Introduction

Irritable bowel syndrome (IBS) is one of the most commonly seen gastrointestinal conditions attended to by general practitioners, with an estimated 2.4-3.5 million physician consultations each year (1,2). IBS is characterized by recurrent abdominal pain and distention, with alteration in bowel habit (diarrhea and/or constipation), increased flatulence, and with no known organic genesis. Often, IBS may inadvertently be confused with a food intolerance, such as for lactose. During instances like these, simply removing the item from the diet alleviates the symptoms; hence, this incident would not be considered to be IBS. As controversy has existed as to how IBS should be diagnosed, the adoption of the Rome (Manning) Criteria (Table 1) was developed in order to have a consensus in the description of symptom patterns and clinical features (3). Due to its multi-symptomatic nature, no single drug treatment has been found to be efficacious; as such, alternative approaches have been tried.

I. Diagnostic criteria for IBS
- A. At least 3 months of continuous or recurrent symptoms of
  - ýAbdominal pain or discomfort that is
    1. Relieved with defecation
    2. Associated with a change in frequency of stool, or
    3. Associated with a change in consistency of stool, and
- B. Two or more of the following, at least on one-fourth of occasions or days:
  - ýAltered stool frequency (>3 bowel movements daily or<3 bowel movements weekly)
  - ýAltered stool consistency (lumpy/hard or loose/watery stool)
  - ýAltered stool passage (straining, urgency, or feeling of incomplete evacuation)
  - ýPassage of mucus,
  - ýBloating or feeling of abdominal distention

Table 1. Rome (Manning) Diagnostic Criteria for Irritable Bowel Syndrome (3).

Since its natural-hybrid-sprouting to England in 1696, peppermint (Mentha x Piperita Lamiaceae) has been used as a flavoring agent for an array of food items. It also has a history of being used for its carminative (flatulence relieving) and digestive effects that are often associated with IBS. Medicinal properties are attributed to a high menthol content (4). There have been an increasing number of studies over the past several years trying to determine if these effects are biological or strictly placebo in nature. Both in vitro and in vivo methods have been employed; in vitro results appear to be promising, while in vivo studies appear to be mixed.

Drug Treatment

IBS is an extremely common disorder, which cannot be attributed to any known organic disease. Often, however, food allergies or intolerance create symptoms found in IBS. During such occurrences, all that is necessary is to identify the food item and remove it from the diet (at times, this is easier said than done). When IBS is identified via careful history taking and implementation of the Rome (Manning) criteria, a physician can take several steps to alleviate the discomfort. Because there is no known cause for IBS, it has been difficult to develop an evidence-based treatment; as a result, current treatments treat symptoms and not the disease. Treatments include the use of smooth muscle relaxants, bulking agents, high fiber diets, psychotherapy and antidepressants. For example the use of anticholinergics, smooth muscle relaxants, seretonin antagonists (5-HT3 and 5-HT4), gonadotrophin-releasing hormone analogues, and tricyclic antidepressants (5). It has long been established that there are many plants that have medicinal value. The use of peppermint oil for the relief of IBS has been explored over the years to see if testimonial results have a biologic or placebo origin.

in vitro Studies

Peppermint oil is extracted from the aerial parts of the flowering plant, the flowering branch tips and the dried leaves (6). For many years, peppermint was presumed to attain its carminative effects by relaxing the intestinal smooth muscle, though the actual mechanism by which this was accomplished had not been

elucidated. The method by which peppermint oil seems to help relax smooth muscle was not described until 1988, by Hawthorn et al. They looked at the action of peppermint and menthol (peppermint's most abundant active ingredient), and studied their effects in intestinal, neuronal and cardiac preparations. Their data shows that both peppermint and menthol have calcium channel blocking properties, with menthol appearing to be twice as effective (7). Both peppermint oil and menthol's calcium-channel blocking activity appear to have pharmacological actions similar to nitrendipine calcium channel blockers. This indicates that there is an inhibition of depolarization in the smooth muscle, which results in smooth muscle relaxation (or antispasmodic activity), that in turn, would explain the relief of IBS symptoms experienced by some individuals who ingest peppermint.

