasing in MDA. Finally, finding showed that the hepatoprotective effect of peppermint and parsley oil may be attributed to its antioxidant content and free radical scavenger effects.[24] A study was performed to investigated the antifibrogenic potential of *Mentha piperita* L. essential oil (MPEO) and its underlying mechanisms. Result showed that MPOE significantly improved the liver injury markers, lipid peroxidation, antioxidant capacity, CYP2E1 gene expression and liver histology. Additionally, extract ameliorated liver fibrosis as evidenced by the reduced expression of desmin, α-smooth muscle actin, transforming growth factor-β1 (TGF-β1), and SMAD3 proteins.[25] The composition and *in vitro* antioxidant activity of *Mentha piperita* leaf essential oil (MpEO) was investigate.The *in vitro* antioxidant activity of MpEO was lower than that of silymarin. Pretreatment of animals with MpEO at a dose of 5 mg/kg did not have a significant effect on ALT, AST, ALP, LDH, γGT, urea or creatinine levels in CCl_4-induced stress. Whereas pretreatment with MpEO at doses of 15 and 40 mg/kg prior to CCl_4, significantly reduced stress parameters (ALT, AST, ALP, LDH, γGT, urea and creatinine) compared to the CCl_4-only group. Moreover, a significant reduction in hepatic and kidney lipid peroxidation (TBARS) and an increase in antioxidant enzymes SOD, CAT and GPx was also observed after treatment with MpEO (40 mg/kg) compared to CCl_4-treated rats.[26]

The effects of peppermint (*Mentha piperita* L.) alcoholic extract on liver injury caused by the oxidant carbon tetrachloride (CCl_4), was evaluated. Peppermint extract significantly increased blood serum concentrations of total protein, albumin, triglyceride and HDL_C, whilst CCl_4 decreased those concentrations (P). Blood serum concentrations of total cholesterol, LDL_C, LDL_C:HDL_C ratio, $VLDL_C$ and glucose were decreased by peppermint extract, whereas those concentrations were increased by CCl_4 (P). A significantly higher level of liver enzymes was found in blood serum of birds treated by CCl_4 than those by peppermint extract (P).[27]

Genotoxicity effect

Genotoxic properties of the essential oils extracted from dill (*Anethum graveolens* L.) herb and seeds, peppermint (*Menthaxpiperita* L.) herb and pine (*Pinus sylvestris* L.) needles were studied in human lymphocytes *in vitro*, and Drosophila melanogaster somatic mutation and recombination test (SMART) *in vivo*. In the CA test, the most active essential oil was from dill seeds, then followed essential oils from dill herb, peppermint herb and pine needles, respectively. In the SCE test, the most active essential oils were from dill herb and seeds followed by essential oils from pine needles and peppermint herb. Essential oils from dill herb and seeds and pine needles induced CA and SCE in a clear dose-dependent manner, while peppermint essential oil induced SCE in a dose-independent manner.[28]

Anti-bacterial activity

Natural compound or active compound of medicinal play significant role as anti-microbial agent and inhibit the growth of microorganism.[29-32] The antibacterial activity of peppermint oil and different extracts of *Mentha piperita* against some Gram-positive and Gram-negative bacterial strains was investigated. It was found that the distilled concentrations of essential oil inhibited the growth of microorganisms and the results were comparable with those of antibiotic gentamycin. Moreover, minimum inhibitory concentrations for the bacterial species ranged from 0.4% to 0.7% v/v.[33]

The antimicrobial activities of peppermint (*Mentha piperita*) extracts against 10 multidrug resistant (MDR) pathogenic bacterial clinical isolates was evaluated. Result showed that ethyl acetate extract of peppermint had strong growth inhibitory effects on the tested pathogens, followed by the chloroform, ethanol and methanol extracts. The inhibitory activity of the ethyl acetate extract against all Gram-

negative pathogens was higher than that of chloroform (10–80 mg/ml), methanol (10– > 80 mg/ml) and ethanol (40– > 80 mg/ml).[34] Volatile oil obtained from the leaves of *Mentha×piperita* L., on MDR strains was investigated. Testing the antibacterial activity of peppermint oil on both reference strains and isolated MDR strains showed its bactericidal effect. Minimum inhibitory concentration (MIC) was lower (20 mg/mL) for *Staphylococcus aureus, Escherichia coli* and *Proteus mirabilis* and higher (40 mg/mL) for *Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Acinetobacter baumannii* strains.[35]

