Clinical Studies on Peppermint (*Mentha* x *piperita* L.)

Gastrointestinal

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Tate, 1997	Postoperative nausea	R, PC, Cm n=18 patients undergoing major gynecological surgery	3 days (day of operation and 2 postoperative days)	Essential peppermint oil vs. peppermint essence (placebo) vs. no treatment	Peppermint oil vs. peppermint essence (placebo) vs. no treatment	Statistically significant differences were demonstrated on day of operation using Kruskal-Wallis test ($p=0.0487$). Using Mann-Whitney U-test, a difference between placebo and experimental groups was shown ($U=3$; $p=0.02$). Experimental group required less conventional antiemetics and received more opioid analgesia postoperatively. Author concludes that peppermint oil may improve postoperative nausea in gynecological patients.
Liu *et al.*, 1997	Irritable bowel syndrome (IBS)	P, R, DB, PC n=110	4 weeks	1 capsule, 3–4x/day, 15–30 minutes before meals vs. placebo	Colpermin® enteric-coated capsule containing 187 mg peppermint oil vs. placebo	Using Mann-Whitney U-test, symptom improvement in peppermint oil group was significantly better ($p<0.05$) compared to placebo. In peppermint group 79% experienced alleviation of severity of abdominal pain (29 were pain-free); 83% had less abdominal distension, 83% had reduced stool frequency; 73% had fewer borborygmi; 79% had less flatulence. Colpermin® peppermint leaf oil was effective and well-tolerated.
Sparks *et al.*, 1995	Spasm during barium enema	R, DB, C n=141 mean age=60 years	3 days bowel preparation before 1 day treatment and examination	Barium suspension with added peppermint oil, 1x/day vs. standard barium sulfate	Barium suspension with 370 ml water and 30 ml peppermint preparation (16 ml peppermint oil BP and 0.4 ml polysorbate) plus 10 ml peppermint preparation added to enema tubing	Significant decrease in spasm was observed in treatment group (60%) compared with control group (35%) ($p<0.001$). Fewer in peppermint group required intravenous buscopan (5 vs. 9) or exhibited spasm (23 vs. 39). Authors concluded that addition of peppermint oil to barium suspension appears to reduce incidence of colonic spasm during examination. Technique is simple, safe and economical and may lessen the need for intravenous administration of spasmolytic agents.
Shaw *et al.*, 1991	Irritable bowel syndrome (IBS)	R, C n=35	Average of 6, 40-minute sessions with physiotherapist over 6 months	40 minutes of stress management with physiotherapist vs. Colpermin® 3x/day	Stress management program vs. treatment with Colpermin® enteric-coated capsule containing 187 mg peppermint oil vs. conventional management	Two-thirds of patients enrolled in the stress management program found it effective in relieving symptoms ($p<0.002$) and experienced fewer attacks ($p<0.004$), of less severity, with benefit maintained for at least 12 months compared to the Colpermin® group.
Fernández, 1990	Irritable bowel syndrome (IBS)	O, MC n=50	4 weeks	1 capsule, 3x/day 30 minutes before meals	Capsule containing 0.2 ml peppermint oil	Evaluation of all signs and symptoms, both pre-treatment and post-treatment, confirmed statistically significant decrease of symptoms.
McKenzie and Gallacher, 1989	Trial 1: Fecal odor in colostomy bags; Trial 2: Effect on colostomy acceptance	O, U Trial 1: n=10 patients, Trial 2: n=20 patients	Trial 1: 1 day Trial 2: 3 days starting on third post-operative day	1 capsule, 3x/day	Enteric-coated capsule containing peppermint oil in a thixotropic paste (brand not stated)	Trial 1: Contents of colostomy bags were checked for intact or partially digested capsules and for smell of peppermint. Only one patient passed capsule unchanged. Trial 2: 14 of 20 patients found odor improved and 1 found it worse. 15 found their colostomies more acceptable and wished to continue taking peppermint. Consistency of feces and frequency of bag-changing appeared to improve.
Carling *et al.*, 1989	Irritable bowel syndrome (IBS)	R, DB, CO n=40	2 weeks		Enteric-coated capsule containing 0.2 ml peppermint oil vs. 0.2 mg hyoscyamine or placebo	Peppermint oil treatment tended to have more pronounced effect on symptoms than placebo or hyoscyamine but was not statistically significant. Findings favor the short-term use of enteric-coated peppermint oil as an antispasmodic for IBS.

