The Longwood Herbal Task Force

(http://www.mcp.edu/herbal/default.htm) and

The Center for Holistic Pediatric Education and Research

(http://www.childrenshospital.org/holistic/)

Peppermint *(Mentha piperita)*

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Principal Proposed Uses: Irritable bowel syndrome, other digestive disorders, decongestant, antitussive

Other Proposed Use: Topical treatment of headaches

Overview

Peppermint 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. Peppermint is on the FDA's GRAS (generally recognized as safe) list and whole herb peppermint has few side effects. However, peppermint oil can cause heartburn or perianal irritaiton, and is contraindicated in patients with bile duct obstruction, gallbladder inflammation and severe liver damage, and caution should be used 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 apnea.

Historical and Popular Uses

Peppermint's Latin name, *Mentha piperita*, comes from the Greek *Mintha*, the name of a mythical nymph thought to have metamorphosed into the plant, and the Latin *piper*, meaning pepper. It is one of the world's oldest medicinal herbs, and is used in both Eastern and Western traditions. Ancient Greek, Roman, and Egyptian cultures used the herb in cooking and medicine.

Peppermint is currently one of the most economically important aromatic and medicinal crops produced in the U.S. The world production of peppermint oil is about 8000 tons per year[1]. Peppermint leaf and oil are used for folk medicine, as flavoring agents, and in cosmetic and

pharmaceutical products throughout the world[2]. Peppermint oil is the most extensively used of all the volatile oils[3]

Peppermint is taken internally as a tea, tincture, oil, or extract, and applied externally as a rub or liniment. Herbalists consider peppermint an astringent, antiseptic, antipruritic, antispasmodic, antiemetic, carminative, diaphoretic, mild bitter, analgesic, anticatarrhal, antimicrobial, rubefacient, stimulant, and emmenagogue[4, 5]. Peppermint oil vapor 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, diarrhea, indigestion, nausea and vomiting, morning sickness and anorexia, and as a spasmolytic to reduce gas and cramping. Peppermint is currently used to treat irritable bowel syndrome, Crohn's disease, ulcerative colitis, gallbladder and biliary tract disorders, and liver complaints[6, 7]. Peppermint oil is used to relieve menstrual cramps[8]. Peppermint oil is used externally for neuralgia, myalgia, headaches, migraines and chicken pox[5, 6].

Botany

Medicinal species: Mentha piperita. It is thought to be a natural hybrid between spearmint *(Mentha spicata)* and water mint *(Mentha aquatica)*[2, 9].

Common names: Peppermint, lamb mint, brandy mint, balm mint, curled mint, amenta, lammint

Botanical family: Leguminosae or pea

Plant description: The plant is a perennial, 50-60 cm (3-4 feet) high. The square stems are usually reddish-purple and smooth[2]. The leaves are short, oblong-ovate and serrate[7]. The flowers are purple-pinkish and appear in the summer months. The plant has runners above and below ground.

Where it's grown: Europe, Canada, and the US.

Biochemistry

Peppermint: Potentially Active Chemical Constituents

- Volatile oils: menthol, menthone, menthyl acetate, neomenthol, isomenthone, menthofuran, limonene, pulegone, alpha and beta pinene, and trans-sabinene hydrate[7]
- Monoterpenes
- Caffeic acids
- Flavonoids
- Tannins

Peppermint contains about 1.2-1.5% *essential oil*. The volatile oil, also known as *menthae piperitae aetheroleum*, contains 30-70% free menthol and menthol esters[10] and more that 40 other compounds. The principal components of the oil are menthol (29%), menthone (20-30%), and menthyl acetate (3-10%). Pharmaceutical grade oil, produced by distilling the fresh aerial parts of the plant at the beginning of the flowering cycle, is standardized to contain no less than 44% menthol, 15-30% methone, and 5% esters, in addition to various terpenoids. Other compounds found in the peppermint are flavonoids (12%), polymerized polyphenols (19%), carotenes, tocopherols, betaine, and choline[3].

Menthol is the primary component of the essential oil of peppermint[2]. It occurs naturally as a colorless crystal or powder. Menthol is mostly responsible for the spasmolytic nature of peppermint. It stimulates bile flow, reduces the tone in the esophageal sphincter, facilitates belching, and has antibacterial properties[7, 8]. It is used as a local anesthetic agent in cold and cough preparations (Vicks Vapo-Rub®, lozenges and syrups) and in liniments for insect bites, eczema, poison ivy, hemorrhoids, toothaches, and musculoskeletal pain (Ben Gay®)[3, 9]. It is used as an antitussive in chest rubs or inhaled as a steam vapor. Its use dates back to 1890, when it was developed as a topical rub to treat whooping cough. It is thought to provide a local anesthetic action on the lungs and throat, suppressing the cough reflex[11].

