Aetheroleum Menthae Piperitae

Definition

Aetheroleum Menthae Piperitae is the essential oil obtained by steam distillation of the fresh overground parts of *Mentha* × *piperita* L. (Lamiaceae) (*1–4*).

Synonyms

Mentha piperita (L.) Huds., *M. piperita* Stokes, *M. balsamea* Willd. (*5*, *6*).

Selected vernacular names

Amentha, american mint, balm mint, brandy mint, cabra-caa, curled mint, doun menta piperita, hierbabuena, hortela pimenta, Katzenkraut, lamb mint, la menta, lamint, menta piemonte, mentea peperina, mentha pepe, menthe, menthe anglaise, menthe poivrée, moto yuyo, nána, ni naa, ni'na el fulfully, pepermin, pepper mint, peppermint, Pfefferminze, Pfefferminzblätter, piperita, pudeena, pum hub, yerba mota (*5–7*).

Geographical distribution

Commercially cultivated in eastern and northern Europe and the United States of America, and is found in Africa (*1*, *5*, *8*, *9*).

Description

A perennial herb, 30–90 cm high. Stems square erect or ascending, branched, the upper portion always quadrangular. Leaves opposite, petiolate, ovate-oblong to oblong-lanceolate, serrate, pointed; dark green on the upper surface. Flowers purplish, occur in thick, terminal, spicoid racemes of verticillasters; each flower shows a tubular calyx with 5 sharp, hairy teeth, a purplish, irregular, 4-cleft corolla, 4 short stamens, a 4-celled ovary and a projecting style ending in a bifid stigma. Fruit consists of 4 ellipsoidal nutlets (*5*, *8*, *10*).

Plant material of interest: essential oil

General appearance

A colourless, pale yellow or pale greenish-yellow liquid (*1*, *2*).

Organoleptic properties

Odour: characteristic, penetrating; taste: characteristic, pungent, followed by a sensation of cold (*1*, *2*).

Microscopic characteristics

Not applicable.

Powdered plant material

Not applicable.

General identity tests

Thin-layer and gas chromatography for characteristic monoterpene profiles (*1*, *2*).

Purity tests

Microbiological

Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on quality control methods for medicinal plants (*11*).

Chemical

Acid value: not more than 1.4 (*1*, *2*).
Relative density: 0.900–0.916 (*1–3*).
Refractive index: 1.457–1.467 (*1–3*).
Optical rotation: –10° to –30° (*1–3*).
Solvent solubility: miscible with ethanol (96%), ether and methylene chloride (*1*, *2*).

Pesticide residues

The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*2*). For other pesticides, see the *European pharmacopoeia* (*2*), and the WHO guidelines on quality control methods for medicinal plants (*11*) and pesticide residues (*12*).

Heavy metals

For maximum limits and analysis of heavy metals, consult the WHO guidelines on quality control methods for medicinal plants (*11*).

Radioactive residues

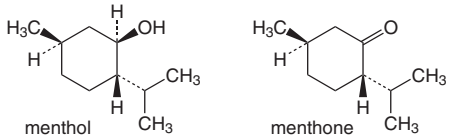
Where applicable, consult the WHO guidelines on quality control methods for medicinal plants (*11*) for the analysis of radioactive isotopes.

Chemical assays

The monoterpene content determined by gas chromatography should be 1,8-cineole (6–14%), limonene (1–5%), menthone (14–32%), menthofuran (1–9%), isomenthone (2–10%), menthyl acetate (3–5%), menthol (30–55%), pulegone (not more than 4.0%) and carvone (not more than 1.0%). The ratio of 1,8-cineole to limonene should be greater than 2.0 (*1*, *2*).

Major chemical constituents

The major constituents are menthol (30–55%) and menthone (14–32%). Menthol occurs mostly in the free alcohol form, with small quantities as the acetate (3–5%) and valerate esters. Other monoterpenes present include isomenthone (2–10%), 1,8-cineole (6–14%), α-pinene (1.0–1.5%), β-pinene (1–2%), limonene (1–5%), neomenthol (2.5–3.5%) and menthofuran (1–9%) (*2*, *6*, *9*, *13*, *14*). The structures of the major monoterpenes, menthol and menthone, are presented below.