Anti-fungal activity

Essential oil of *Mentha piperita* was analyzed and evaluated for *in vitro* antifungal activity against *Dreschlera spicifera*, *Fusarium xysporum* f.sp. *ciceris* and *Macrophomina phaseolina.* Result showed that oil was found to be effective against these fungal pathogens. The antifungal activities of the oil increased with an increase in the concentration.[36] Antifungal activity of "Mentha of Pancalieri" EO, either alone or in combination with azole drugs against a wide panel of yeast and dermatophyte clinical isolates was evaluated. The results suggest that this EO exerts a fungicidal activity against yeasts and a fungistatic activity against dermatophytes. Interaction studies with azoles indicated mainly synergistic profiles between itraconazole and EO vs. Candida spp., Cryptococcus neoformans, and Trichophyton mentagrophytes.[37] The vapors of peppermint oil and two of its chief ingredient constituents (menthol and menthone), and sweet basil oil and its major constituents (were evaluated tested against Sclerotinia sclerotiorum, Rhizopus stolonifera Vuill and Mucor sp. (Fisher). The essential oils, their major individual aroma constituents and blends of the major individual constituents at different ratios inhibited the growth of the fungi in a dose-dependent manner. Menthol was found to be the individual aroma constituent responsible for the antifungal properties of peppermint essential oil their concentrations in the original oil was found to enhance the antifungal properties of basil oil indicating a synergistic effect.[38]

Anti-viral activity

The virucidal effect of peppermint oil, against herpes simplex virus was evaluated. Peppermint oil showed high levels of virucidal activity against HSV-1 and HSV-2 in viral suspension tests. At noncytotoxic concentrations of the oil, plaque formation was significantly reduced by 82% and 92% for HSV-1 and HSV-2, respectively. Higher concentrations of peppermint oil reduced viral titers of both herpesviruses by more than 90%.[39] An experiment was performed to investigate the antiviral, anti-inflammatory, and antioxidant effects of the ethanol extract of *Mentha piperita* L. leaves (MPE). MPE contained high levels of phenolic acid and flavonoid, showed antiviral activity against RSV with a high selectivity index, and significantly decreased the production of NO, TNF-α, IL-6.[40] Aqueous extracts from species of the Lamiaceae family were examined for their antiviral activity against Herpes simplex virus (HSV). Extracts from lemon balm (Melissa officinalis), peppermint (Mentha x piperita), prunella (Prunella vulgaris), rosemary (Rosmarinus officinalis), sage (Salvia officinalis) and thyme (Thymus vulgaris) were screened. All test compounds showed a high antiviral activity against HSV-1, HSV-2 and ACV . In order to identify the mode of antiviral action, the extracts were added to the cells or viruses at different stages of infection. Both types of Herpes virus including ACV (res) were considerably neutralized after treatment with the extracts prior to infection.[41] Antiviral, anti-inflammatory, and antioxidant effects of the ethanol extract of *Mentha piperita* L. leaves (MPE) was investigated. MPE contained high levels of phenolic acid and flavonoid, showed antiviral activity against RSV with a high selectivity index, and significantly decreased the production of NO, TNF-α, IL-6, and PGE2 in lipopolysaccharide-stimulated RAW 264.7 cells.[42]

Larvicidal activity

Oil of *Mentha piperita* Lwas investigated for larvicidal activity against different mosquito species: *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus*. Of the three species tested *Cx. quinquefasciatus* was most susceptible followed by *Ae. aegypti and An. stephensi.* Application of oil at 3 ml/m^2 of water surface area resulted in 100% mortality within 24 h for *Cx. quinquefasciatus*, 90% for *Ae. aegypti* and 85% for *An. stephensi*. For *Ae. aegypti* 100% mortality was achieved at 3 ml/m^2 in 48 h or 4 ml/m^2 in 24 h. For *An. stephensi* 100% mortality was observed at 4 ml/m^2 in 72 h.[43]

Anti-tumour effect

Medicinal plants or active compounds play an important role in the management of cancer.[44-46] The methanol extracts prepared from ten kinds of herbs including M. piperita were examined for the cytotoxcic effect againt L1210 cancer cells and its mode of action. The considerable cytotoxic effects were observed in all cases with the most prominent effect demonstrated by lemon verbena extract. The cytotoxic effect was found to be dose and culture period dependent. With respect to the mechanism of the cytotoxicity, the augmented generation of *O2−ion* and the dramatically escalated activities of antioxidant enzymes.

Role in Respiratory system

The effects of inhalation of L-menthol, D-isomenthol and D-neomenthol, upon nasal resistance and sensation to airflow were evaluated in 40 subjects. L-menthol caused a highly significant enhancement of nasal sensation of airflow. These findings show that L-menthol has a specific pharmacological action on nasal sensory nerve endings which is not related to its peppermint smell. The effects of oral administration of a lozenge containing menthol on nasal resistance to airflow (NAR) and nasal sensation of airflow in 62 subjects suffering from nasal congestion associated with naturally acquired common cold infection was examined. Nasal resistance to airflow showed a significant increase in both the menthol and placebo groups over the 2 h experiment with no difference between the groups at any time. The VAS scores showed significant changes of subjective improvement in nasal sensation of airflow in the menthol-treated group 10 min after dosing whereas the placebo group showed no change. Menthol inhalation showed no steady effect on nasal resistance whereas the majority of subjects showed an increased sensation of nasal airflow as well as a cooling effect of menthol. The results advocate that menthol encourages cold receptors in the nasal mucosa to make an increased sensation of airflow.

