



Effects of *Pistacia lentiscus* and Coriander Triphala on Adult Gastroesophageal Reflux Disease: A Randomized Double-Blinded Clinical Trial

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Abstract

Background: The cardinal symptoms of gastroesophageal reflux disease include heartburn (pyrosis) and regurgitation. Conventional treatment is done by proton pump inhibitors. In Persian traditional medicine, several herbs (single or combined) have been used to treat gastrointestinal disorders.

Objectives: This study aimed to assess the effects of *Pistacia lentiscus* (mastic) and Coriander Triphala on reflux symptoms compared to omeprazole in a double-blinded randomized clinical trial.

Methods: In a double-blinded, multicenter, randomized clinical trial, we assessed the effects of *Pistacia lentiscus* L., Coriander Triphala, and omeprazole on the symptoms of GERD in Tabriz, Iran, in 2018 - 2019. Thus, 105 patients with GERD symptoms were assigned randomly to three groups as group A (*Pistacia lentiscus* L., 1000 mg/TDS), group B (Coriander Triphala, 1000 mg/TDS), and group C (omeprazole, 20 mg/day plus five placebo capsules per day). The assessments were done at the beginning and the end of the study using FSSG, VAS, RS, and GERD-HRQL questionnaires.

Results: In the beginning, no significant differences were observed between the groups in the background characteristics. There was no statistically significant difference between *Pistacia lentiscus*, Coriander Triphala, and omeprazole in the improvement of FSSG, VAS, GERD-HRQL, and reflux scores. In all groups, the FSSG, VAS, reflux, and GERD-HRQL scores significantly decreased and improved after four weeks of intervention compared to the respective baselines. The FSSG score improvements after four weeks of intervention were 73.68%, 83.33%, and 68.62%, in groups A, B, and C, respectively. The VAS score improvements were 66.66%, 75.00%, and 62.50% in groups A, B, and C, respectively. Improvements in GERD-HRQL were 90.00%, 91.28%, and 82.00%, in groups A, B, and C, respectively. Reflux improvements were 66.66%, 80.00%, and 66.66% in groups A, B, and C, respectively.

Conclusions: The results showed that *Pistacia lentiscus* and Coriander Triphala are as effective as omeprazole in the treatment of GERD.

Keywords: Coriandrum, GERD, *Pistacia lentiscus*, Pyrosis, Reflux, Triphala

1. Background

Gastroesophageal reflux disease (GERD) is to encompass a family of conditions with commonality caused by gastroesophageal reflux resulting in either troublesome symptoms or an array of potential esophageal and extraesophageal manifestations (1). Heartburn and regurgitation are cardinal esophageal symptoms that occur when gastric contents regurgitate into the esophagus or oral cavity. Various factors are associated with GERD, such as sliding hiatal hernia, increased transient lower esophageal

sphincter (LES) relaxation, low LES pressure, delayed gastric emptying, and risk factors of reflux such as obesity and smoking (2). The GERD prevalence is estimated to be 10% to 27.8% in the Western and European populations (2-5) and 3 - 7% in Asia (6). Approximately 20% of Iranian people suffer from this disease (7). The complications of GERD include esophageal ulcer, peptic esophageal strictures, and Barrett's esophagus, which can lead to adenocarcinoma (4). Regarding these complications, GERD can impose a heavy therapeutic and socioeconomic burden and impair

the quality of life and overall work productivity of patients (8).

Proton pump inhibitors (PPI) and histamine-2 receptor (H₂) blockers are used for the GERD treatment (1). However, the daily use of a standard dose of PPI has not proven to clinically eliminate the GERD symptoms in 20% - 30% of patients (4, 9). Furthermore, many patients should receive these medications for a long time or even life-long, which causes side effects such as *Clostridium difficile* infections (10), kidney problems (11), hip fractures (12), and respiratory infections (13). The symptoms easily relapse after stopping PPIs (1, 14). Due to the failure of conventional treatments, a growing interest has been developed in herbal medicine. Among many different herbaceous plants, *Pistacia lentiscus* L. (Mastic) from the Anacardiaceae family (15) has the potential to strengthen gastric innate heat, which proper digestion is dependent on, and it is recommended for such a purpose in the Persian traditional medicine (PTM) literature. *Pistacia* species possess anti-inflammatory (16), anti-ulcerogenic (17), and anti-*Helicobacter pylori* (18) properties. Mastic is a good source of tonic, varnishing, tendering, astringent, and stubbing agents (19). Based on reliable PTM references, mastic has been a potent medicinal herb in the management of gastrointestinal (GI) tract disorders since ancient times (20). According to the European medicine agency, there are no medicinal products authorized or registered in the EU/EEA containing preparations from the Resin form of *Pistacia lentiscus* L., called "mastic", as a single active substance (15). Nowadays, only is mastic oil or its combination with honey used for therapeutic purposes in PTM, but as far as we know, its powdered form does not exist in Iran's medicinal market. This study was designed to evaluate the efficacy of a specific dose of the capsulized powder of *Pistacia lentiscus* L. as a single active substance in the management of GERD patients.

Triphala is composed of the fruits of three herbal plant trees, *Phyllanthus emblica* L. (Amla), *Terminalia bellerica* Retz., and *Terminalia chebula* Retz (21). It possesses anti-inflammatory (22), antimicrobial (23), antiulcer (24), antiviral, and antibacterial (25) properties. Even though Triphala has a long history in many different therapeutic applications in PTM and ayurvedic medicine such as the treatment of digestive disorders (21-26), its combination with Coriander (as Coriander Triphala) is unique to PTM. *Coriander sativum* belongs to the Apiaceae family (27) and has antimicrobial (28), anti-*H. pylori* (29), and antioxidant (30) properties. To the best of our knowledge, no clinical trial has been conducted so far to evaluate the efficacy of this combination (Coriander Triphala) in the treatment of GERD. Therefore, a randomized, double-blinded clinical trial was designed to evaluate its efficacy in the improve-

ment of patients with GERD symptoms.