Medicinal uses

Uses supported by clinical data

Internally for symptomatic treatment of irritable bowel syndrome (*15–20*), and digestive disorders such as flatulence and gastritis (*21–23*). Externally for treatment of myalgia and headache (*21*, *24–27*).

Uses described in pharmacopoeias and in traditional systems of medicine

Internally and externally for the symptomatic treatment of catarrh and coughs (*21*, *22*).

Uses described in folk medicine, not supported by experimental or clinical data

Treatment of dysentery, diabetes, dysmenorrhoea, fevers, jaundice and urinary infections (*7*).

Pharmacology

Experimental pharmacology

Antimicrobial activity

Aetheroleum Menthae Piperitae inhibited the growth in vitro of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Enterococcus faecalis* and *Escherichia*

coli (*28–30*), but did not affect the growth of *Bacillus cereus*, *Penicillium cyclopium* or *Aspergillus aegyptiacus* (*28*, *30*). The essential oil inhibited the growth in vitro of *Trichophyton equinum* and *T. rubrum* (at a concentration of 0.4 µg/ml) (*31*), *Aspergillus flavus*, *A. fumigatus* and *A. niger* (*32*).

Antispasmodic activity

The essential oil had smooth muscle relaxant activity in guinea-pig ileum (ED_{50} 26.0 mg/l) and trachea (ED_{50} 87.0 mg/l) in vitro (*33*), and inhibited electrically induced contractions of guinea-pig ileum (IC_{50} 0.176 mg/ml) in vitro (*34*). The essential oil decreased both the number and amplitude of spontaneous contractions, and inhibited spasms induced by barium chloride, pilocarpine and physostigmine in isolated segments of rabbit and cat ileum (inhibitory concentrations 0.05 µg/ml) (*35*). The essential oil (0.5 µmol/l) inhibited smooth muscle contractions of guinea-pig ileum in vitro induced by barium chloride, carbachol, histamine and potassium chloride (*36*). Both the essential oil and menthol act as calcium antagonists, since they inhibited the influx of calcium ions through smooth muscle of guinea-pig ileum and taenia coli isolated from humans (*36–39*). The essential oil and menthol inhibited smooth muscle contractions of guinea-pig ileum induced by potassium chloride (IC_{50} 28.1 and 21 µg/ml, respectively) and induced electrically (11.5 and 7.7 µg/ml, respectively) (*40*). Both also inhibited $^{45}Ca^{2+}$ uptake induced by potassium ion-dependent depolarization in brain synaptosomes and retinal neurons, and inhibited specific binding of [^{3}H]nitrendipine to ileal smooth muscle, synaptosomes and retinal neurons (*40*). The essential oil relaxed carbachol-contracted guinea-pig taenia coli (IC_{50} 22.1 µg/ml), and inhibited spontaneous contractions in isolated guinea-pig colon (IC_{50} 25.9 µg/ml) and rabbit jejunum (IC_{50} 15.2 µg/ml) (*41*). The essential oil also attenuated contractile responses in guinea-pig taenia coli induced by acetylcholine, histamine, serotonin (5-hydroxytryptamine) and substance P (*41*). Contraction of Oddi's sphincter induced by morphine was reversed after intravenous administration of the essential oil to guinea-pigs (1.0 mg/kg body weight). However, intravenous injection of the essential oil to guinea-pigs (25 mg/kg body weight) was found to increase spasms of the sphincter (*42*). Intragastric administration of the essential oil exhibited cholagogic activity in rats. This activity was attributed to (–)-menthol, a major constituent of the essential oil (*43*).

Antifoaming activity

The essential oil (0.1%) had antifoaming and carminative activity in vitro; however, the antifoaming effect was less than that observed with a combination of dimethicone and silica (*44*).

Toxicology

Intragastric administration of the essential oil (100 mg/kg body weight) to rats daily for 28 days induced histopathological changes (scattered cyst-like spaces)

in the white matter of the cerebellum. No behavioural or clinical symptoms due to the encephalopathy were observed (*45*).