As it became more clear that smooth muscle relaxation was a result of blocked calcium channels, the question that naturally arose was, are there any other mechanism by which peppermint influences biologic processes? Beesley et al. explored this question. They designed their study in order to investigate whether peppermint oil is able to influence transport across the small intestine by examining peppermint's effects on absorptive and secretory processes in a rat model. They measured transintestinal electrical activity, glucose uptake by brush border membrane vesicles, and non-specific glucose binding to bush border membrane vesicles. In the presence of peppermint oil (on either the serosal or mucosal side of the intestinal preparation), basal electrical activity was not affected, suggesting that the basal ionic transport systems remain unaffected by peppermint. However, data indicates that peppermint oil can also reduce sodium dependent glucose uptake when it is introduced into the mucosal side of the preparation at a concentration 0.5 mg/ml (by 10% ($p<0.05$)) at 10 seconds. Higher values, explain Beesley et al., would indicate non-specific binding and disruption of the membranes, as can be seen with the introduction of Triton X-100. Observations on secretory effects were limited to acetylcholine-induced reactions; the acetylcholine process was not inhibited by peppermint. In summary, peppermint oil appears to affect glucose uptake in a specific manner, while not affecting basal ionic transport systems or acetylcholine-related secretions (4). It is interesting to note many over-the-counter drugs for the treatment of IBS contain peppermint oil.

Clinical Trials

Multiple studies have been conducted over the past 10-15 years testing the efficacy in the oral administration of peppermint oil on IBS. The use of an enteric capsule (Colpermin) for delivery has been implemented, so as to decrease the side effects of peppermint oil ingestion, mainly in the form of heartburn (believed to be associated with the rapid absorption in the proximal gut (8). Pittler et al. performed a systematic review and metaanalysis of several of these studies to determine the usefulness of peppermint oil for treating IBS (2). Of the eight studies originally targeted for analysis, three were excluded from metaanalysis due to the fact that two of them failed to present data in sufficient detail (one was an abstract), and the third study was not double-blind, nor was it placebo controlled. Overall, Pittler et al. showed a significant ($p<0.001$) improvement of IBS symptoms in patients treated with peppermint oil compared to those given a placebo; however, only one of the studies (9) used the Rome (Manning) Criteria for IBS. That particular study, although excluded from the metaanalysis, showed that peppermint oil had no effect on IBS. The highest rated, metaanalyzed study, conducted by Nash et al. (10), did not show an improvement with peppermint oil; however, this study failed to use the Rome (Manning) Criteria for IBS. Such failure may have included individuals that may have otherwise not been diagnosed with IBS. Studies that showed subject improvement of IBS symptoms did not rate as highly in their data collection methods.

More recently, Liu et al. (11) have conducted a randomized, double-blind, placebo-controlled study on 110 Chinese outpatients, using Colpermin. This study shows a significant improvement in IBS symptoms. Of the 101 subjects that finished the study, 52 were on Colpermin and 49 on placebo (3 subjects on Colpermin and 6 on placebo did not return for a follow-up). Subjects on Colpermin reported improvement with various IBS symptoms, with the majority of subjects having diarrhea-predominant IBS (Table 2):

SYMPTOMS	COLPERMIN	PLACEBO
Improvement of abdominal pain severity.	79%	43%
Less abdominal distension.	83%	29%
Reduced Stool Frequency.	83%	32%
Fewer Borborygmi (rumbling in the bowels).	73%	31%
Less flatulence.	79%	22%

Table 2. Symptom improvement seen in study conducted by Liu et al. (11).

