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Topical Mastic Oil for Treatment of Functional Dyspepsia: A Randomized Triple-Blind Controlled Trial

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Abstract

Background: The main goal of the present study was to evaluate the effect of topical mastic oil, compared to placebo on treatment of functional dyspepsia (FD). **Materials and Methods**: Sixty-three patients with FD were included. Thirty-two subjects received the topical mastic oil (10 drops/TDS after meal) with massage and 31 patients received topical sesame oil with massage. Both groups received pantoprazole (40 mg daily) along with oil and massage. The severity of early satiation, postprandial fullness, epigastric pain and epigastric burning was assessed after 4 weeks using the Visual Analogue Scale (VAS) as well as frequency of symptoms. Satisfaction with the treatment was also assessed using a researcher-made questionnaire. Changes in the severity of symptoms were evaluated by Friedman's test. **Results**: Mean and standard deviation of age of the subjects were equal to 36.95±13.64 and 50 (79.4%) patients were female. Both groups experienced a significant decrease in the severity of all the four symptoms (P<0.001). The percentage of decrease in the severity of early satiation was significantly higher in the mastic group than the control group (76.03±34.91% vs. 37.24±38.86%, P=0.003). No significant differences were found in the percentage of decrease in the severity of postprandial fullness, epigastric pain and burning between the study groups (P=0.05, 0.06, and 0.13, respectively). The frequency of symptoms was decreased similarly in both groups. Satisfaction with the treatment was reported to be significantly higher in the mastic group than the sesame group (P=0.01). There were no intolerable side effects in both groups. **Conclusion**: Mastic oil reduced early satiation better than the placebo. In addition, satisfaction with the treatment was higher in the mastic group than the sesame group. **[GMJ.2021;10:e1965]** **DOI:10.31661/gmj.v10i0.1965**

Keywords: Functional Dyspepsia; Persian Medicine; Herbal Medicine; Clinical Trial; Mastic

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Introduction

Functional Dyspepsia (FD) as a non-ulcer dyspepsia [1] involves more than half of the patients with dyspepsia [2] and is a common gastrointestinal problem with a prevalence rate of 5-11% [3]. Its prevalence ranges from 2.2 to 29.9% in Iran [4]. FD does not cause death [5] but because it is considered a chronic condition [2], in addition to disrupting the quality of life [6], it also imposes significant financial and economic costs [4]. The main symptoms of dyspepsia are bothersome postprandial fullness, early satiation, epigastric pain, and epigastric burning in the absence of systemic, organic, or metabolic diseases existed in the past 3 months and at least started 6 months before diagnosis [2-8]. Drugs, such as acid suppressors, prokinetics, proton pump inhibitors, *H*. pylori eradication therapy, anti-anxiety medications, and antidepressants are used to mitigate the symptoms of FD, but no definitive treatment has been introduced for it [2, 3, 9, 10] thus, there is a need to evaluate new therapeutic methods. The frequent use of CAM, especially medicinal plants has increased in the recent years [11, 12]. Medicinal plants are widely used in treatment of gastrointestinal disorders [13, 14]. Persian traditional medicine (PM) is a branch of complementary and alternative medicine (CAM), which is also known in the world due to the presence of Persian scholars, such as *Avicenna* (*Ibn Sina*, 980-1032 C.E.) and other Persian physicians and philosophers like *Khwarazm*i (780- 850 C.E.) and *Razi* (865-925 C.E) [15]. About 105 plants from 37 families have been identified in the literature related to PM, which have been shown to treat various symptoms of dyspepsia [16]. Some of them, such as *Asparagus racemosus*, *Brassica oleracea*, *Mentha longifolia*, *Mentha pulegium*, *Mentha piperata, Ocimum basilicum*, *Pimpinella anisum, Nigella sativa, Curcuma longa, Glycyrrhiza glabra*, and *Zingiber officinale* have been evaluated in the previous scientific studies [17-19]. According to the PM, topical use of mastic gum and some other medicinal plants, such as *Cyperus rotundus* L., *Cyperus longus* L., *Eugenia caryophyllata* Thunb, and *Melilotus officinalis* (L.) Lam., *Olea europaea* L., and *Rosa damascena* Mill has been recommended for treatment of gastrointestinal diseases [20]. *Pistacia lentiscus* L. (var.chia) commonly known as Mastic is one of the herbal remedies recommended for treatment of gastrointestinal diseases in the traditional medicine , which belongs to the Anacardiaceae family [21] and is known by different names including masticha, mastiha, mastika, and mastix. Mastic has been known as gastric sedative and has been used for treatment of stomach pain (gastralgia), gastric ulcers, and bowel ulcers [22]. According to the PM, mastic oil has a warm and dry temperament and is used as a medicine to treat gastralgia and gastroparesis (which are mainly among the cold and wet diseases) [23]. The use of mastic gum has also been recommended topically in treatment of gastrointestinal diseases, such as gastroparesis (weakness of the stomach), difficulty swallowing (dysphagia), pain and inflammation, anorexia, dyspepsia, hiccups, severe nausea, intestinal ulcers, and diarrhea [20]. Oral mastic has anti-*Helicobacter pylori* (*H. pylori*) effect [24-26] as well as digestive aid [16] and antioxidant [27] properties and has been studied as a complementary treatment in the Inflammatory Bowel Disease (IBD) and Irritable Bowel Syndrome (IBS) [28]. In a previous study, the effect of applying 350 mg/BD of *Pistacia atlantica* resin for 4 weeks was compared with placebo and a significant decrease was observed in the severity and frequency of early satiation, pain, and nausea in the *Pistacia atlantica*-treated group compared to the placebo group [4]. Results of a clinical trial conducted on 148 patients with FD in 2010 in Greece showed that oral administration of 350 mg of mastic gum/ TDS for 3 weeks reduced the symptoms of dyspepsia compared to the placebo [29]. Since mastic oil is available in the Iran's medicinal plants̀ market and considering that there is no scientific evidence regarding its effectiveness in treatment of dyspepsia, this study was designed to evaluate the effect of mastic oil, compared to the placebo on the symptoms of the patients with FD.

