

A review of medicinal uses and pharmacological effects of *Mentha piperita*

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Abstract

Mentha piperita Linn. emend. Huds. is widely used in food, cosmetics and medicines. It has been proven helpful in symptomatic relief of the common cold. It may also decrease symptoms of irritable bowel syndrome and decrease digestive symptoms such as dyspepsia and nausea, although more research is needed. It is used topically as an analgesic and to treat headaches. Though *M. piperita* is on the FDA's GRAS (Generally recognized as safe) list but herb has few side effects. The peppermint oil can cause heartburn or perianal irritation, and is contraindicated in patients with bile duct obstruction, gallbladder inflammation and severe liver damage, and caution should be taken in patients with GI reflux. Menthol products should not be used directly under the nose of small children and infants due to the risk of apnoea.

Keywords: *Mentha piperita*, Peppermint, Peppermint oil, Menthol, Medicine, Toxicity.

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reddish-purple and smooth. The leaves are short 2.5-5cm long, oblong-ovate and serrate. The flowers are purple-pinkish and appear in the summer months. The plant has runners above and below ground and propagation takes place through these runners. It is originally native of Europe, Canada, and the US and have been naturalized in many parts of India. It is cultivated in India, China, Europe, America, Australia, South Africa and some other countries. The leaves and flower tops are collected as soon as flowers begin to open and dried as crude drug for its oil and peppermint (Fleming, 1998; Wealth of India – Raw Materials, 1962).



Mentha piperita

Introduction

Mentha species are used for their flavouring and medicinal properties widely throughout different countries of the world. *Mentha piperita* Linn. emend. Huds. is currently one of the most economically important aromatic and medicinal crops. It is commonly known as Peppermint, Brandy mint, Candy mint, Lamb mint, Balm mint, *Vilayati pudina* or *Paparaminta* and belongs to the family *Lamiaceae*. The world production of peppermint oil is about 8000 tonnes per year (Eccles, 1994). It is a popular medicinal plant in several

traditional systems of medicine. In Ayurveda, this is an important ingredient of several compound formulations used in management of gastro-intestinal and skin disorders. It is thought to be a natural hybrid between spearmint (*M. spicata* Linn. emend. Nathh.) and water mint (*M. aquatica* Linn), the latter itself being a hybrid of *M. longifolia* (Linn.) Huds. and *M. rotundifolia* (Linn.) Huds., so *M. piperita* is a triple hybrid (Fleming, 1998; Wealth of India – Raw Materials, 1962).

The plant is a strongly scented, perennial, glabrous, herb 30-90 cm in height. The square stems are usually



Medicinal uses

Peppermint oil vapour is used as an inhalant for respiratory congestion. Peppermint tea is used to treat coughs, bronchitis, and inflammation of the oral mucosa and throat. It has traditionally been used to treat a variety of digestive complaints such as colic in infants, flatulence, diarrhoea, indigestion, nausea and vomiting, morning sickness and anorexia, and as a spasmolytic to reduce gas and cramping. The oil is also used in toothache, rheumatism, muscular pains and to relieve menstrual cramps. *M. piperita* is currently used to treat irritable bowel syndrome, Crohn's disease, ulcerative colitis, gallbladder and biliary tract disorders, and liver complaints (Fleming, 1998; Tyler, 1992; Robbers & Tyler, 1999).

Chemical composition

The major constituent reported is volatile oil of which the principal component is usually (–) menthol, together with menthol stereoisomers such as (+) neomenthol and (+) isomenthol. Other monoterpenes include menthone (10-40%), menthyl acetate (1-10%), menthofuran (1-10%), cineol (eucalyptol, 2-13%) and limonene (0.2-6%). Monoterpenes like pinene, terpinene, myrcene, β -caryophyllene, piperitone, piperitenone, piperitone oxide, pulegone, eugenol, menthone, isomenthone, carvone, cadinene, dipentene, linalool, α -phellendrene, ocimene, sabinene, terpinolene, γ -terpinene, fenchone, *p*-menthane and β -thujone are also present in small quantities (Baslas, 1977; Baslas & Saxena, 1984).