Chemopreventive action

Shamma, a mixture of powdered tobacco, slaked lime, oils, ash, spices and other flavors, has been associated to oral cancer in Saudi Arabia. Chloroform extract of a brand named 'white shamma' (WSH) was found to be mutagenic, while that of a brand called 'brown shamma' (BSH), which is known to contain mint as a flavouring agent, was found to be non-mutagenic. A carcinogenicity assay was performed to test the effects of WSH and BSH in the hamster cheek pouch model showed that the former was tumorigenic, while the latter was not. However, when crushed leaves of mint were mixed with powdered WSH (in 1:1 proportion), the tumorigenic effect of the latter was abolished. These data strongly suggested that mint has a chemopreventive effect agaizst shamma-induced carcinogenesis.

Radiation protective action

Mentha extract administered orally for three consecutive days prior to whole body irradiation showed modulation of activity of serum phosphatases in albino mice. Moreover, irradiated animals pretreated with extract showed important drop in acid phosphatase activity as

compared to untreated irradiated animals. A marked decrease in serum alkaline phosphatase activity was recorded in both irradiated groups. However, in ME pretreated irradiated group, values of alkaline phosphatase activity remained significantly higher than untreated irradiated animals. The modulatory influence of mentha oil (*Mentha piperita* Linn.) against a lethal dose (8.0 Gy) of gamma irradiation on the activities of serum phosphatases in Swiss albino mice was studied. Mentha oil (40 microL/animal/day) given orally for 3 consecutive days prior to whole-body irradiation (8.0 Gy) showed a modulation of activity of serum phosphatases. The values of acid phosphatase activities were significantly higher in the irradiated groups throughout the experiment compared with the mentha treated unirradiated animals. However, the acid phosphatase activity of mentha treated irradiated animals showed a significant decline over untreated irradiated animals at all autopsy intervals.

CONCLUSION

In this review, we discussed the current evidence on the potential role of peppermint and its active compounds in management of diseases. The health-promoting property of peppermint are well recognised. It plays an important role in diseases cure via modulation of various biological activities. Research advocates that peppermint can help in the management of diseases through modulation inflammatory conditions, diabetes, microbes growth inhibition, liver disease, and respiratory diseases.

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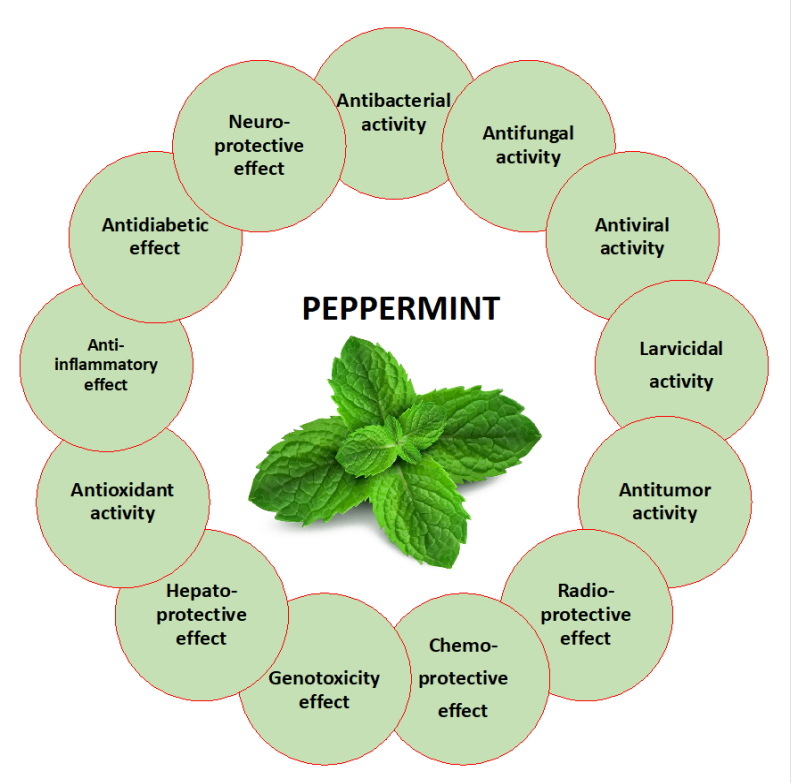
GRAPHICAL ABSTRACT



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