Materials and Methods

Preparation of the Mastic Oil and Placebo

The drug used in this study was the mastic

gum oil prepared as a traditional medicine product by the Yas Daru Company (Tehran, Iran) (license number: S 93-0331). The used gum was registered in the School of Pharmacy, at Tehran University of Medical Sciences (herbarium code: PMP-880). The used mastic oil was prepared based on traditional medicine sources so that, 134 g of mastic gum with 536 g of sesame oil were placed in a glass container and were mixed. Then, they were placed in a water bath until the mastic was completely melted and well mixed with the sesame oil. Finally, the resulting mixture was filtered (according to the book of Qarabadin-e- Kabir written by *Aghili Khorasani*) [30]. The sesame oil was used as placebo prepared from the Barij Essence Pharmaceutical Company (Tehran, Iran).

Study Design

In this randomized, triple-blind parallel clinical trial, 63 patients with FD referred to the Gastrointestinal Clinic at Imam Khomeini Hospital from April 16, 2019 to November 10, 2019 were examined. Pilot study information and mean-comparison formula were used in both study groups to calculate the sample size. Twenty-eight subjects were considered for each group taking into account the alpha error of 0.05 and the study power of 80% to observe the effect size of 75% (for the four symptoms of dyspepsia). Inclusion criteria were having the age between 18-60 years old, both sexes, FD diagnosed based on the Rome IV Diagnostic Criteria (symptoms including pain or burning in the upper abdomen, early satiation, and postprandial fullness in the absence of a specific cause confirmed by endoscopic examination, for at least 12 weeks in the last 6 months), the negative test result regarding *Helicobacter pylori* status (negative *H. pylori*) (confirmed by endoscopic examination) [2, 31], not taking chemical or herbal medications from two weeks before beginning the study, and signing an informed written consent. Exclusion criteria were being diagnosed with dyspepsia along with dominant symptoms of heartburn; warning signs (including weight loss of more than 10% over a period of 6 months or losing 5% of previous weight in the last month progressively without dieting, gastrointestinal bleeding in the form of hematemesis (vomiting of the blood), pitch-like stools or iron-deficiency anemia, dysphagia or odynophagia, frequent vomiting or return of the food, abdominal mass, lymphadenopathy or ascites, family history of gastric malignancies in the first-degree relatives as well as IBD; gastritis; duodenitis; peptic ulcer; reflux (the most important complaint); taking nonsteroidal anti-inflammatory drugs or corticosteroids for more than a month; taking other herbal and chemical medications for treatment of dyspepsia; obstruction of the gastrointestinal tract in the endoscopy; the presence of malignant tumors in the gastrointestinal tract; history of gastric surgery; body mass index (BMI) above 30; pregnancy and lactation; smoking and consumption of alcohol and drugs; chronic heart, kidney, liver ,and gallbladder diseases; diabetes; and other metabolic diseases causing the dyspepsia. Attrition criteria included not taking the prescribed medication (taking less than 80% of the prescribed dose), personal desire to leave the study, intolerance to severity of the symptoms of dyspepsia and the need for other necessary interventions and treatments, and intolerance to the drugs prescribed in the study. Patients were initially assessed by the gastroenterologists through examination, medical history, and endoscopy (if necessary). Upper gastrointestinal (UGI) endoscopy was performed to rule out other organic causes and have a more accurate diagnosis. Block randomization method was used to randomly assign the subjects into two groups [intervention (n=32) and control (n=31)]. After selecting the four blocks randomly, random list was prepared by the statistical consultant and given to the executor. The treatments were presented as A and B with the same shape and appearance in order to blind the patients, executor, and analyst. Closed envelopes were used for allocation concealment, with the patient's number written on the envelope and type of intervention in the envelope. The statistician generated random allocation sequence, the gastroenterologists enrolled participants, and then they were assigned to groups to receive interventions. The first group received the pantoprazole (40 mg daily) along with mastic oil. The patients were asked to massage their upper abdomen (the epigastrium or epigastric region) with 10 drops of