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Clinical Studies on Peppermint (*Mentha* x *piperita* L.) (cont.)

Gastrointestinal (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Lawson *et al.*, 1988	Irritable bowel syndrome (IBS)	R, DB, CO n=18	4 weeks	3 capsules, 3x/day	Enteric-coated capsule containing 0.2 ml peppermint oil (brand not stated)	Peppermint group had small, but statistically significant increase in frequency of defecation but no significant change in scores for global severity of symptoms or scores for specific symptoms of pain, bloating, urgent defecation, and sensation of incomplete evacuation.
Nash *et al.*, 1986	Irritable bowel syndrome (IBS)	R, DB, PC, CO n=34	4 weeks	2 capsules, 3x/day	Capsule containing 0.2 ml peppermint oil vs. placebo Colpermin®	In terms of overall symptoms, patients' assessments at end of 2 and 4 weeks of treatment showed no significant difference between peppermint oil and placebo.
Dew *et al.*, 1984	Irritable bowel syndrome (IBS)	R, DB, PC, CO, MC n=29 mean age 42 years	2 weeks	1–2 capsules, 3x/day depending on severity of symptoms	Elanco LOK gelatin capsules containing 0.2 ml peppermint oil coated with cellulose acetate phthalate vs. placebo capsules containing 0.2 ml of arachis oil.	Patients in peppermint group were relieved of symptoms, while the number of their daily bowel movements was unaffected. Patients felt significantly better while taking peppermint compared with placebo ($p<0.001$) and considered peppermint better than placebo in relieving abdominal symptoms ($p<0.001$). Study suggested beneficial effect of peppermint for treatment of IBS based on patient data.
Somerville *et al.*, 1984	Pharmacokinetics of peppermint oil in spastic colon syndrome	Cm, U n=12 6 healthy volunteers (17–37 years) and 6 ileostomy patients (22–49 years)	24 hours	2 capsules, 3x/day	Colpermin® enteric-coated capsule containing 187 mg peppermint oil vs. peppermint oil in soft-gel capsules	Total 24-hour urinary excretion of menthol was similar in both preparations, but peak menthol excretion levels were lower and were delayed with enteric-coated capsule vs. soft gelatin capsules. Menthol excretion was reduced in ileostomy patients taking enteric-coated capsules, and moderate amounts of unmetabolized menthol were recovered from ileostomy effluent. Enteric-coated capsules can deliver unmetabolized oil directly to the colon.
Leicester and Hunt, 1982	Colonic spasm during endoscopy	U n=20	1 day	Peppermint oil injected along the biopsy channel of colonoscope into lumen of colon, 1x	Peppermint oil BP	Peppermint oil caused a relaxant effect on gastrointestinal tract that relieved colonic spasms within 30 seconds after injection in all 20 patients, allowing easier passage of the instrument or assisting in polypectomy.
Duthie, 1981	Colonic motility	R, PC, CO n=6	1 day	Peppermint oil injected into the lumen of the colon, 1x	Peppermint oil 0.2 ml in 50 ml of 0.9% sodium chloride with 1 in 10,000 polysorbate as suspending agent vs. vehicle alone (placebo)	Period of inhibition of all motor activity in all 6 subjects began within 2 minutes of peppermint oil administration lasting 7–23 minutes (mean 12 minutes). Decrease in percentage activity and motility index seen in all 6 subjects during first 10 minutes after introducing oil. Differences were statistically significant (actual statistics not stated). Decrease in motility index 10–20 minutes after oil was also statistically significant.
Rees *et al.*, 1979	Irritable bowel syndrome (IBS)	DB, PC, CO n=16	6 weeks (3 weeks each)	1–2 capsules, 3x/day depending on severity of symptoms	Elanco LOK gelatin capsules containing 0.2 ml peppermint oil coated with cellulose acetate phthalate vs. placebo capsules containing 0.2 ml of arachis oil	Overall assessment showed that patients felt significantly better ($p<0.01$) during peppermint treatment period compared to placebo and considered peppermint oil more effective than placebo in relieving abdominal symptoms ($p<0.005$).

