THE PHYTOCHEMICAL AND CLINICAL EVALUATION OF
PEPPERMINT OIL (MENTHA PIPERITA L.) WITH OLIVE OIL (OLEA
EUROPAEA L.) IN THE TREATMENT OF IRRITABLE BOWEL
SYNDROME (IBS)

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ABSTRACT

Background: Irritable bowel syndrome (IBS) is a common public health problem. Different therapeutic agents including natural products had been used for its treatment. Peppermint oil has been suggested for treatment of IBS but its combination with olive oil was not studied previously. Methods: Peppermint oil have been extracted and evaluated phytochemically. Patient with IBS were divided into three groups; the first group was given pure peppermint oil capsules, the second was given mixed peppermint oil with olive oil (30%:70%) respectively, the third was given traditional therapeutic agent (Mebeverine) as control group. Results: There was a significant effect of peppermint oil with olive oil (mixed oils) on IBS symptoms compared with both peppermint oil only and control groups. The percentages of responders to control, peppermint oil only and mixed oils were reached to 72, 77 and 88% after 2 week from the end of treatment, respectively. Conclusions: This study suggests a new modality for treatment of IBS in the form of mixed peppermint oil with olive oil which gave a better result than traditional therapeutic agents.

KEYWORDS: phytochemically, Mebeverine, peppermint oil.

INTRODUCTION

Irritable bowel syndrome [IBS] is a common chronic functional bowel disorder characterized by abdominal pain or discomfort, bloating and alterations in bowel habits. It is a symptom-based diagnosis according to Rome III criteria; the primary symptoms of IBS are abdominal...
pain or discomfort in association with frequent diarrhea or constipation, as alternating bowel habits.\(^2\) IBS can be classified as either diarrhea predominant (IBS-D), constipation predominant (IBS-C) or IBS with alternating stool pattern (IBS-A) or pain predominant.\(^2\)

Several conditions with similar symptoms may present as IBS including coeliac disease, fructose malabsorption, mild infections, parasitic infection like giardiasis, and inflammatory bowel diseases, which should be excluded.\(^3\) People with IBS may also have gastroesophageal reflux, chronic fatigue syndrome, headache, backache and psychiatric symptom, such as depression and anxiety.\(^4,5\)

Various carminative plants have been used to relieve intestinal colic including chamomile, lemon balm, dill, caraway, fennel and etc.\(^6,7\) Among these plants, peppermint plant (\textit{Mentha piperita} L.) is the most frequently recommended.\(^8\)

The beneficial effect of peppermint leaves is attributed to its volatile oil.\(^9\) The main constituents of the essential oil from peppermint (\textit{Mentha piperita} L.) were menthol, menthone, menthyl acetate, 1,8-cineole, limonene, beta-pinene and beta-caryophyllene.\(^9,10\) Peppermint oil possessed antiradical and antioxidant activity.\(^9\) Peppermint is widely used in food, cosmetics and medicines. It has proven helpful in symptomatic relief of the common cold.\(^11\) 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.\(^11\)

Olive oil is the fatty oil extracted from the drupes of olive using the cold press method.\(^12\) Olive oil is composed of the mixed triglyceride esters of oleic acid, palmitic acid and other fatty acid, along with traces of squalene (up to 0.7\%) and sterols (about 0.2), phytosterol and tocosterols.\(^12\) Olive oil contains a group of related natural products with potent antioxidant property, also is contain a soluble vitamins in oil such as E, D, A and K.\(^13\) Olive oil have great health benefits including the reduction in coronary heart disease risk, prevention of some cancers, modification of immune and anti-inflammatory responses, olive oil and its extracts protect against oxidative damage of hepatic tissue.\(^14\)

Although peppermint leaves and oil is on the FDA (Food and Drug administration) GRAS (Generally Recognized As Safe) list, but when it is used alone or in a higher concentration may cause heartburn, gastrointestinal irritation and perianal irritation.\(^11,15\) therefore the aim
of this study was to evaluate the activity of the combination between mentha oil with olive oil at (30:70) percentage of mentha oil and olive oil respectively for treatment of Irritable bowel syndrome and to assess the side effects of this formula compared with mentha oil alone.