the oil using their hands in a clockwise direction three times a day after meals. The second group received the pantoprazole along with the placebo (topical sesame oil). Interventions were administered during 4 weeks. Adherence to the treatment was measured using a checklist so that, the participants wrote a checkmark after doing the orders.

Follow-Up

Before beginning the intervention and at the end of the week, the patients were visited four times and the outcomes were measured. Treatment process and evaluation of the symptoms were followed up by making phone calls weekly during the intervention and 4 weeks after the intervention.

Outcome Measurement

Primary outcomes included severity of early satiation, postprandial fullness, epigastric pain, and epigastric burning. Secondary outcomes were patients' satisfaction with the treatment and possible complications. At the beginning of the study, patients' characteristics form including the age, sex, marital status, occupation, educational level, weight, height, etc. and patients' medical information form including the (individual and family) history of the disease and medication use, warning signs, duration of dyspepsia, tests and previous paraclinical examinations, pregnancy and lactation, and smoking and alcohol consumption were completed for each patient. A checklist was designed to collect the information about severity and frequency of the patients' symptoms. Dyspepsia symptoms were recorded at the beginning of the study and during the follow-ups [32, 33]. Severity of the symptoms was measured quantitatively using the VAS (visual analogue scale) and the frequency of symptoms was assessed qualitatively using the multiple-choice questions [34]. The rating was done as follows: without symptom (0), less than one day per month (1), between once a month and once a week (2), between once a week and once a day (3), and once a day or more (4). A researcher-made questionnaire called the TSTMQ (treatment satisfaction with traditional medicines questionnaire) was used to measure the patients' satisfaction with the treatment. The paper related to development of the above-mentioned scale is under publication. TSTMQ is a fourteen-item questionnaire designed in three domains (efficacy, convenience ,and overall satisfaction) that has been confirmed after measuring content validity ratio (>0.62) , content validity index (> 0.79) ,and exploratory factor analysis. Intraclass correlation coefficient (ICC) for the entire questionnaire was equal to 0.99 (95% CI: 0.95-0.99), (P<0.001) and Cronbachs alpha was equal to 0.87. In confirmatory factor analysis, all factor loadings and t-values were greater than 0.3 and 1.96, respectively. Also, $\chi 2/df$, root mean score error of approximation (RMSEA), and goodness of fit index (GFI) were equal to 2.6, 0.062, and 0.94, respectively. The observed or reported side effects were also compared in the two study groups after the intervention.

Statistical Analysis

SPSS Statistics for Windows, version 17 (SPSS Inc., Chicago, Ill., USA) was used to analyze the data. The missing data were replaced using the Last Observation Carried Forward (LOCF) method and Intention to treat (ITT) analysis was conducted. Quantitative data were described by mean and standard deviation and qualitative data were presented by the number and percentage of frequency.
The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normal distribution of data. The Friedman's test was used to evaluate changes in the severity of symptoms during the study. The Chi-Square and Mann-Whitney U tests were used to compare the variables between groups. The P-value of 0.05 was considered as statistically significant.