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Gastrointestinal

Combination Preparations

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Micklefield *et al.*, 2000	Gastro-duodenal motility	P, C, Cm, CO n=6 healthy volunteers (24–40 years)	1 day	1 capsule/day	Enteroplant® enteric-coated capsule; 90 mg peppermint oil and 50 mg caraway oil vs. non-enteric-coated capsule of peppermint-caraway oil combination	Both enteric-coated and non-enteric-coated preparations have effects on migrating motor complex (MMC), primarily a decrease in the number of contractions and contraction amplitudes. Non-enteric-coated preparation shows effect mainly during first MMC after administration, and enteric-coated preparation has a temporarily delayed effect during the second MMC after administration. Authors conclude that both preparations are safe, acting locally to cause smooth muscle relaxation. No adverse effects were noted.
Freise and Köhler, 1999	Non-ulcer dyspepsia	P, Cm, R, DB, C, MC n=223	29 days plus a 1-week washout phase before study	1 capsule, 3x/day with water before meals	Enteroplant® enteric-coated capsule; 90 mg peppermint oil and 50 mg caraway seed oil vs. enteric-soluble formulation containing 36 mg peppermint oil and 20 mg caraway oil	Statistically significant decline in pain intensity observed in both groups. Equivalent efficacy of both preparations was demonstrated ($p<0.001$). Concomitant variable results were similar in both groups. Test preparation significantly better ($p= 0.04$) in pain frequency. Authors conclude that the enteric-coated capsule provides an advantage over the acid-soluble formulation because it not only reduces pain intensity, it also potentially decreases the number of side effects, including nausea and eructation, with peppermint taste.
Madisch *et al.*, 1999	Functional dyspepsia	Cm, R, DB, C, MC n=118	4 weeks plus a 1-week washout phase before study	1 capsule, 2x/day with water, morning and noon, plus 1 placebo capsule/day in evening vs. 10 mg cisapride, 3x/day before meals	Enteroplant® enteric-coated capsule; 90 mg peppermint oil and 50 mg caraway seed oil vs. prokinetic agent Propulsid® cisapride	Reduction in visual analogue scale (VAS) pain intensity scores was comparable with drop of 4.62 points in peppermint/caraway group and 4.60 points in cisapride group ($p=0.021$). Reduction in frequency of VAS pain scores was equivalent by week 4 ($p=0.0034$). Flatulence decreased in peppermint group by 71.8% and 65.7% in cisapride group. Treating physicians concluded that 78.6% of peppermint group were very much or much improved compared to 70.9% in cisapride group. Peppermint/caraway oil preparation provides comparable effect to cisapride, is well-tolerated, is only one quarter the cost of cisapride therapy, and has fewer potential side effects.
May *et al.*, 1996	Non-ulcer dyspepsia for at least 14 days	R, DB, PC, PG, MC n=45 mean age Enteroplant group=42 years, mean age placebo=47 years	4 weeks	1 capsule, 3x/day with water before meals	Enteroplant® enteric-coated capsule; 90 mg peppermint oil and 50 mg caraway seed oil vs. placebo	Clinical Global Impression (CGI) values were improved in 94.7% of treatment group vs. 55% placebo group ($p=0.004$). In treatment group, 63.2% were pain-free compared to only 25% in placebo group ($p=0.005$). Improvement in pain intensity was 89.5% in treatment group vs. 45% in placebo group ($p=0.015$). Authors conclude that treatment was equally successful for patients diagnosed with IBS and dyspepsia and that Enteroplant® has a risk-to-benefit ratio more favorable than standard treatment with synthetic chemical medicaments.
May *et al.*, 2000	Functional dyspepsia	R, DB, PC n=96	4 weeks	1 capsule, 2x/day with water before meals	Enteroplant® (PCC) enteric-coated capsule; 90 mg peppermint oil and 50 mg caraway seed oil vs. placebo	Primary efficacy variables were the intra-individual change in (1) pain intensity, and (2) sensation of pressure, heaviness, and fullness between days 1 and 29, and the investigators' rating of (3) global improvement (Clinical Global Impressions [CGI] item 2) on day 29. The average intensity of pain was reduced by 40% vs. baseline in the PCC group and by 22% in the placebo group. Regarding pressure, heaviness, and fullness, a 43% reduction was observed for PCC vs. 22% for placebo. In CGI item 2, 67% (PCC) vs. 21% (placebo) of patients were described as much or very much improved. In all three target parameters, the superiority of PCC over a placebo was statistically significant.