Although Liu et al. claim that peppermint should be the treatment of choice for IBS, they failed to strengthen their study by the control of an additional variable that Nash et al. accounted for. That is, the aroma associated with peppermint, which may inadvertently create a placebo effect. Nash et al. controlled for this by injecting peppermint oil in the lid of the placebo bottle. As well, Liu et al. may have seen varied results, had their study incorporated a crossover protocol.

Discussion

IBS affects millions of people each year. Because there is no known etiology, symptom-based therapy appears to be the treatment of choice. The use of current treatments includes muscle relaxants, bulking agents, high fiber diets, psychotherapy, and antidepressants. However, alternative medicines are being explored due to the pharmacological side-effects and low efficacy of some of the drugs being utilized. Peppermint has long been used for its carminative properties, and continues to be a subject of controversy as to whether it is effective against IBS. In vitro studies show that peppermint has antispasmodic properties that are achieved by blocking calcium channels. Clinical studies, however, give conflicting results. The potential of using peppermint oil instead of other pharmacological agents includes a lower price and not having to take unnecessary agents, such as tricyclic antidepressants, which may have many unwanted, associated side-effects. Additionally, other possible applications are being explored. One such double-blind study conducted by Sparks et al. (12), looked at the effectiveness of relieving colonic muscle spasms when peppermint is mixed with a barium enema slurry. Their results showed 60% of the patients receiving the peppermint-barium enema did not have colonic muscle spasms, compared to 35% ($p<0.001$) who's enema did not contain peppermint.

The use of peppermint to alleviate IBS-associated symptoms looks promising but is far from conclusive. Future studies need to be well designed (e.g., a large number of subjects, double-blind crossover, use of the Rome (Manning) criteria, etc.), in order to see if peppermint is effective against any or all IBS symptoms.

REFERENCES

1. Farthing MJG. Irritable Bowel, Irritable Body, Irritable Brain? British Medical Journal. 1995;310:171-5.

2. Pittler MH, Ernst, E. Peppermint Oil for Irritable Bowel Syndrome: A Critical Review of Metaanalysis. American Journal of Gastroenterology. 1998;93:1131-5.

3. Drossman DA, Richter JE, et al. Functional Gastrointestinal Disorders: Diagnosis, Pathophysiology and Treatment: A Multinational Consensus. Boston: Little Brown, 1994:13-19.

4. Beesley A, Hardcastle J, et al. Influence of Peppermint Oil on Absorptive and secretory Processes in Rat Small Intestine. Gut. 1996;39:214-9.

5. Physicians' Desk Reference for Herbal Medicines. Montvale, NJ: Medical Economics Company. 1998:971-5.

6. Farthing MJG. New Drugs in the Management of IBS. Drugs. 1998;56:11-21.

7. Hawthorn M, Ferrante J, et al. The Actions of Peppermint Oil and Menthol on Calcium Channel Dependent Processes in Intestinal, Neuronal and Cardiac Preparations. Alimentary Pharmacology and Therapeutics. 1988;2:101-18.

8. Somerville KW, Richmond CR, et al. Delayed-Release peppermint oil capsules (Colpermin) for the Spastic Colon Syndrome: A Pharmacokinetic Study. British Journal of Clinical Pharmacology. 1984;18:638-40.

9. Lawson MJ, Knight RE, et al. Failure of Enteric-Coated Peppermint Oil in the Irritable Bowel Syndrome: A Randomized, Double-Blind Crossover Study. Journal of Gastroenterology and Hepatology. 1988;3:235-8.

10. Nash P, Gould PR, et al. Peppermint Oil Does Not Relieve the Pain of Irritable Bowel Syndrome. Britrish Journal of Clinical Practice. 1986;40:292-3.

11. Liu JH, Chen GH, et al. Enteric-Coated Peppermint-Oil Capsules in the Treatment of Irritable Bowel Syndrome: A Prospective, Randomized Trial. Journal of Gastroenterology. 1997;32:765-8.

12. Sparks MJW, O'sullivan P, et al. Does Peppermint relieve Spasm During Barium Enema? British Journal of Radiology. 1995;68:841-3.