Ethical Considerations

This study was approved by the Ethics Committee of Islamic Azad University of Medical Sciences in Tehran, Iran on December 30, 2018 (code: IR.IAU.PS.REC.1397.322) and was registered in the Iranian registry of clinical trials (IRCT) (No. IRCT20090527001957N8).

Results

Three patients were excluded from the study

(out of 63 subjects) and LOCF and ITT analysis were done. Figure-1 shows the CONSORT flow diagram of the study.

Table-1 shows the frequency of age, sex, educational level, occupation, and BMI among the subjects. According to Table-1, there was

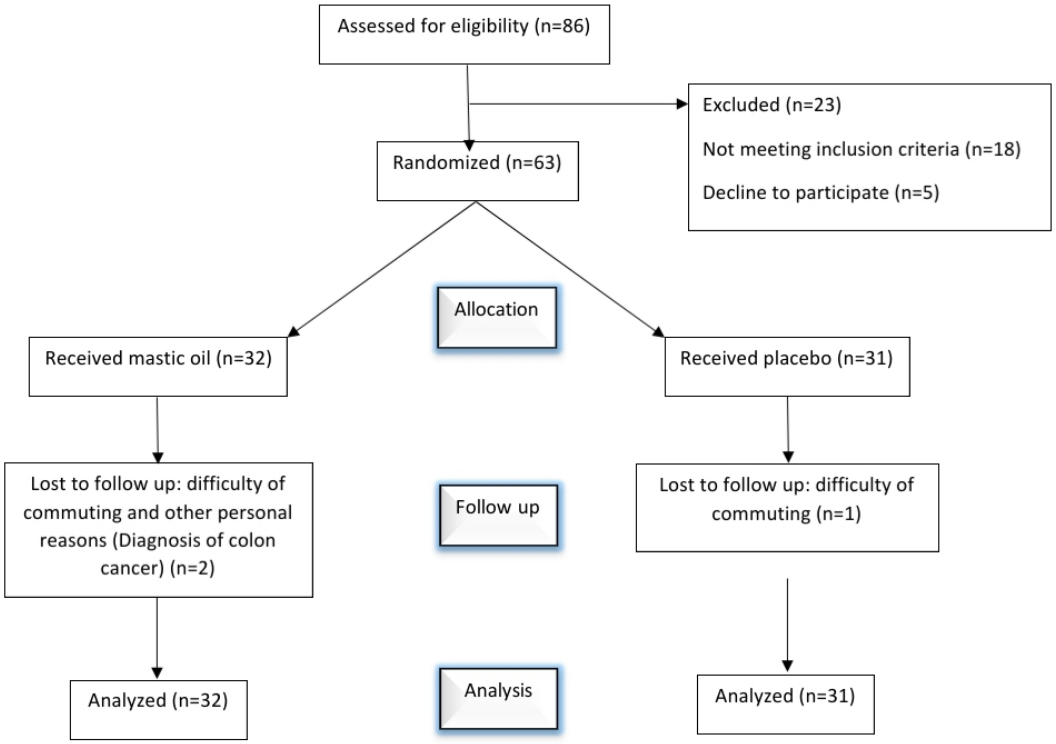

Figure 1. CONSORT flow diagram of the study

Table 1. Demographic Characteristics of Participants

	Mastic oil	Placebo	P-value*
Age (mean ± SD) (year)	37.3412.43	35.8713.20	0.8
Sex n (%)	Female: 27(84.4%) Male: 5(15.6%) f	Female: 23(74.2%) Male: 8(25.8%)	0.36
BMI (mean ±SD)	25.653.77	24.234.08	0.12
Marriage n (%)	Single: 10(31.3%) Married: 22(68.8%)	Single: 10(32.3%) Married: 21(67.7%)	1
Education n (%)	Uneducated: 1(3.1%) Elementary and middle school:10(31.3%) Highschool and diploma: 13(40.6%) University/college: 8(25%	Uneducated: 3(9.7%) Elementary and middle school: 10(32.3%) Highschool and diploma: 13(41.9%) University/college: 5(16.1%)	0.3
Job n (%)	Housewife: 16(50.0%) White- collar:10(31.2%) Blue- collar: 5(15.6%) Retired: 1(3.1%)	Housewife: 16(51.6%) White- collar: 8(25.8%) Blue- collar: 3(9.6%) Retired: 4(12.9%)	0.55

SD: standard deviation; *comparison between groups; **White- collar:** student, service, sales, clerical, administrative managerial, professional/technical; **Blue- collar:** agricultural/forestry/fishery, transport, production/machine operation/ laborer, protective/ inspective [30].