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Neurology, Psychiatry

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Sullivan *et al.*, 1998	Effects on vigilance performance in brain injury	R, C n=40 patients with brain injury	30-minute vigilance task	Periodic whiffs of peppermint-scented air delivered by pumps that force air through plastic tubing into a glass reservoir	Peppermint-scented air vs. unscented air	Under fragrance conditions, controls reduced frequency of commissive errors (false alarms) over course of vigil, an adaptive strategy given the low probability of signals employed. False alarm rate of observers with brain injury increased precipitously toward end of vigil in unscented air condition. Exposure to scent of peppermint rendered false alarm scores of observers with brain injury similar to controls, a result that is consistent with evidence that olfactory stimulation activates brain areas vital for planning and judgement.
Göbel *et al.*, 1996	Tension headaches	R, DB, PC, Cm, CO n=41 male and female patients (18–65 years)	Four headache episodes per patient	Topical application of peppermint oil or placebo solution to forehead and temples, repeated 1x after 15 or 30 minutes vs. oral 1,000 mg acetaminophen or 1,000 mg placebo vs. simultaneous application of 1,000 mg acetaminophen and 10% peppermint oil in ethanol solution	Euminz® (containing 10 g peppermint oil with ethanol 90%) vs. Paracetamol® (500 mg acetaminophen) vs. 90% ethanol solution with traces of peppermint oil for blinding purposes	Study involved analyses of 164 headache attacks of patients suffering from tension headaches. Compared to placebo, peppermint leaf oil significantly reduced clinical headache intensity within 15 minutes ($p<0.01$) with a continuing effect over the one hour observation period. No significant difference between acetaminophen and peppermint. Simultaneous acetaminophen and peppermint use did not result in significant additive effect. Authors conclude that peppermint oil efficiently alleviates tension-type headaches as well as acetaminophen. It is well-tolerated and a cost-effective alternative to conventional therapies.
Göbel *et al.*, 1994	Neurophysiological, psychological, and experimental algesimetric parameters	Cm, CO, R, DB, PC n=32 healthy subjects	1 day	Oil and ethanol mixture applied to forehead and temples with small sponge	Peppermint oil and ethanol vs. peppermint oil with eucalyptus oil and ethanol vs. placebo (brands not stated)	Peppermint oil demonstrated significant analgesic effect with reduction in sensitivity to headache. Peppermint oil with eucalyptus oil had little influence on pain sensitivity but increased cognitive performance and had a muscle-relaxing and mentally relaxing effect.
Warm *et al.*, 1991	Effects on signal detectability in tasks demanding sustained attention	R, C n=36 college students (men and women with normal or corrected-to-normal vision)	40 minutes divided into 4 consecutive 10-minute periods	Repeated exposure time of 150 milliseconds per 10-minute period	Peppermint-scented air vs. muguet-scented air (International Flavors and Fragrances, Inc.) vs. unscented air	A statistical difference was found between groups exposed to air scented with fragrance of peppermint ($p<0.05$) or muguet ($p<0.05$) vs. placebo. Authors concluded that this scented air can enhance rate of signal detections in a vigilance task without a concomitant increase in errors of commission vs. placebo. It is suggested that exposure to fragrance may serve as an effective form of ancillary stimulation in tasks demanding close attention for prolonged periods.

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