About 85 constituents of the oil have been identified and a further 40 are unidentified. The composition is considerably influenced by environmental factors like temperature, photoperiod, nutrition, salinity, water stress, plant age, harvesting and planting time (Chales *et al*, 1990). Flavanoids like luteolin and its 7-glucoside (cynaroside), menthoside, isorhoifolin and others including a number of highly oxygenated flavones have been reported (Orani *et al*, 1991; Rastogi *et al*, 1990).

Phenolic acids including caffeic, chlorogenic and rosmarinic acid and "Pseudotannins" derived from them are reported to be present. Triterpenes in small amounts including squalene, α -amyrin, urosolic acid and sitosterol and other constituents, azulene and minerals are also reported (Lucida & Wallace, 1998).

Peppermint oil possesses greater antihydrolytic effect than the commercial preservative such as butylated hydroxytoluene (Singh *et al*, 1998).

Pharmacokinetics

In a pharmacokinetic study of treatment with peppermint oil in enteric-coated capsules (containing 91-97 mg menthol) or soft gelatin capsules urinary excretion of menthol glucuronide represented 17% of the dose from two coated capsules and 29% of the dose from the capsules 24 hr after administration (Somerville *et al*, 1984). When an enteric-coated capsule containing 130 mg peppermint oil was fed to four subjects, the average 14 hr urinary excretion of menthol glucuronide was 40% of the dose (range, 20-64%) (Kaffenberger & Doyle, 1990). The major metabolite found in the

bile was menthol glucuronide; various oxidation products were also found in the urine (Yamaguchi *et al*, 1994). The oxidation products of menthol include *para*-menthane-3,8-diol, *para*-menthane-3,9-diol, and 3,8-dihydroxy-*para*-menthane-7-carboxylic acid. Additional oxidation metabolites that have been identified include a primary alcohol, a triol, and hydroxy acids (Madyastha & Srivatsan, 1988; Yamaguchi *et al*, 1994). When 750 mg (–)-menthol was given orally to three human volunteers, followed by oral or intravenous administration of 200 mg [6-13C]-glucuronolactone or [6-13C]-sodium glucuronate, menthyl glucuronide was excreted for two days, in average daily yields ranging from approximately 27 to 84% (Eisenberg *et al*, 1955).

Pharmacological effects

Respiratory

Inhibition of respiration — Menthol stimulates upper airway cold receptors that causes a reflex inhibition of respiration and inhibits upper airway accessory respiratory muscle activity. In guinea pigs and dogs, but not cats, menthol causes reflex inhibition of respiration (Orani *et al*, 1991; Davies & Eccles, 1987).

Nasal decongestant — In cats and dogs, vaporized menthol stimulated cold receptors in the respiratory tract (Schafer *et al*, 1986). In a double blind randomized controlled trial, 62 subjects with nasal congestion secondary to common cold infections were given a lozenge containing 11 mg menthol or placebo. The subjects given the menthol reported a significant improvement in the



sensation of nasal airflow after ten minutes (Eccles *et al*, 1990).

Antitussive—In a randomized trial, 20 healthy subjects received a citric acid cough challenge every hour for five hours. Five minutes before each challenge the subjects inhaled either menthol in eucalyptus oil or one of two placebos (pine oil or air). Menthol inhalation caused a reduction in evoked cough when compared with either placebo (Morice *et al*, 1994).

Gastrointestinal/Hepatic disorders

Digestive aid—In a blinded controlled study, 20 healthy males (ages 21-23 and 34-35) and six subjects with non-obstructive dyspepsia were fed a radio labeled solid test meal with and without peppermint oil (25 ml of water with 0.2 ml of peppermint oil). After administration of peppermint oil, gastric emptying rate accelerated in both normal and patients with dyspepsia. None of the volunteers complained of any side effects (Dalvi *et al*, 1991).