Table 2. The Severity of Dyspepsia Symptoms in Both Study Groups During the Study

	Group	Baseline (mean± SD)	Week 1 (mean± SD)	Week 2 (mean± SD)	Week 3 (mean± SD)	Week 4 (mean± SD)	P- value*	Percent Change (mean± SD)	P-value**
Postprandial fullness	mastic oil	7.372.16	3.202.44	2.512.59	1.882.15	1.772.02	<0.001	75.85	0.05
	placebo	7.472.50	3.283.41	3.323.30	3.213.09	3.583.16	<0.001	55.49	
Early satiation	mastic oil	7.711.59	4.073.41	2.152.96	1.782.67	1.682.53	<0.001	76.03	0.003
	placebo	6.442.90	2.973.03	2.732.37	3.702.78	3.822.79	<0.001	37.24	
Epigastric pain	mastic oil	6.642.57	2.562.54	1.412.53	1.162.23	1.482.60	<0.001	80.93	0.06
	placebo	6.602.70	2.433.04	2.063.19	2.123.05	2.563.23	<0.001	64.33	
Epigastric burning	mastic oil	6.332.50	1.672.03	.851.48	.601.57	.751.60	<0.001	89.36	0.13
	placebo	6.352.81	3.203.34	1.572.67	2.373.23	1.872.72	<0.001	74.24	

*Friedman test,**Mann-Whitney U test

Table 3. Change in the Severity of Symptoms after Stopping the Interventions

	Group	Mean± Standard deviation	P-value*
Postprandial fullness	mastic oil	-17.77± 110.45	0.68
	placebo	7.50 ± 44.34	
Early satiation	mastic oil	24.48 ±51.97	0.73
	placebo	4.77±34.94	
Epigastric pain	mastic oil	25±74.53	0.81
	placebo	-11.25±163.57	
Epigastric burning	mastic oil	-40.62±170.05	0.60
	placebo	29.06±49.03	

*Mann-Whitney U test

no statistical difference in the frequency of age, sex, marital status, educational level, occupation, and BMI between the study groups. At baseline, the two study groups had the same severity of postprandial fullness, early satiation, epigastric pain, and epigastric burning. Table-2 presents the changes in the severity of dyspepsia symptoms in the two study groups during the study. According to Table-2, severity of all the four symptoms of dyspepsia was significantly reduced in the two study groups during the study (P<0.001). The decrease in the early satiation was significantly higher in the mastic oil-treated group than the control group (P=0.003). In the other three symptoms, although there was a further decrease in the mastic oil-treated group, but there was no statistically significant difference between the two study groups. Table-3 shows percentage of change in the severity of symptoms after stopping the interventions. Negative numbers indicate an increase in the severity of symptoms. As shown in Table-3, after stopping the interventions, percentage of

Table 4. The Frequency of Dyspepsia Symptoms in Both Study Groups at Different Time Points