Experimental Studies

Peppermint: Potential Clinical Benefits

1. Cardiovascular: Vasodilation
2. Pulmonary: Inhibition of respiration, nasal decongestant, antitussive
3. Renal and electrolyte balance: none
4. Gastrointestinal/hepatic: Digestive aid, antiemetic, antispasmodic, irritable bowel syndrome, cholesterol gallstones
5. Neuro-psychiatric: Headaches
6. Endocrine: none
7. Hematologic: none
8. Rheumatologic: none
9. Reproductive: none
10. Immune modulation: Anti-inflammatory
11. Antimicrobial: Antiviral, antibacterial, antifungal
12. Antineoplastic: none
13. Antioxidant: none
14. Skin and mucus membranes: Analgesic and coolant
15. Other/miscellaneous: none

1. **Cardiovascular:** Vasodilation
   i. *In vitro data:* In rat and guinea pig atrial and papillary muscle, both menthol and peppermint demonstrated Ca^{2+} channel blocking properties[12].
   ii. *Animal data:* In rabbits, topical application of menthol led to vasodilation of blood vessels in the ear. Menthol, thymol, and methyl salicylate caused decreases in blood pressure but had no effects on respiration, heart rate, or blood flow in the femoral artery or gastrocnemius muscle[13].
   iii. *Human data:* Peppermint has traditionally been used as a rubefacient. No clinical studies.
2. **Pulmonary:** Inhibition of respiration, nasal decongestant, antitussive

a. Inhibition of respiration: Stimulation of upper airway cold receptors causes a reflex inhibition of respiration and inhibits upper airway accessory respiratory muscle activity[14]. Menthol stimulates the same reflex inhibition of respiration in humans[15].

   i. *In vitro data:* none

   ii. *Animal data:* In guinea pigs and dogs, but not cats, menthol causes reflex inhibition of respiration[14, 16, 17].

   iii. *Human data:* In a clinical study of 44 newborn premature infants with gestational ages of 19-37 weeks, administration of menthol vapors from an open container of menthol crystals 1 cm from the nostril resulted in brief periods of apnea or a drop in respiratory rate in 43% of the infants[18].

b. Nasal decongestant: Although menthol is widely used in medications to relieve common cold and flu symptoms such as nasal congestion and cough, studies show that peppermint and menthol do not have nasal decongestant properties. However, menthol does cause subjective improvement in nasal breathing.

   i. *In vitro data:* none

   ii. *Animal data:* In animals, topical application of menthol to nasal mucosa leads to nasal congestion[19]. In cats and dogs, vaporized menthol stimulated cold receptors in the respiratory tract[20, 21].

   iii. *Human data:* Although nasal decongestion is not objectively decreased by menthol, there is a subjective improvement in the sensation of easier breathing by subjects[22]. This is thought to be due to menthol's stimulation of cold receptors served by the trigeminal nerve in the nose, the vapor action on the sensory nerve endings of the nasal mucosa, and stimulation of the major palatine nerve[1, 22, 23].

   In two studies, l-menthol significantly enhanced the subjective sensation of nasal airflow compared to d-isomenthol, and d-neomenthol. It was l-menthol's specific action on nasal sensory nerve that caused the subjective enhancement of nasal airflow, not its peppermint smell[24, 25].

   In 31 normal volunteers, five minutes of exposure to menthol vapor did not decrease nasal airflow resistance, but it did increase the sensation of nasal airflow and cause a cooling effect in the majority of the subjects[26]. In another study of 11 normal

adult subjects, nasal inhalation of l-menthol stimulated cold receptors in the upper airway, reducing the sensation of respiratory discomfort associated with loaded breathing. In both flow-resistive loading and elastic loading, inhalation of l-menthol significantly reduced the sensation of respiratory discomfort without significantly changing breathing pattern or ventilation[27].

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. Nasal resistance to airflow significantly increased in both groups over the two-hour experiment, while the subjects given the menthol reported a significant improvement in the sensation of nasal airflow after ten minutes[28, 29].

In a clinical trial, 30 subjects were exposed to normal air or the vapors of 1 g menthol crystals, 1 g camphor crystals, or 10 ml of eucalyptus for five minutes, and asked to exercise for five minutes. Inhalation of camphor, eucalyptus or menthol had no effect on nasal airflow resistance (NAR), but exercise decreased NAR. The majority of the subjects reported a cold sensation in the nose and a sensation of improved airflow when exposed to the camphor, eucalyptus or menthol vapor[30].

c. Antitussive

i. *In vitro data:* Menthol vapor lowered the surface tension on synthetic surfactant films. The authors theorized that it may affect lung surface tension and lung function[31].

ii. *Animal data:* In guinea-pigs who received a cough-inducing citric acid challenge, menthol vapor significantly decreased cough in a dose-dependent fashion[32].

iii. *Human data:* 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[33].

A mixture of aromatic oils including menthol applied as a chest rub significantly reduced citric acid-induced cough for 30 and 60 minutes after administration[34].

In a four-week randomized placebo controlled study, 23 subjects with chronic mild asthma received either nebulized menthol (10 mg twice a day) or placebo. There were no significant differences in vital capacity, forced expiratory volume in one

second, or change in peak expiratory flow rate, between the placebo group and the menthol group. The menthol group had a decrease in peak expiratory flow rate, had fewer wheezing episodes and used fewer bronchodilators[35].