Anti-emetic—In a placebo-controlled study of gynaecological surgery patients, there was a statistically significant effect of peppermint in reducing postoperative nausea (Tate, 1997).

Antispasmodic—Peppermint relaxes gastro-intestinal smooth muscle by reducing calcium influx in both guinea pig large intestine and rabbit jejunum (Hills & Aaronson, 1991; Taylor *et al*, 1983). Peppermint oil and menthol have calcium channel blocking activity in rat and guinea pig atrial and papillary muscle, rat brain synaptosomes, and chick retinal neurones (Taylor *et al*, 1983; Taylor, 1984).

In anesthetized guinea pigs, peppermint oil resolved a morphine-

induced spasm on the sphincter of Oddi (Giachetti *et al*, 1987).

In 20 subjects who were undergoing colonoscopy, administration of peppermint oil during the procedure relieved colon spasm within 30 seconds in each patient (Leicester & Hunt, 1982). Similarly, in a placebo controlled trial in six adults, injection of 0.2 ml peppermint oil suspension into the colon led to a statistically significant decrease in motor activity at two minutes and lasting 7-23 minutes (Duthie, 1981).

In a double blind, placebo-controlled randomized study of 141 patients receiving a Barium enema, those who had 40 ml of topical peppermint oil preparation added to the Barium suspension reported a significantly lower rate of residual spasm compared to placebo group (64% vs. 35%). In patients with diverticular disease, 72% were spasm-free, compared to 21% of diverticular disease patients in the placebo group. No adverse effects were reported (Sparks *et al*, 1995).

Irritable bowel syndrome (IBS)—In rat small intestine, peppermint oil at concentrations of 0.5 and 1 mg/ml inhibited enterocyte glucose uptake via a direct action at the brush border membrane. Inhibition of secretion by serosal peppermint oil is consistent with a reduced availability of calcium (Beesley *et al*, 1996).

A meta-analysis of four randomized controlled studies indicated that peppermint oil could be efficacious for the symptoms of IBS. However, it has been noted that methodological flaws in the studies prevented this recommendation beyond a reasonable doubt (Pittler & Ernst, 1998; Dew *et al*,

1984; Rees *et al*, 1979; Nash *et al*, 1986).

In two double blind, placebo-controlled crossover studies, 16 to 29 subjects with active IBS were given either enteric-coated peppermint oil (one or two 0.2 ml capsules three times daily) or placebo for three to four weeks. The peppermint oil capsules significantly increased the feeling of well being and decreased abdominal pain compared to placebo. There was no significant effect on stool frequency. The frequency of symptom-free days increased and severe symptoms decreased in the peppermint oil group but the data were not statistically significant. Two subjects developed heartburn (Dew *et al*, 1984; Rees *et al*, 1979).

In a double blind clinical trial, 34 patients with IBS in whom pain was a prominent symptom took two peppermint oil (0.2 mg) capsules or placebo three times daily for two and four weeks. The patients' assessment of their overall symptoms showed no significant difference between peppermint oil and placebo (Nash *et al*, 1986).

The enteric-coated peppermint capsules were found to dissolve in the colon and gelatin-coated peppermint capsules in the stomach of human volunteers. To be effective in the treatment of spastic colon syndromes, the oil must reach the colon in an unmetabolized state (Somerville *et al*, 1984).

In human volunteers, both enteric-coated (Enteroplant®) and non-enteric-coated preparations (a combination of peppermint oil 90 mg and 50 mg of caraway oil) showed a decrease in the number of contractions and contraction amplitudes during the various phases of the MMC (Migrating Motor Complex).



Non-enteric-coated preparations showed their effects mainly during the second MMC after administration. Enteric-coated and non-enteric-coated peppermint-caraway oil combinations are safe preparations, acting locally to cause smooth muscle relaxation (Micklefield *et al*, 2000).