Group		Baseline n (%)							P- value*	Week 4 n (%)							P-value*
		0	1	2	3	4	5	6		0	1	2	3	4	5	6	
A	mastic oil	5 (15.6)	0 (0.0)	1 (3.1)	2 (6.3)	9 (28.1)	3 (9.4)	12 (37.5)	0.45	17 (53.1)	0 (0.0)	3 (9.4)	2 (6.3)	5 (15.6)	0 (0.0)	5 (15.6)	0.73
	placebo	8 (25.8)	0 (0.0)	2 (6.5)	0 (0.0)	5 (16.1)	5 (16.1)	11 (35.5)		17 (54.8)	0 (0.0)	1 (3.2)	3 (9.7)	3 (9.7)	1 (3.2)	6 (19.4)	
B	mastic oil	13 (40.6)	0 (0.0)	1 (3.1)	0 (0.0)	4 (12.5)	1 (3.1)	13 (40.6)	0.61	25 (78.1)	0 (0.0)	1 (3.1)	1 (3.1)	1 (3.1)	0 (0.0)	4 (12.5)	0.36
	placebo	14 (45.2)	0 (0.0)	1 (3.2)	2 (6.5)	4 (12.9)	2 (6.5)	8 (25.8)		20 (64.5)	0 (0.0)	2 (6.5)	3 (9.7)	4 (12.9)	0 (0.0)	2 (6.5)	
C	mastic oil	1 (3.1)	2 (6.3)	3 (9.4)	0 (0.0)	9 (28.1)	4 (12.5)	13 (40.6)	0.32	22 (68.8)	0 (0.0)	3 (9.4)	2 (6.3)	1 (3.1)	0 (0.0)	4 (12.5)	0.27
	placebo	2 (6.5)	0 (0.0)	5 (16.1)	3 (9.7)	9 (29.0)	4 (12.9)	8 (25.8)		15 (48.4)	0 (0.0)	4 (12.9)	2 (6.5)	4 (12.9)	3 (9.7)	3 (9.7)	
D	mastic oil	4 (12.5)	1 (3.1)	3 (9.4)	2 (6.3)	6 (18.8)	7 (21.9)	9 (28.1)	0.18	24 (75.0)	1 (3.1)	4 (12.5)	1 (3.1)	1 (3.1)	0 (0.0)	1 (3.1)	0.57
	placebo	11 (35.5)	1 (3.2)	0 (0.0)	4 (12.9)	5 (16.1)	3 (9.7)	7 (22.6)		22 (71.0)	0 (0.0)	2 (6.5)	1 (3.2)	1 (3.2)	2 (6.5)	3 (9.7)	

*Chi- square test for comparison between groups; **A:** postprandial fullness; **B:** early satiation; **C:** epigastric pain; **D:** epigastric burning; **0:** never; **1:** One day a month; **2:** 2-3 days a month; **3:** 1 day a week; **4:** 2-3 days a week; **5:** More than 3 days a week; **6:** everyday

change in the severity of all the four symptoms was equal in both study groups. Table-4 presents the frequency of symptoms. According to Table-4, the frequency of all the four dyspepsia symptoms was decreased in both study groups during the study, and there was no significant difference in this respect between both groups. Table-5 presents a comparison of the patients' satisfaction with the treatment in both study groups. As shown in Table-5, satisfaction with the treatment, the rate of overall opinions, and the total score of the questionnaire were significantly higher in the mastic oil-treated group compared to the control group. Although, for simplicity of the analysis, there was no difference between the two study groups. No serious complications were observed in the study groups.

Discussion

Our results showed that consumption of topical mastic oil along with oral pantoprazole for 4 weeks reduced severity and frequency of FD symptoms. Although, mastic oil was better in reducing all the four symptoms of dyspepsia than the sesame oil, only severity of early satiation was reduced significantly. Satisfaction with the treatment was significantly higher in the mastic oil-treated group than the control group, and patients in the mastic oil-treated group more frequently tended to re-use the mastic oil or introduce it to other patients with FD. No serious side effects were observed regarding the use of mastic oil in this study. Dobbs *et al*., (2010) evaluated the effect of using 350 mg of the Chios mastic gum three times a day on improvement of FD symptoms in 148 patients through a randomized, double-blind clinical trial. They showed that the mastic gum significantly improved the symptoms of dyspepsia in 77% of the patients, especially gastric pain (1.05±0.05 vs. 0.43±0.03, P<0.05) and heartburn (0.77±0.03 vs. 0.21±0.01, P<0.05) compared to the placebo (lactose). They found no significant difference in reducing the severity of upper abdominal bloating, stomach pain before meals, nausea and vomiting, burping, acid reflux, gastric acidity, and anorexia between the two study groups [29]. They stated that possible mechanism for the effect of oral mastic on epigastric burning is related to its prokinetic effect, which could result from a gel formed by the polymer under acidic conditions [29]. In their study, mastic gum was used orally and alone, while in the present study, all the subjects received routine treatment of dyspepsia along with mastic oil and placebo for taking into account the ethical considerations. They diagnosed the dyspepsia based on the Rome II Diagnostic Criteria and their intervention was administered during 3 weeks. But in the present study, diagnosis was made on the basis of the Rome IV Diagnostic Criteria, and the intervention was administered during 4 weeks and follow-up study was conducted one month after the intervention.

