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FILE: ■Peppermint Oil (*Mentha x piperita*)
■Irritable Bowel Syndrome
■Gastrointestinal Ailments

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RE: Peppermint Oil Examined in the Treatment of Gastrointestinal Ailments

Grigoleit HG, Grigoleit P. Gastrointestinal clinical pharmacology of peppermint oil. *Phytomed.* 2005;12:607-611.

Peppermint (*Mentha x piperita*) oil is often used in aromatherapy and as an external topical treatment for arthritis and muscle pain. Menthol and other terpenes are the main chemical constituents of peppermint oil. In herbal medicine, peppermint oil is used internally to treat irritable bowel syndrome and other gastrointestinal ailments, as well as coughs and colds.

The aim of this review was to study the effect of peppermint oil on the gastrointestinal tract, especially in the treatment of irritable bowel syndrome (IBS). The authors reviewed pharmacodynamic and pharmacokinetic studies.

Pharmacodynamics

Nine clinical trials on peppermint oil and its gastrointestinal effects, including a total of 269 subjects, have been conducted. Most studies of orally administered peppermint oil demonstrate a substantial spasmolytic effect on the gut (single dose range: 0.1 to 0.24 ml/subject.) When peppermint oil is applied topically to the intestinal tract, this anti-spasm effect begins within 0.5 minutes of application and lasts up to 23 minutes. In order to treat IBS, a sustained release formula is necessary.

Gut motility is slowed after prolonged use of peppermint oil internally, however lower doses (<0.2 ml) do not seem to slow the emptying of the gut. When peppermint oil is added to a barium sulfate enema, the spasmolytic effect is also observed. Heartburn is an adverse event associated with peppermint oil being released in the upper gastrointestinal tract, causing the sphincter muscle to relax. A delayed release formula is necessary to prevent this effect.

Pharmacokinetics

Several in vivo animal studies have focused on the pharmacokinetics of peppermint oil. In rats, peppermint oil is rapidly absorbed and eliminated mainly by the bile; the main biliary metabolite is menthol glucuronide. The main constituents of peppermint oil, menthol and terpenes, are highly fat soluble, so they absorbed rapidly from the proximal gut. This confirms that a sustained release

formulation of peppermint oil is needed to treat the lower intestinal tract, the target organ in humans with IBS.

The pharmacokinetics of two galenic sustained released peppermint oil formulations have been studied in clinical trials. The formulations, Colpermin® (Tillots Pharma AG, Ziefen, Switzerland) and Mintec® (Key Pharmaceuticals, Rhodes, NSW, Australia), were compared to softgel capsules of peppermint oil.

In a 1984 crossover study, investigators compared the urinary excretion patterns of six healthy volunteers over 24 hours after they were administered either Colpermin (a sustained release preparation) or softgels (non-sustained release) delivered 0.8 ml of peppermint oil total. The investigators found that Colpermin released in the lower digestive tract and the colon in a sustained release pattern at therapeutic levels, while the softgels did not. Although the total amount of urinary metabolites released was equivalent for both Colpermin and the softgels, when Colpermin was administered, the urinary metabolites were released over a longer period of time. The study was extended in five patients with an ileostoma, or hole in the large intestine, and the investigators found that urinary menthol excretion was reduced by more than 50% when the ileostoma patients (n=5) were administered Colpermin, compared to healthy subjects (n=6). Upon administration of the softgel formulation to the ileostoma patients, the reduction was less than 30% in comparison to healthy subjects. This confirms that Colpermin is absorbed in the large intestine, the target organ in IBS treatment.

An earlier crossover study compared Colpermin and Mintec in 13 healthy subjects. The patients were randomized to receive three enteric-coated capsules of either Mintec or Colpermin (0.6ml peppermint oil each). Urine samples were collected from the subjects for 24 hours and analyzed for menthol and glucuronide metabolites of menthol. The two formulations showed significantly different urinary metabolite release patterns in both lag time and time to peak (Colpermin: $P < 0.017$; Mintec: $P < 0.047$). Metabolites were released faster and peaked sooner for Mintec (lag time: 0.5 hour, time to peak: 2.8 hour) than for Colpermin (lag time: 1.07 hour, time to peak: 5 hours). The average total urinary metabolite excretion was higher for Mintec (130.9 mg) than for Colpermin (95.5 mg), indicating that after 24 hours metabolism and excretion of Colpermin was not finished. Five subjects taking Mintec experienced nausea and vague abdominal pain; no adverse events were reported for Colpermin.

The authors conclude that available evidence indicates that the formulation of peppermint oil capsules is important in both reaching the target organ in IBS: the large intestine, and in minimizing adverse events, such as heartburn and nausea. The authors state the ideal formulation would have "a peak release at about 4 hours after ingestion with a release time of up to 24 hours." An enteric coated sustained release peppermint oil capsule is the ideal formulation when treating patients with IBS.

—*Marissa Oppel, MS*

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