Biliary disorders—In animal studies, flavanoids found to possess cholerectic effect (Lucida & Wallace, 1998). Menthol and related terpenes exert a cholerectic effect. Several clinical studies with the drug Rowachol® (a mixture of six cyclic monoterpenes: menthol, menthone, pinene, borneol, camphene, and cineol) have shown success in the treatment of patients with cholesterol stones in their gallbladders and bile ducts (Somerville *et al*, 1985; Ellis & Bell, 1981; Ellis *et al*, 1984; Doran *et al*, 1979).

In a controlled prospective double blind trial, 23 patients with cholesterol gallstones were treated with ursodeoxycholic acid (UDCA) (11.1 mg/kg per day) or Ursomenth, a combination of UDCA plus menthol (4.75 mg/kg per day). After 17 months, complete dissolution had occurred in 53% of the Ursomenth group, versus 38% of the UDCA group (Leuschner *et al*, 1988).

Skin and mucus membranes

Analgesic and coolant — Peppermint oil stimulates cold receptors on the skin and dilates blood vessels, causing a sensation of coldness and an analgesic effect. Menthol is a topical vasodilator that enhances the absorption of other topical skin medications. On hairless mice, menthol (1-5% w/v) enhances the absorption of cortisone,

mannitol, indomethacin, morphine hydrochloride and propranolol (Katayama *et al*, 1992; Morimoto *et al*, 1993; Kunta *et al*, 1997). In low concentrations, topical application of menthol causes a cooling sensation; while in high concentrations it causes irritation and local anaesthesia (Eccles, 1994).

In a three-fold crossover clinical trial on the arms of 15 healthy males, topical application of menthol-reduced histamine-induced itch (Kokate & Varma, 1970).

Local anaesthetic—Both the enantiomers of menthol (0.0001 mg/ml) drastically reduced the electrically evoked contractions of rat phrenic nerve hemidiaphragm while increases the number of stimuli in rabbit necessary to provoke the reflex in a dose dependent manner (Thorup *et al*, 1983a,b; Galeotti *et al*, 2001).

Anti-inflammatory

The ethanolic extract possesses anti-inflammatory effect in acute (xylene induced ear oedema) and chronic (cotton pellet granuloma) inflammation (Atta & Alkofahi, 1998).

Azulene found in oil of peppermint have shown to have anti-inflammatory effects in laboratory animals (Lucida & Wallace, 1998).

Antimicrobial

The peppermint oil exerts antidermatophytic activity against (+) and (–) strains of *Narinzia fulva* and *N. gypsea* (Gautam *et al*, 1980) and antibacterial activity against *Staphylococcus aureus*, *S.*

pyrogenes, *Escherichia coli*, *Bacillus subtilis* and *Proteus vulgaris* (Kokate & Varma, 1970; Sawhney *et al*, 1977). It possesses repellent activity against *Tribolium castaneum* and is moderately effective fumigant on both *Callosobruchus maculatus* and *T. castaneum* (Tripathi *et al*, 2000). Moderate antimyotic property against *Aspergillus fumigatus*, *Candida albicans*, *Geotrichum candidum* and *Rhodotarula rubra* (Blaszcy *et al*, 2000), *Phytophthora cinnamoni*, *Pyrenochaeta lycopersici* and *Verticillium dahliae* (Giamperi *et al*, 2002) has been reported. Peppermint oil showed antifungal activity against *Aspergillus niger*, *Alternaria alternata* and *Fusarium* sp. by agar well diffusion method (Aqil *et al*, 2000).

Radioprotective

M. piperita leaf extract pre-treatment provides protection against radiation induced alterations in intestinal mucosa of swiss albino mice. A significant promotion was obtained in various hematological parameters and modulates activity of serum phosphates in albino mice against γ -radiation (Samarth *et al*, 2001, 2002; Tripathi *et al*, 1999).