3. **Renal and electrolyte imbalance:** none
4. **Gastrointestinal/hepatic:** Digestive aid, antiemetic, antispasmodic, irritable bowel syndrome, bilary disorders
   a. Digestive aid
      i. *In vitro data:* none
      ii. *Animal data:* none
      iii. *Human data:* In a blinded controlled study, 20 healthy males (ages 21-23 and 34-35) and six subjects with non-obstructive dyspepsia were fed a radiolabeled 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[36].
   b. Antiemetic
      i. *In vitro data:* none
      ii. *Animal data:* none
      iii. *Human data:* In a placebo-controlled study of gynecological surgery patients there was a statistically significant effect of peppermint in reducing postoperative nausea[37].
   c. Antispasmodic
      i. *In vitro data:* Peppermint relaxes gastrointestinal smooth muscle by reducing calcium influx in both guinea pig large intestine and rabbit jejunum[38-40]. 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[12, 39, 41, 42].
      ii. *Animal data:* In anesthetized guinea pigs, peppermint oil resolved a morphine-induced spasm on the sphincter of Oddi[43].
      iii. *Human data:* In 20 subjects who were undergoing colonoscopy, administration of peppermint oil during the procedure relieved colon spasm within 30 seconds in each patient[44]. 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[45].

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[46].

d. Irritable bowel syndrome (IBS): Enteric-coated capsules of peppermint oil are used to treat IBS and spastic colon.

i. *In vitro data:* none

ii. *Animal data:* 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[47].

iii *Human data:* Of eight studies, five showed a positive effect of peppermint on IBS symptoms and three showed no effect.

A meta-analysis of five randomized controlled studies indicated that peppermint oil could be efficacious for the symptoms of IBS. However, the authors noted that methodological flaws in the studies prevented this recommendation beyond a reasonable doubt[48-53].

In an open multicenter trial, 50 subjects suffering from IBS received three peppermint oil capsules (0.2 ml) 30 minutes before each meal daily for four weeks. There was a statistically significant decrease in signs and symptoms[54].

In a one-month prospective, randomized, double blind, placebo-controlled trial, 110 outpatients with symptoms of IBS (66 men and 44 women, ages 18–70) took either Colpermin® (187 mg enteric-coated peppermint oil in a thixotropic gel) three to four times daily before meals or placebo. There was a statistically significant improvement in abdominal pain, distention, stool frequency and consistency, and flatulence in the Colpermin group compared to the placebo group. One patient in the peppermint oil

group reported heartburn (because of chewing the capsules) and one developed a mild transient skin rash[55].

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[49, 52].

In a double-blind crossover study, 40 patients with IBS received one to two capsules (0.2 ml peppermint oil, 0.2 mg hyoscyamine, or placebo) three times daily for two weeks. Treatment with peppermint oil tended to have a more pronounced effect on symptoms than placebo or hyoscyamine, but this was not statistically significant[51].

In a double-blind, randomized, placebo-controlled, multicenter trial, 39 patients with non-ulcerative dyspepsia received Enteroplant® (an enteric-coated capsule with 90 mg peppermint oil and 50 mg caraway oil) or placebo three times daily for four weeks. Eighty-nine percent of the subjects noted improvement in pain intensity, compared to 40% in the placebo group. In the peppermint/caraway group, improvement of secondary symptoms such as the sensation of pressure, heaviness, tension, fullness, eructation and flatulence was statistically significant compared to the placebo group. Four subjects taking the Entroplant noted substernal burning, belching, and nausea[50].

In a double-blind, placebo-controlled crossover trial, 25 subjects with IBS were given enteric-coated peppermint oil capsules (0.2 ml) three times daily for four weeks and then were changed to placebo for four weeks. There was a small but significant increase in stool frequency with peppermint. There was no significant change in scores for severity of symptoms or specific symptoms such as urgent defecation, pain, bloating or the sense of complete evacuation. Three subjects left the study due to perianal burning and one patient due to heartburn. Compliance was reported to be poor[56].

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[53].

In human volunteers, enteric-coated peppermint capsules were found to dissolve in the colon and gelatin-coated peppermint capsules to dissolve in the stomach. To be effective in the treatment of spastic colon syndromes, the oil must reach the colon in an unmetabolized state[57].

e. Biliary disorders

i. *In vitro data:* none

ii. *Animal data:* In animal studies, peppermint enhanced bile production[58]. Menthol inhibited hepatic S-3-hydroxy-3- methylglutaryl-CoA reductase activity in animal studies[58-60]

iii. *Human data:* Menthol and related terpenes exert a choleretic 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[61-64].

In a controlled prospective double blind trial, 23 patients with cholesterol gallstones were treated with ursodeoxy-cholic 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[65].

5. **Neuro-psychiatric:** Headaches

i. *In vitro data:* Peppermint oil blocks smooth muscle contraction induced by serotonin and substance P[58].

ii. *Animal data:* In frogs, menthol noncompetitively blocked neuromuscular transmission[66].

iii. *Human data:* In a double blind, placebo-controlled, randomized crossover study, 32 healthy subjects underwent artificial painful stimulation and received four different topical test preparations: a) peppermint and eucalyptus oil with ethanol, b) peppermint

with ethanol, c) eucalyptus with ethanol, or d) ethanol alone. The combination of peppermint oil, eucalyptus oil and ethanol inproved cognitive performance and had a muscle relaxing and mentally relaxing effect, but had little influence on pain sensitivity. Peppermint oil and ethanol exerted a significant analgesic effect and reduction in sensitivity to headache[67].