MATERIALS AND METHODS

Extraction and chemical analysis of volatile oil

The leaves of the peppermint plant have been collected during the year 2012 from the medicinal plants garden in the College of Pharmacy/ University of Kerbala. The volatile oil was extracted by hydro-distillation using an apparatus of Clevenger type. The extraction took 3 hours for mixing 100 g leaves in 500 ml of distilled water, after isolation of volatile oil was stored at 4°C in obscurity till the beginning of analysis. The chemical composition of peppermint volatile oil was determined by GLC (Gas liquid chromatography). The analysis equipped with flame ionization detector (GC-FID), Varian capillary column temperature was programmed from 40°C to 280°C for 5°C/min. The temperature of the injector was fixed to 250°C and the one of the detector (FID) to 260°C. The debit of gas vector (nitrogen) was fixed to 1ml./min. The volume of injected specimen was 0.5µl of diluted oil in solution (10%) constituent in the oil was determined by area peaks.

PREPARATION OF OIL CAPSULES

Olive oil was obtained from company then mixed with Peppermint volatile oil at (70:30) percent for both oils respectively. The gelatin capsules size 250 mg were filled by using manual gelatin filling machine. Polishing, finishing, packaging and labeling processes were completed respectively.

PATIENTS

The clinical study was conducted during the period from April 2012 till September 2013 and carried out in Karbala-Iraq. This clinical trial had been approved by the Herbal Medicine Center in The Ministry of Health. Three hundred thirty patients were enrolled in this study, which were divided into three groups. The number of patients who completed the study period was 292 patients.

A detailed medical history was taken from the patients in addition to clinical examination and investigation. All patients were diagnosed as irritable bowel syndrome (IBS) according to Rome III diagnostic criteria. Patients were randomly assigned into three groups: Group A received conventional treatment (Mebeverine) as control, Group B received peppermint oil
(Mentha oil) only, and Group C received mixed peppermint oil with olive oil. The time of onset and duration, the quality and severity of pain, and associated symptoms in addition to side effects were recorded.

Figure (1) showed the patients’ assignment diagram.

**Statistical analysis**

Statistical analysis was carried out with the statistical analysis system (SAS) Program and all data recorded were subjected to analysis of variance (ANOVA) and least significant difference (L.S.D.) at 0.01 level implemented to compare the parameters studied.\(^{[17]}\)

**RESULTS AND DISCUSSION**

**Phytochemical evaluation**

**Peppermint (Mentha Piperita) oil**

The results revealed that the leaves of peppermint plant contained 3% of volatile oils. The major components of peppermint volatile oil were menthol 37%, menthone 27%, menthofuran 9%, isomenthone 7%, 1,8 cineole 9%, limonene 5%, carvone 0.6%, pulegone 4%, α-pinen 0.6%, piperitone 0.2% and caryophline 0.6%. These results were comparable with other researchers.\(^{[9,10,18]}\) Also the evaluation showed many physical properties of peppermint volatile oil such as relative density, refractive index and optical rotation and the values of these properties were (0.916), (1.466) and (-30\(^{\circ}\)) respectively.

**Olive (Olea Europaea) oil**

The oil extracted from the ripe fruit and obtained from Rew Company. Olive oil is the fatty oil extracted from the drupes of *olea europaea* using the cold press method. An important variety is virgin oil which is produced by lightly pressing the peeled pulp devoid of endocarp. Olive oil is pale yellow or light greenish-yellow oily liquid which has faint but characteristic odour. It has a bland to slightly acrid taste. The constituents of oil were 75% of oleic acid, 10% palmitic acid and 9% of linoleic acid, with lesser amounts of stearic, myristic, hexadecenoic and arachidic acids.

**CLINICAL EVALUATION**

The age and sex distribution in this study is presented in table (1). The age groups (20-30), (31-40), (41-50) and (51-60) were about 25%, 29%, 28% and 18% respectively. The percentage of males who were suffered from IBS was about 44% while the percentage of
females was about 56%.

The results in table (2) showing the significant effect of peppermint oil with olive oil (mixed oils) on IBS symptoms compared with control and peppermint oil only. The same trend of response to the mixed oils was observed after 2 weeks from the end of treatment. There was no significant difference between control and peppermint oil only during the treatment period, nevertheless there was a significant difference between them after 2 week form the end of treatment. The percentages of responders to control, peppermint oil only and mixed oils were reached to 72, 77 and 88% after 2 week from the end of treatment, respectively.

The reduction percentages of abdominal pain, flatulence and altered bowel motion as major symptoms of IBS were shown in Table (3).

Table (4) illustrates the overall clinical response of the three groups of patients to treatments during this study. It is obvious that the two groups of peppermint oil were better than control and the group of mixed oil was the best.

The beneficial effect of peppermint oil in the treatment of IBS may be attributed to its relaxing effect on gastrointestinal motility and also to the potential antibacterial activity of its components on the inhibition of growth of some gastrointestinal pathogens.