Differences in the results of both studies can be attributed to differences in the diagnostic criteria used for diagnosis of the disease, sample size, and type of drug administration. The sample size in the study by Dobbs *et al*., was much larger than that of the present study. It seems that oral type of mastic can reduce gastric pain and burning in the people with dyspepsia. While the use of mastic oil is more effective than only embrocating in reducing postprandial fullness and early satiation. Herein, reduction of other symptoms of dyspepsia in the two study groups was related to the effect of pantoprazole along with embrocating and it cannot be attributed to the mastic oil. Besides, the effect size was less than the extent considered initially for determining the sample size, so a larger sample size is required

Table 5. Patients' Satisfaction with the Treatment in Both Study Groups

	Efficacy (mean± SD)	Convenience (mean± SD)	Overall satisfaction (mean± SD)	Total score (mean± SD)
Mastic oil	23.202.55	26.932.98	14.131.81	69.265.30
Placebo	21.103.41	26.333.08	13.162.30	65.536.17
P-value*	0.006	0.36	0.03	0.01

*Mann- Whitney U test for comparison between groups; **SD:** Standard deviation

to show the differences between the two study groups in the present study. *Eftekhar Afzali et al.,* (2018), in a clinical trial evaluated the effect of *Pistacia atlantica* on patients with FD (diagnosed based on the Rome IV Diagnostic Criteria). One group received a capsule containing 350 mg of *Pistacia atlantica* resin twice a day along with 150 mg of sugar, and the other group received a capsule containing 350 mg of starch along with 150 mg of sugar for 4 weeks. At the end of the study, a significant decrease was found in the severity and frequency of early satiation, nausea, pain, and burning in the *Pistacia atlantica*-treated group compared to the placebo group, but no significant difference was observed in the severity of bloating, abdominal fullness, burping, and vomiting compared to the control group [4].
In this study, another type of *Pistacia* was investigated that seemed to be more effective than the placebo, compared to our study in terms of sample size.
According to the results of the above-mentioned studies, it seems that oral form of mastic works better than topical form, however, it is necessary to compare the effect of topical oil in larger sample size without standard treatment and with oral form to prove this hypothesis. Another important point is that, herein, the sesame oil was used to apply blinding because there is no study investigated the effect of sesame oil on dyspepsia. But according to the traditional medicine, rubbing with oil can influence the body even without medication [35]. Therefore, the small difference between the two groups in the present study could be due to selection of the control group.
There are several reasons regarding development of dyspepsia including excessive secretion of gastric acid, gastric motor disorders, delayed gastric emptying [2], visceral hypersensitivity to physical and chemical stimuli, *H. pylori* infection, food allergies, social and psychological factors, alcohol consumption, smoking [2], air swallowing, obesity, and overeating [36]. The probable mechanism of action for oral mastic gum in FD is related to its antacid [37] and anti-inflammatory effect [26] and its cellular protective effects on gastrointestinal tract [38]. Some studies have indicated that mastic gum is a potentially effective treatment for *H. pylori* infection [39, 40], which can prevent the inflammation caused by *H. pylori* infection through inhibiting neutrophil activity under laboratory conditions [26]. According to the PM, symptoms of dyspepsia occur due to predominance of cold temperament and weakness of the stomach [23]. Mastic gum has been reported to be warm and dry in terms of temperament and is known as a diluent, digestive, and laxative agent and also is able to strengthen the stomach, intestines, and liver. It eliminates the stomach gas and noises and relieves indigestion, strengthens the stomach, decreases difficulty in swallowing, decreases pain and inflammation, alleviates severe nausea, intestinal ulcers, and diarrhea, and also stimulates appetite [41]. Also, topical utilization of mastic has been found to be effective in addition to its oral form [20].
This study is the first clinical trial evaluated the effect of mastic oil on FD. Given preliminary nature of the research on this formulation, sample size was considered to be small, which was a limitation in the present study. Therefore, it is recommended to conduct more studies with a larger sample size.
Besides, combining the pantoprazole with mastic oil did not allow us to determine the mastic oil's net effect. Also, it is suggested to conduct a comparative study for comparing the effect of mastic oil with its oral form in FD.

Conclusion

Our results showed that mastic oil reduced early satiation better than the placebo. Also, satisfaction with the treatment was higher in the mastic group than the control group.

Conflict of Interest

There is nothing to declare.

Acknowledgement

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