In a double blind, placebo-controlled crossover study, 41 male and female subjects (18 to 65 years old) with tension headaches were treated with two capsules of acetaminophen (1000 mg) or placebo and topical peppermint oil or topical placebo solution. Compared to topical placebo, 10% peppermint oil in ethanol solution significantly reduced the clinical headache intensity within 15 minutes for over an hour. There were no reported adverse events[68].

6. **Endocrine function:** none
7. **Hematologic:** Iron deficiency anemia
   i. In *vitro data:* none
   ii. *Animal data:* In rats, peppermint extract increased the intestinal absorption of iron[69].
   iii. *Human data:* none
8. **Rheumatologic:** none
9. **Reproductive:** none
10. **Immune modulation:** Anti-inflammatory
    i. *In vitro data:* In LPS-stimulated monocytes from healthy volunteers, l-menthol had an anti-inflammatory effect on IL-1 beta production[70]. In rat peritoneal mast cells, 1-menthol, menthone, and 1,8-cineole suppressed antigen-induced histamine release[71].
    ii. *Animal data:* In guinea pigs, intraperitoneal administration of menthol inhibited homologous passive cutaneous anaphylaxis (PCA) mediated by IgE antibody[71].
    iii. *Human data:* none
11. **Antimicrobial:** Antiviral, antibacterial, antifungal
    a. Antiviral
       i. *In vitro data:* Peppermint has significant antiviral activity[72]. Menthol is virucidal against *Influenza*, *Herpes* and other viruses *in vitro*. Aqueous extracts of peppermint

leaves were antiviral against *Influenza A, Newcastle disease virus, Herpes simplex virus,* and *Vaccinia virus* in egg and cell-culture systems[73].

ii. *Animal data:* none

iii. *Human data:* none

b. Antibacterial

i. *In vitro data:* Peppermint oil and menthol have moderate antibacterial effects against both Gram-positive and Gram-negative bacteria[74-78]. Peppermint extracts are bacteriostatic against *Streptococcus thermophilus* and *Lactobacillus bulgaricus*[79]. Menthol is bactericidal against *Staphylococcus pyogenes, S. aureus, Streptococcus pyogenes, Serratia marcescens, Escherichia coli,* and *Mycobacterium avium*.

ii. *Animal data:* none

iii. *Human data:* none

c. Antifungal

i. *In vitro data:* Menthol and peppermint oil are fungicidal against *Candida albicans, Aspergillus albus* and dermatophytic fungi[74-76, 80].

ii. *Animal data:* none

iii. *Human data:* none

12. **Antineoplastic:** none

13. **Antioxidant:** none

14. **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[81].

i. *In vitro data:* none

ii. *Animal data:* 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[82-84].

iii. *Human data:* Menthol moderates oral sensations of warmth and coldness[85, 86]. In low concentrations, topical application of menthol causes a cooling sensation, while in high concentrations it causes irritation and local anesthesia[87].

Thirty-one young adults given an oral .02% menthol aqueous solution for five seconds experienced a sensation of both warmth and coolness[88].

In a clinical placebo-controlled study, ten normal subjects had Eucalyptamint® applied to one anterior forearm and a placebo to the other. There was a statistically significant increase in cutaneous blood flow, muscle temperature, and skin temperature after the application of Eucalyptamint, with the effects lasting up to 45 minutes[89].

In a three-fold crossover clinical trial on the arms of 15 healthy males, topical application of menthol reduced histamine-induced itch[90]. However, in a clinical trial in 18 healthy subjects, menthol did not affect histamine-induced itch or pain sensation[91].

15. **Other/miscellaneous:** none

Toxicity and Contraindications

All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, pharmaceuticals, etc. This is particularly concerning with imports from developing countries.

Furthermore, allergic reactions can occur to any natural product in sensitive persons.

Allergic reactions to peppermint have been reported.

Potentially toxic compounds in peppermint: Pulegone, 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 pulgeone 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[92]. 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[93, 94].

Acute toxicity: Adverse reactions to enteric coated peppermint oil capsules are rare but can include hypersensitivity reaction, contact dermatitis, abdominal pain, heartburn, perianal burning, bradycardia and muscle tremor[3, 52, 56, 57, 95-100].

Inhalation of menthol can cause apnea and larygoconstriction in susceptible individuals[58]. In one case series, 12 patients noted contact sensitivity to menthol and peppermint with oral symptoms including burning mouth syndrome, recurrent oral ulceration, or a lichenoid reaction[101].

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[102]. 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[102].

Chronic toxicity: In rat studies, chronic exposure to high concentrations of menthol vapor have shown no gross toxic effects[1]. There are no chronic toxicity studies in humans.

Limitations during other illnesses or in patients with specific organ dysfunction: Peppermint oil is contraindicated in obstruction of the bile ducts, gallbladder inflammation, and severe liver

damage[6]. Patients with achlorhydria should use peppermint oil only in enteric coated capsules[52]. 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.

Interactions with other herbs or pharmaceuticals: Unknown

Safety during pregnancy and/or childhood: Direct application of peppermint oil to the nasal area or chest to infants should be avoided because of the risk of apnea, laryngeal and bronchial spasms, acute respiratory distress with cyanosis and respiratory arrest[103, 104]. Several case reports of adverse effects of menthol in infants led to an international symposium in 1966 to debate the safety of menthol preparations. The conclusion of the symposium was that menthol products are safe to use in infants but that they should not be applied directly to the nostrils[11, 105].