Clinical pharmacology

Antispasmodic activity

Irritable bowel syndrome

Aetheroleum Menthae Piperitae is a carminative with antispasmodic activity that reduces intracolonic pressure (*22*). In an open study of 20 patients, an aqueous suspension of peppermint oil (British Pharmacopoeia Standard) injected along the biopsy channel of a colonoscope relieved colonic spasms within 30 seconds, allowing easier passage of the instrument or facilitating polypectomy (*16*). The essential oil relaxed the oesophageal sphincter when administered orally (15 drops [about 0.88 ml] oil in 30 ml water), decreasing the pressure differential between the stomach and oesophagus, and allowing reflux to occur (*46*).

In a double-blind, placebo-controlled, crossover clinical trial, 18 patients with symptoms of irritable bowel syndrome were treated daily with three enteric-coated gelatin capsules, each containing either 0.2 ml essential oil or a placebo for 3 weeks. Patients reported feeling significantly better while taking capsules containing the essential oil than when taking those containing placebo ($P < 0.01$) and considered the essential oil significantly better than the placebo in relieving abdominal symptoms ($P < 0.005$) (*19*). These results were confirmed in a later study (*15*). A matched-pair, placebo-controlled trial assessed the efficacy of the essential oil in the treatment of 40 patients with symptoms of irritable bowel syndrome. After 14 days of treatment with 1–2 enteric-coated gelatin capsules containing either 0.2 ml essential oil or a placebo three times daily, patients treated with the essential oil showed an increase in intestinal transit time, and subjective improvement in the feeling of fullness, bloating, bowel noises and abdominal pain, as compared with patients who received the placebo (*20*).

Administration of the essential oil to patients undergoing barium enemas relieved the associated colonic spasms (*47, 48*). However, two earlier trials failed to confirm the antispasmodic and analgesic activity of the essential oil in the treatment of irritable bowel syndrome (*49, 50*). A double-blind, placebo-controlled trial assessed the effects of peppermint oil in 34 patients with symptoms of irritable bowel syndrome. After 4 weeks of treatment with two capsules containing either 0.2 ml essential oil or a placebo three times daily, patients treated with the essential oil showed no significant difference in their overall symptoms, as compared with those who received the placebo treatment (*49*).

A prospective, randomized double-blind, placebo-controlled trial assessed the efficacy and safety of enteric-coated capsules containing 0.2 ml essential oil (one capsule 3–4 times daily for 1 month) for the symptomatic treatment of 110 patients with irritable bowel syndrome. After treatment, 79% of patients

in the treatment group and 43% of those in the placebo group experienced alleviation of severe abdominal pain; 83% of the treated group and 32% of the placebo group had reduced abdominal distention and a reduced stool frequency; 73% of the treated group and 31% of the placebo group had fewer bowel noises; and 79% of the treated group and 22% of the placebo group had less flatulence (*17*).

A review of five randomized, double-blind, placebo-controlled clinical trials assessed the efficacy of the essential oil in the symptomatic treatment of irritable bowel syndrome (*18*). By measuring the improvement of symptoms, the meta-analysis showed that two of the trials (*49*, *51*) did not show a significant difference between the essential oil and the placebo. However, three of the trials demonstrated significant improvements in symptoms after treatment with the essential oil (*15*, *19*, *52*). Although there were methodological flaws in most of the trials analysed, the analysis suggested that there was a significant positive effect of the essential oil ($P < 0.001$) on the symptomatic treatment of irritable bowel syndrome, as compared with the placebo (*18*).

Dyspepsia

A double-blind, placebo-controlled multicentre study involving 45 patients with non-ulcer dyspepsia assessed the change in pain intensity and Clinical Global Impression Scale after treatment with an enteric-coated capsule containing a combination of the essential oil (90 mg) and caraway oil (50 mg). After 4 weeks of treatment with the essential oil/caraway oil capsules (one capsule three times daily), 63% of patients were free of pain; 89.5% had less pain; and 94.5% showed improvements in the Clinical Global Impression Scale (*23*). In another study, oral administration of the essential oil (0.2 ml) delayed the gastric emptying time in healthy volunteers and in patients with dyspepsia (*53*).