Although the peppermint oil is commonly used to treat abdominal pain, bloating and relax smooth muscle such as found in the colon, but the excessive doses may cause heartburn, also when used for long term and high doses it may cause kidney problem. The peppermint oil when diluted with olive oil at (30% to 70%) respectively in this study was giving excellent effect on IBS without side effects such as heartburn and kidney problem. The enhancing activity of peppermint oil for IBS with preventing the side effects when mixed with olive oil at (30: 70%) presenting peppermint and olive oils respectively may be attributed to different health benefits of olive oil, such as the activity of this oil in treatment of gastritis and colitis by affecting agents that may aggravate the inflammatory response. The result of this study was agreed with conclusion of other researchers who were estimated that around half of the cases of colitis could be prevented if larger amount of oleic acid were consumed. Some patients who were received peppermint oil only treatment were suffered from heartburn may be due to some component of peppermint oil such as menthol which causes mild irritation of stomach that may lead to dyspepsia or heartburn. The results of this study were agreed with
conclusion of other researchers who were found that enteric-coated peppermint oil capsules decreasing the side effects of peppermint oil when used alone.[23] The role of olive oil in enhancing the activity for IBS with preventing the side effects may be due to regulating bowel motility and may include calcium channel blocking on local level causing smooth muscle cells relaxation.[24] The long-term consumption of olive oil provide other cardiovascular and general health benefits such as cholesterol regulation and oxidation, and also exerts anti-inflammatory, antihypertensive as well as vasodilator effects.[25]

Figure 1: Patient randomization, allocation and drop-outs.
### Table (1) Age and sex distribution in the study population.

<table>
<thead>
<tr>
<th>Age (year)</th>
<th>Control</th>
<th>M.O.</th>
<th>M.O. + O.O.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>20-30</td>
<td>23</td>
<td>23.7</td>
<td>26</td>
<td>27.0</td>
</tr>
<tr>
<td>30-40</td>
<td>27</td>
<td>27.8</td>
<td>28</td>
<td>29.2</td>
</tr>
<tr>
<td>41-50</td>
<td>31</td>
<td>31.9</td>
<td>25</td>
<td>26.0</td>
</tr>
<tr>
<td>50-60</td>
<td>16</td>
<td>16.5</td>
<td>17</td>
<td>17.8</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100</td>
<td>96</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Control</th>
<th>M.O.</th>
<th>M.O. + O.O.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Male</td>
<td>43</td>
<td>44.3</td>
<td>43</td>
<td>43.4</td>
</tr>
<tr>
<td>Female</td>
<td>54</td>
<td>55.7</td>
<td>54</td>
<td>56.6</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100</td>
<td>96</td>
<td>100</td>
</tr>
</tbody>
</table>

### Table (2) Response of patients to treatments.

<table>
<thead>
<tr>
<th>Groups</th>
<th>2 weeks on treatment</th>
<th>4 weeks on treatment</th>
<th>2 weeks after end of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>70 % a</td>
<td>74 % a</td>
<td>72 % a</td>
</tr>
<tr>
<td>M.O.</td>
<td>73 % a</td>
<td>80 % a</td>
<td>77 % b</td>
</tr>
<tr>
<td>M.O. + O.O.</td>
<td>85 % b</td>
<td>91 % b</td>
<td>88% c</td>
</tr>
<tr>
<td>L.S.D</td>
<td>2.6</td>
<td>4.8</td>
<td>3.4</td>
</tr>
</tbody>
</table>

M.O: Mentha Oil. O.O: Olive Oil.

L.S.D: Least significant differences: \( P \leq 0.01 \).

### Table (3) The percentage of reduction of main symptoms of IBS 2 weeks after the end of treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Control</td>
<td>73%</td>
</tr>
<tr>
<td>M. O.</td>
<td>75%</td>
</tr>
<tr>
<td>M.O. + Olive oil</td>
<td>88%</td>
</tr>
</tbody>
</table>
Table (4): The overall response to treatments during the study.

<table>
<thead>
<tr>
<th>Result</th>
<th>Range</th>
<th>Control</th>
<th>M.O.</th>
<th>M.O + O.O</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2weeks on treatment</td>
<td>4weeks on treatment</td>
<td>2weeks after treatment</td>
</tr>
<tr>
<td>Excellent</td>
<td>More than 90%</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Very good</td>
<td>80-89%</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Good</td>
<td>70-79%</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Satisfactory</td>
<td>Under 70%</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
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REFERENCES

1061: 31-9.