There are reports that menthol can cause jaundice in newborn babies. In some cases this has been linked to a glucose 6-phosphatase dehydrogenase deficiency[106, 107].

There are no data available of the safety of peppermint in pregnancy.

Typical Dosages

Provision of dosage information does NOT constitute a recommendation or endorsement, but rather indicates the range of doses commonly used in herbal practice.
Doses are given for single herb use and must be adjusted when using herbs in combinations.
Doses may also vary according to the type and severity of the condition treated and individual patient conditions.

Example of typical adult dosages:

Tea/infusion: 1-2 teaspoons of dried leaf steeped in 8 ounces of water and taken as needed

Internal use of peppermint oil:

For digestive disorders: 0.2-0.4 ml 0 three times daily in dilute preparations or in suspension

For irritable bowel syndrome: 0.2-0.4 ml, three times daily in enteric coated capsules

As an inhalation: 3-4 drops added to hot water; or as lozenge containing 2-10 mg[58].

External use of peppermint oil: In dilute liquid or semi solid preparations as analgesic, anesthetic, or antipruritic (0.1-1.0% m/m), or as a counter-irritant (1.25-16 % m/m) rubbed onto the affected area[58] no more than 3-4 times a day.

Pediatric dosages: Unknown

Availability of standardized preparations: Yes

Dosages used in herbal combinations: Variable

REFERENCES

1. Eccles R. Menthol and related cooling compounds. J Pharm Pharmacol 1994; 46:618-30.
2. Foster S. Peppermint: Mentha piperita. American Botanical Council - Botantical Series 1996; 306:3 - 8.
3. Murray MT. The healing power of herbs : the enlightened person's guide to the wonders of medicinal plants. Rocklin, CA: Prima Pub., 1995:xiv, 410.
4. Hoffman D. The complete illustrated holistic herbal. Rockport, MA: Element Books Inc., 1996.
5. Bove M. An encyclopedia of natural healing for children & infants. New Canaan, CT: Keats Publishing, Inc., 1996.
6. Blumenthal M. The complete German Commission E monographs : therapeutic guide to herbal medicines. Austin: American Botanical Council, 1998.
7. Fleming T. PDR for herbal medicines. Montvale, NJ: Medical Economics Company, Inc., 1998.
8. Tyler VE. The honest herbal : a sensible guide to the use of herbs and related remedies. New York: Pharmaceutical Products Press, 1992:xviii, 375.
9. Peirce A. The American Pharmaceutical Association practical guide to natural medicines. New York: William Morrow and Company, Inc., 1999.
10. Anonymous. Peppermint. In: Dombek C, ed. Lawerence Review of Natural Products. St. Louis: Facts and Comparisons, 1990.
11. Robbers JE, Tyler VE. Tyler's Herbs of choice : the therapeutic use of phytomedicinals. New York: Haworth Herbal Press, 1999:x, 287.
12. Hawthorn M, Ferrante J, Luchowski E, Rutledge A, Wei XY, Triggle DJ. The actions of peppermint oil and menthol on calcium channel dependent processes in intestinal, neuronal and cardiac preparations. Alimentary Pharmacology & Therapeutics 1988; 2:101-18.
13. Futami T. [Actions and mechanisms of counterirritants on the muscular circulation]. Nippon Yakurigaku Zasshi 1984; 83:219-26.
14. Orani GP, Anderson JW, Sant'Ambrogio G, Sant'Ambrogio FB. Upper airway cooling and l-menthol reduce ventilation in the guinea pig. J Appl Physiol 1991; 70:2080-6.
15. De Cort S, al e. Cardiorespiratory effects of inhalation of L-menthol in healthy humans. J. Physiol 1993; 473:47.
16. Sant'Ambrogio FB, Anderson JW, Sant'Ambrogio G. Menthol in the upper airway depresses ventilation in newborn dogs. Respir Physiol 1992; 89:299-307.
17. Davies AM, Eccles R. Electromyographic responses of a nasal muscle to stimulation of the nasal vestibule in the cat. J Physiol (Lond) 1987; 391:25-38.
18. Javorka K, Tomori Z, Zavarska L. Protective and defensive airway reflexes in premature infants. Physiol Bohemoslov 1980; 29:29-35.
19. Fox N. Effect of camphor, eucalyptol and menthol on the vascular state of the mucousmenbrane. Archiv. Otolaryngol Head Neck Surg. 1027; 6:112-122.