Toxicity and contraindications

Potentially toxic compounds in peppermint are pulegone and menthol. Pulegone, the toxic compound in pennyroyal, is also found in peppermint in much smaller proportions. In rats, doses of 80 and 160 mg of pulegone for 28 days caused atonia, weight loss,



decreased blood creatinine content, and histopathological changes in the liver and the white matter of the cerebellum. Menthol causes hepatocellular changes in rats. In rats, peppermint oil caused cyst-like changes in the white matter of the cerebellum and nephropathy at doses of 40-100 mg/kg per day for 28-90 days (Spindler & Madson, 1992; Thorup *et al*, 1983a,b).

Direct application of peppermint oil to the nasal area or chest to infants should be avoided because of the risk of apnoea, laryngeal and bronchial spasms, acute respiratory distress with cyanosis and respiratory arrest (Blake *et al*, 1993).

Acute toxicity

Adverse reactions to enteric-coated peppermint oil capsules are rare but can include hypersensitivity reaction, contact dermatitis, abdominal pain, heart burn, perianal burning, bradycardia and muscle tremor (Rees *et al*, 1979; Nash *et al*, 1986; Weston, 1987; Bromm *et al*, 1995). The excessive inhalation of mentholated preparation has caused reversible nausea, anorexia, cardiac problems, ataxia, and other CNS problems, which are thought to be due to the presence of volatile oils. There is a case report of a 13-year-old boy who, following inhalation of 5 ml of Olbas oil (containing 200 mg menthol) instead of the recommended few drops, experienced ataxia, confusion, euphoria, nystagmus, and diplopia (O'Mullane *et al*, 1982).

Chronic toxicity

In rat studies, chronic exposure to high concentrations of menthol vapour

has shown no gross toxic effect (Eccles, 1994). Peppermint oil is contraindicated in obstruction of the bile ducts, gallbladder inflammation, and severe liver damage (Lucida & Wallace, 1998). Patients with achlorhydria should use peppermint oil only in enteric-coated capsules (Rees *et al*, 1979). Patients with GI reflux should use caution because peppermint may make GI reflux symptoms worse. Caution is recommended in patients with hiatal hernia, kidney stones, or GI reflux.

Conclusion

It can be concluded that with its vast and diversified pharmacological potentials *M. piperita* has a strong future in the world market. This plant is now well-acclimatized and cultivated in different parts of India and enjoys a strong export potential for the volatile oil extracted from it. Various formulations like Pudín Hara® for gastro-intestinal disturbances like flatulence and indigestion and Itch-gard® for skin disorders are available in the market.

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Adulterants of Peppermint oil

Total amount of menthol is the most important indication to examine the peppermint oil. The English oil contains 60 to 70 per cent of menthol, the Japanese oil containing 85 per cent, and the American about 50 per cent. The odour and taste also afford a good indication of the quality of the oil, and help to distinguish between English, American and Japanese oils. The oils produced from *M. arvensis var. piperascens*, *M. arvensis var. glabrata* and *M. incana* are greatly inferior to those distilled from *M. piperita*, but have the advantage of containing a large proportion of menthol. *M. arvensis* (Hindi-*Pudina*), has to be carefully removed from the fields of peppermint to avoid spoiling of the flavour of the peppermint oil when the herb is distilled.

Adulteration of American Peppermint oil with dementholized Japanese oil, known as menthene, which is usually cheaper than American oil, is frequently practiced. Camphor oil, Cedarwood oil and oil of African Copaiba are also occasionally used as adulterants of Peppermint oil. Some times the oil is adulterated with one-third part of rectified spirit, which may be detected by the milkiness produced when the oil is agitated by water. Oil of Rosemary and oil of Turpentine are occasionally used for the same purpose. If the oil contains turpentine it will explode with iodine. If quite pure, it dissolves in its own weight of rectified spirits of wine. (<http://www.botanical.com/botanical/mgmh/m/mints-39.html>).