Analgesic activity

A randomized, double-blind, placebo-controlled, crossover study assessed the efficacy of a combination product of the essential oil (peppermint oil) and Aetheroleum Eucalypti (eucalyptus oil) for headache relief in 32 patients. Five different preparations were used (all in 90% ethanol, to a final weight of 100 g): 10 g peppermint oil and 5 g eucalyptus oil; 10 g peppermint oil and traces of eucalyptus oil; traces of peppermint oil and 5 g eucalyptus oil; and traces of both peppermint oil and eucalyptus oil; or a placebo. The test preparations or placebo were applied topically to large areas of the forehead and temples, and the effects on neurophysiological, psychological and experimental algesimetric parameters were measured. The preparations improved cognitive performance, and induced muscle relaxation and mental relaxation, but had no effect on sensitivity to headache (*27*). A randomized, double-blind, placebo-controlled study assessed the efficacy of the essential oil in the treatment of 41 patients suffering from chronic tension headache. At each headache episode, patients were treated orally with two capsules of either paracetamol (1 g) or placebo, or exter-

nal application of 10% essential oil in ethanol, or a placebo solution. Compared with the placebo solution, the 10% essential oil preparation produced a significant ($P < 0.05$) reduction in headache intensity within 15 minutes. Paracetamol was also more effective than the oral placebo but did not differ significantly from topical treatment with the essential oil (*54*).

Contraindications

Preparations of Aetheroleum Menthae Piperitae should not be used internally by patients with inflammation of the gastrointestinal tract or gall bladder, or with impaired liver function (*21*). Hypersensitivity to the essential oil has been reported (*55–57*).

Warnings

Aetheroleum Menthae Piperitae preparations should not be applied to the face, especially the nose, of infants or young children (*21*, *22*). Keep out of reach of children.

Precautions

General

Patients with achlorhydria (due to medication with histamine H_2 receptor antagonists) should only use enteric-coated preparations (*19*, *58*).

Carcinogenesis, mutagenesis, impairment of fertility

Aetheroleum Menthae Piperitae was not mutagenic in the *Salmonella*/microsome assay using *S. typhimurium* strains TA98 and TA1535 (*59*).

Paediatric use

No information available. Therefore, Aetheroleum Menthae Piperitae should not be administered to children without medical supervision. (See also Contraindications and Warnings.)

Other precautions

No information available on precautions concerning drug interactions; drug and laboratory test interactions; teratogenic and non-teratogenic effects in pregnancy; or nursing mothers. Therefore, Aetheroleum Menthae Piperitae should not be administered during pregnancy or lactation without medical supervision.

Adverse reactions

Following internal administration of Aetheroleum Menthae Piperitae, gastric complaints have been reported in individuals sensitive to the essential oil (*21*). The use of non-enteric-coated essential oil preparations has occasionally caused

heartburn, especially in patients suffering from reflux oesophagitis (*58*). Skin rashes, headache, heartburn, perianal burning, bradycardia, muscle tremors and ataxia have been reported as rare side-effects, usually associated with overdose (*18*, *56*, *60–65*). Recurrent muscle pain has been associated with the ingestion of the essential oil (*66*). Following external administration of Aetheroleum Menthae Piperitae, skin irritation has been reported (*58*).

Dosage forms

Essential oil, concentrated peppermint emulsion, peppermint spirit and other galenic preparations (*1*, *21*). Store in a well-closed container, protected from light (*1*, *2*).

Posology

(Unless otherwise indicated)

Internal use

For digestive disorders, daily dosage: 0.2–0.4 ml essential oil three times daily in dilute preparations (*58*, *67*) or suspensions (*19*). By inhalation: 3–4 drops essential oil in hot water (*21*). Lozenges: 2–10 mg essential oil per lozenge (*58*).

For irritable bowel syndrome, daily dosage: 0.2–0.4 ml essential oil three times daily in enteric-coated capsules (*21*, *58*).

External use

5–20% essential oil in dilute, semisolid or oily preparations; 5–10% essential oil in aqueous-ethanol; nasal ointments containing 1–5% crude drug (*21*).

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