20. Sant'Ambrogio FB, Anderson JW, Sant'Ambrogio G. Effect of l-menthol on laryngeal receptors. J Appl Physiol 1991; 70:788-93.
21. Schafer K, Braun HA, Isenberg C. Effect of menthol on cold receptor activity. Analysis of receptor processes. J Gen Physiol 1986; 88:757-76.
22. Naito K, Ohoka E, Kato R, Kondo Y, Iwata S. The effect of L-menthol stimulation of the major palatine nerve on nasal patency. Auris Nasus Larynx 1991; 18:221-6.
23. Naito K, Komori M, Kondo Y, Takeuchi M, Iwata S. The effect of L-menthol stimulation of the major palatine nerve on subjective and objective nasal patency. Auris Nasus Larynx 1997; 24:159-62.
24. Eccles R, Griffiths DH, Newton CG, Tolley NS. The effects of menthol isomers on nasal sensation of airflow. Clinical Otolaryngology & Allied Sciences 1988; 13:25-9.
25. Eccles R, al e. The effects of D and L Isomers of menthol upon nasal sensation of airflow. The Journal of Laryngology and Otology 1988; 102:506-508.
26. Eccles R, Jones AS. The effect of menthol on nasal resistance to air flow. J Laryngol Otol 1983; 97:705-9.
27. Nishino T, Tagaito Y, Sakurai Y. Nasal inhalation of l-menthol reduces respiratory discomfort associated with loaded breathing. Am J Respir Crit Care Med 1997; 156:309-13.
28. Eccles R, Jawad MS, Morris S. The effects of oral administration of (-)-menthol on nasal resistance to airflow and nasal sensation of airflow in subjects suffering from nasal congestion associated with the common cold. J Pharm Pharmacol 1990; 42:652-4.
29. Eccles R, Morris S, Jawad MS. The effects of menthol on reaction time and nasal sensation of airflow in subjects suffering from the common cold. Clin Otolaryngol 1990; 15:39-42.
30. Burrow A, Eccles R, Jones AS. The effects of camphor, eucalyptus and menthol vapour on nasal resistance to airflow and nasal sensation. Acta Otolaryngol (Stockh) 1983; 96:157-61.
31. Zanker KS, Tolle W, Blumel G, Probst J. Evaluation of surfactant-like effects of commonly used remedies for colds. Respiration 1980; 39:150-7.
32. Laude EA, Morice AH, Grattan TJ. The antitussive effects of menthol, camphor and cineole in conscious guinea-pigs. Pulm Pharmacol 1994; 7:179-84.
33. Morice AH, Marshall AE, Higgins KS, Grattna TJ. Effect of inhaled menthol on citric acid induced cough in normal subjects. Thorax 1994; 49:1024-1026.
34. Packman EW, London SJ. The utility of artificially induced cough as a clinical model for evaluating the antitussive effects of aromatics delivered by inunction. Eur J Respir Dis Suppl 1980; 110:101-9.
35. Tamaoki J, Chiyotani A, Sakai A, Takemura H, Konno K. Effect of menthol vapour on airway hyperresponsiveness in patients with mild asthma [see comments]. Respir Med 1995; 89:503-4.
36. Dalvi SS, Nadkarni PM, Pardesi R, Gupta KC. Effect of peppermint oil on gastric emptying in man: a preliminary study using a radiolabelled solid test meal [letter]. Indian Journal of Physiology & Pharmacology 1991; 35:212-4.
37. Tate S. Peppermint oil: a treatment for postoperative nausea. Journal of Advanced Nursing 1997; 26:543-9.

38. Hills JM, Aaronson PI. The Mechanism of Action of Peppermint Oil On Gastrointestinal Smooth Muscle an Analysis Using Patch Clamp Electrophysiology and Isolated Tissue Pharmacology in Rabbit and Guinea-Pig. Gastroenterology 1991; 101:55-65.
39. Taylor B. Inhibitory effect of peppermint oli on gastrointestinal smooth muscle. Gut 1983; 24:992.
40. Kolbel CB, Layer P. [Peppermint oil and the smooth muscles of the gastrointestinal tract]. [German]. Zeitschrift fur Gastroenterologie 1992; 30:885-6.
41. Hawthorn M, Ferrante J, Luchowski E, Rutledge A, Wei XY, Triggle DJ. The actions of peppermint oil and menthol on calcium channel dependent processes in intestinal, neuronal and cardiac preparations. Aliment Pharmacol Ther 1988; 2:101-18.
42. Taylor B. The mechanism of the inhibitory action of menthol on gut smooth muscle. British Journal of Surgery 1984; 71:902.
43. Giachetti D, al e. Pharmacological Activity of the Essential Oils on Oddi's Sphincter. Planta Medica 1987; 54:389-92.
44. Leicester RJ, Hunt RH. Peppermint oil to reduce colonic spasm during endoscopy [letter]. Lancet 1982; 2:989.
45. Duthie H. The effect of peppermint oil on colonic motility in man. British Journal of Surgery 1981; 68:820.
46. Sparks MJ, O'Sullivan P, Herrington AA, Morcos SK. Does peppermint oil relieve spasm during barium enema? British Journal of Radiology 1995; 68:841-3.
47. Beesley A, Hardcastle J, Hardcastle PT, Taylor CJ. Influence of peppermint oil on absorptive and secretory processes in rat small intestine. Gut 1996; 39:214-9.
48. Pittler MH, Ernst E. Peppermint oil for irritable bowel syndrome: a critical review and metaanalysis. Am J Gastroenterol 1998; 93:1131-5.
49. Dew MJ, Evans BK, Rhodes J. Peppermint oil for the irritable bowel syndrome: a multicentre trial. British Journal of Clinical Practice 1984; 38:394, 398.
50. May B, Kuntz HD, Kieser M, Kohler S. Efficacy of a fixed peppermint oil/caraway oil combination in non-ulcer dyspepsia. Arzneimittel-Forschung 1996; 46:1149-53.
51. Carling L, Svedberg L, Hultsen S. Short term treatment of the irritable bowel syndrome:a placebo controlled trial of peppermint oil againt hyoscyamine. Opusc Med 1989; 34:55-57.
52. Rees WD, Evans BK, Rhodes J. Treating irritable bowel syndrome with peppermint oil. Br Med J 1979; 2:835-6.
53. Nash P, Gould SR, Bernardo DE. Peppermint oil does not relieve the pain of irritable bowel syndrome. British Journal of Clinical Practice 1986; 40:292-3.
54. Fernandez F. mentha piperita en el tratamiento de sindrome de colon irritable. Invest Med Intr 1990; 17:42-46.
55. Liu JH, Chen GH, Yeh HZ, Huang CK, Poon SK. Enteric-coated peppermint-oil capsules in the treatment of irritable bowel syndrome: a prospective, randomized trial. Journal of Gastroenterology 1997; 32:765-8.
56. Lawson M, Knight R, Tran K. Failure of enteric coatd peppermint oil in the IBS: a randomized, double blind cross over study. Journal Gastroenterol Hepatol 1988; 3:235-238.

57. Somerville KW, Richmond CR, Bell GD. Delayed release peppermint oil capsules (Colpermin) for the spastic colon syndrome: a pharmacokinetic study. British Journal of Clinical Pharmacology 1984; 18:638-40.
58. Anonymous. Monographs on the medicinal uses of plants. Exeter: European Scientific Cooperative on Phytotherapy, 1997.
59. Clegg RJ, Middleton B, Bell GD, White DA. The mechanism of cyclic monoterpene inhibition of hepatic 3-hydroxy-3- methylglutaryl coenzyme A reductase in vivo in the rat. J Biol Chem 1982; 257:2294-9.
60. Clegg RJ, Middleton B, Bell GD, White DA. Inhibition of hepatic cholesterol synthesis and S-3-hydroxy-3-methylglutaryl-CoA reductase by mono and bicyclic monoterpenes administered in vivo. Biochem Pharmacol 1980; 29:2125-7.
61. Somerville KW, Ellis WR, Whitten BH, Balfour TW, Bell GD. Stones in the common bile duct: experience with medical dissolution therapy. Postgrad Med J 1985; 61:313-6.
62. Ellis WR, Bell GD. Treatment of biliary duct stones with a terpene preparation. Br Med J (Clin Res Ed) 1981; 282:611.
63. Ellis WR, Somerville KW, Whitten BH, Bell GD. Pilot study of combination treatment for gall stones with medium dose chenodeoxycholic acid and a terpene preparation. Br Med J (Clin Res Ed) 1984; 289:153-6.
64. Doran J, Keighley MR, Bell GD. Rowachol--a possible treatment for cholesterol gallstones. Gut 1979; 20:312-7.
65. Leuschner M, Leuschner U, Lazarovici D, Kurtz W, Hellstern A. Dissolution of gall stones with an ursodeoxycholic acid menthol preparation: a controlled prospective double blind trial. Gut 1988; 29:428-32.
66. Futami T. [Actions of counterirritants on the muscle contractile mechanism and nervous system]. Nippon Yakurigaku Zasshi 1984; 83:207-18.
67. Goebel H, Schmidt G, Soyka D. Effect of peppermint and eucalyptus oil preparations on neurophysiological and experimental algesimetric headache parameters. Cephalalgia 1994; 14:228-234.
68. Goebel H, Fresenius J, Heinze A, Dworschak M, Soyka D. Effectiveness of peppermint oil and paracetamol in the treatment of tension headache. [German]. Nervenarzt 1996; 67:672-681.
69. El-Shobaki F, Saleh Z, Saleh N. The effect of some beverage extracts on intestinal iron absorption. *Z Ernahrungswiss* 1990; 29:264-69.
70. Juergens UR, Stober M, Vetter H. The anti-inflammatory activity of L-menthol compared to mint oil in human monocytes in vitro: a novel perspective for its therapeutic use in inflammatory diseases. Eur J Med Res 1998; 3:539-45.
71. Arakawa T, Shibata M, Hosomi K, et al. Anti-Allergic Effects of Peppermint Oil Chicle and Jelutong. Journal of the Food Hygienic Society of Japan 1992; 33:569-575.
72. Kerman E, Kucera L. Antiviral substances in plants of the mint family. Peppermint and other mint plants. Proc SOc Exper Biol Med 1967; 124:874-5.
73. Herrmann EC, Jr., Kucera LS. Antiviral substances in plants of the mint family (labiatae). 3. Peppermint (Mentha piperita) and other mint plants. Proceedings of the Society for Experimental Biology & Medicine 1967; 124:874-8.

74. El-Kady IA, El-Maraghy SSM, Mostafa ME. Antibacterial and antidermatophyte activities of some essential oils from spices. Qatar University Science Journal 1993; 13:63-69.
75. Pattnaik S, Subramanyam VR, Kole C. Antibacterial and antifungal activity of ten essential oils in vitro. Microbios 1996; 86:237-46.
76. Pattnaik S, Subramanyam VR, Bapaji M, Kole CR. Antibacterial and antifungal activity of aromatic constituents of essential oils. Microbios 1997; 89:39-46.
77. Moleyar V, Narasimham P. Antibacterial activity of essential oil components. Int J of Food Microbiology 1992; 16:337 - 342.
78. Janssen AM, Chin NL, Scheffer JJ, Baerheim Svendsen A. Screening for antimicrobial activity of some essential oils by the agar overlay technique. Pharm Weekbl [Sci] 1986; 8:289-92.
79. Bayoumi S. Bacteriostatic Effect of Some Spices and Their Utilization in the Manufacture of Yoghurt. Chemie Mikrobiologie Technologie der Lebensmittel 1992; 14:21-26.
80. el-Naghy MA, Maghazy SN, Fadl-Allah EM, el-Gendy ZK. Fungistatic action of natural oils and fatty acids on dermatophytic and saprophytic fungi. Zentralblatt fur Mikrobiologie 1992; 147:214-20.
81. Anonymous. Peppermint: Drugdex Drug Evaluations, Micromedex Inc. Healthcare Series, 1999.
82. Katayama K, Takahashi O, Matsui R, et al. Effect of l-menthol on the permeation of indomethacin, mannitol and cortisone through excised hairless mouse skin. Chem Pharm Bull (Tokyo) 1992; 40:3097-9.
83. Morimoto Y, al e. A new enhacer-coenhancer system to increase skin permeation of morphine hydrochloride in vitro. Int. J. Pharm 1993; 91:9-14.
84. Kunta JR, Goskonda VR, Brotherton HO, Khan MA, Reddy IK. Effect of menthol and related terpenes on the percutaneous absorption of propranolol across excised hairless mouse skin. J Pharm Sci 1997; 86:1369-73.
85. Green BG. The sensory effects of l-menthol on human skin. Somatosens Mot Res 1992; 9:235-44.
86. Green BG. Menthol inhibits the perception of warmth. Physiol Behav 1986; 38:833-8.
87. Eccles R. Menthol and related cooling compounds. Journal of Pharmacy & Pharmacology 1994; 46:618-630.
88. Green B. Menthol modulates oral sensations of warmth and cold. Physiol Behav 1985; 35:427-434.
89. Hong CZ, Shellock FG. Effects of a topically applied counterirritant (Eucalyptamint) on cutaneous blood flow and on skin and muscle temperatures. A placebo- controlled study. Am J Phys Med Rehabil 1991; 70:29-33.
90. Bromm B, Scharein E, Darsow U, Ring J. Effects of menthol and cold on histamine-induced itch and skin reactions in man. Neurosci Lett 1995; 187:157-60.
91. Yosipovitch G, Szolar C, Hui XY, Maibach H. Effect of topically applied menthol on thermal, pain and itch sensations and biophysical properties of the skin. Arch Dermatol Res 1996; 288:245-8.
92. Thorup I, Wurtzen G, Carstensen J, Olsen P. Short term toxicity study in rats dosed with pulegone and menthol. Toxicology Letters 1983; 19:207-10.
93. Spindler P, Madsen C. Subchronic toxicity study of peppermint oil in rats. Toxicology Letters 1992; 62:215-20.
94. Thorup I, Wurtzen G, Carstensen J, Olsen P. Short term toxicity study in rats dosed with peppermint oil. Toxicology Letters 1983; 19:211-5.

95. Nash P, Gould SR, Bernardo DE. Peppermint oil does not relieve the pain of irritable bowel syndrome. Br J Clin Pract 1986; 40:292-3.
96. Wilkinson SM, Beck MH. Allergic contact dermatitis from menthol in peppermint. Contact Dermatitis 1994; 30:42-3.
97. Parys BT. Chemical burns resulting from contact with peppermint oil mar: a case report. Burns, Including Thermal Injury 1983; 9:374-5.
98. Weston CF. Anal burning and peppermint oil [letter]. Postgraduate Medical Journal 1987; 63:717.
99. Dooms-Goossens A, Degreef H, Holvoet C, Maertens M. Turpentine-induced hypersensitivity to peppermint oil. Contact Dermatitis 1977; 3:304-8.
100. Sainio EL, Kanerva L. Contact allergens in toothpastes and a review of their hypersensitivity. Contact Dermatitis 1995; 33:100-5.
101. Morton CA, Garioch J, Todd P, Lamey PJ, Forsyth A. Contact sensitivity to menthol and peppermint in patients with intra-oral symptoms. Contact Dermatitis 1995; 32:281-4.
102. O'Mullane NM, Joyce P, Kamath SV, Tham MK, Knass D. Adverse CNS effects of menthol-containing olbas oil [letter]. Lancet 1982; 1:1121.
103. Wyllie JP, Alexander FW. Nasal instillation of 'Olbas Oil' in an infant [letter]. Arch Dis Child 1994; 70:357-8.
104. Blake KD, Fertleman CR, Meates MA. Dangers of common cold treatments in children [letter] [published erratum appears in Lancet 1993 Mar 27;341(8848):842]. Lancet 1993; 341:640.
105. Dost S, Leiber B. Menthol and Menthol containig External Remedies. Use, Mode of Effect and Tolerance in Children. Stuttgart: George Thieme Verlag, 1967.
106. Olowe SA, Ransome-Kuti O. The risk of jaundice in glucose-6-phosphate dehydrogenase deficient babies exposed to menthol. Acta Paediatr Scand 1980; 69:341-5.
107. Familusi JB, Dawodu AH. A survey of neonatal jaundice in association with household drugs and chemicals in Nigeria. Ann Trop Paediatr 1985; 5:219-22.