2. Objectives

The current work aimed to assess the effects of *Pistacia lentiscus* (Mastic) and Coriander Triphala on the reflux symptoms compared to omeprazole via a double-blinded randomized clinical trial.

3. Methods

3.1. Study Design

This study was a multicenter, randomized, outpatient, double-blinded clinical trial. We evaluated the effects of *Pistacia lentiscus* and Coriander Triphala capsules compared to omeprazole on the frequency of reflux symptoms in patients with GERD.

3.2. Participants

Male and female patients aged 18 years or older with confirmed symptomatic GERD were included in the study. The diagnosis was made by a gastroenterologist based on the endoscopic findings and/or clinical symptoms. No other medication was used by the patients during the study. The study was carried out in Shahid Madani and Sina hospitals and Sheikhalraeis Clinic, as governmental, referral, specialized, and subspecialized centers, affiliated to the School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran, from September 2018 to December 2019. The aim and process of the study were explained to all patients, and they completed and signed informed consent forms before participation.

The exclusion criteria were taking anti-reflux medications, warning signs such as anemia, significant unintentional weight loss, Barrett's esophagus, vomiting, and esophagitis with non-reflux causes, using non-steroidal anti-inflammatory drugs (NSAIDs), systemic diseases such as liver and kidney disease, uncontrolled diabetes, pregnancy, and lactation.

The follow-up procedure was performed by telephone contacts and/or visits. Patients were visited three times: Before the intervention, two weeks later (for follow-up), and at the end of the treatment. Symptoms were evaluated and recorded based on the questionnaires of GERD-health-related quality of life (GERD-HRQL), reflux syndrome score, Visual Analog scale (VAS), and the Frequency scale for the symptoms of GERD (FSSG).

3.3. Intervention

First, 105 patients were randomized into three groups (A, B, and C). According to traditional recommendations and a previous experimental study on the administrative dose of mastic, the first group (A) received 500 mg powders in capsules (1000 mg TDS). The B group received Coriander Triphala 500 mg in capsules (1000 mg TDS), and the C group received a 20 mg capsule of omeprazole and five placebo capsules per day for four weeks.

Mastic gum was purchased from a local herb market in Tabriz, Iran. Its effective pharmaceutical ingredient was analyzed and verified by the Pharmacognosy Laboratory of Drug Applied Research Center of Tabriz University of Medical Sciences. Coriander Triphala capsules (500 mg) were purchased from a medicinal plant market (Toba), approved by the Ministry of Health, Treatment, and Medical Education, in Tehran, Iran. After the screening of patients by a gastroenterologist, they were referred to a PhD candidate in Persian traditional medicine who used FSSG, VAS, RS, and GERD-HRQL questionnaires. The patients received the respective interventions in line with randomization. The physician completed the same questionnaires after treatment.

3.4. Preparation of *Pistacia lentiscus*

The dry resin (without stone) was purchased from an herbal market in Tabriz, Iran. The resin was completely ground. The culture results showed that the powder was free of any microbes and fungi. We prepared capsules containing 500 mg powders using a capsule press machine under the supervision of a pharmacist, and then the appearance, shape, and weight of the capsules were checked.

3.4.1. The Isolation of Essential Oil

Essential oil of the mentioned gum was obtained by the hydrodistillation method using a Clevenger type apparatus for 3 h. The oil was dried over anhydrous sodium sulfate and stored in sealed vials before chemical analyses.

3.4.2. GC-MS Analysis

About 1 μ L of volatile oil/hexane solution was injected into a GC-MS analyzer using a Shimadzu capillary GCMS-QP5050A gas chromatograph-mass spectrometer and DB1 capillary column (60 m \times 0.25 mm, I.D. film thickness 0.25 μ m) using helium (He) as the carrier gas with a flow rate 1 mL/min along with a split ratio of 1:24, which was equipped with a flame ionization detector (FD). The condition of GC was as follows: The range of column temperature started at 50°C for 3 min, finally holding 2 minutes at 270°C. The injector and detector temperatures were 240°C and 280°C, respectively. Moreover, all mass spectra were recorded in

an electron-impact mode with an ionization voltage of 70 eV. Other parameters were as follows: Solvent delay 3 min, scan speed 2000 amu/s, scan range 30 - 600 amu, and eV voltage 3000 V. Essence was obtained with 0.375% v/w, and Triterpenoid acids were identified as the main components of mastic resin. Placebo capsules were prepared in the same color, shape, size, and weight with starch powder. The packs and labels of all treatment groups were also similar.

3.5. Outcome Measures

In this study, the primary outcome was the changes in the scores of the FSSG questionnaire regarding the heartburn frequency based on the number of days of having heartburn. The secondary outcomes were changes in the frequency of heartburn, regurgitation, nausea, quality of sleep with burning and reflux, other drugs used in addition to previously prescribed medications to relieve reflux symptoms, quality of life, and drug side effects. The physician and participants completed all questionnaires at the beginning and the end of the treatment.

3.6. Sample Size

According to a previous study, we estimated the sample size with the power of 80%, the significance level of 0.05, and a 10% dropout rate in each group. The sample size was calculated to be 35 patients in each group, and a total of 105 patients were randomly assigned to three groups.

3.7. Safety Assessment

All patients had follow-up visits for possible side effects, and if present, the symptoms were documented in a form.

3.8. Randomization

In this trial, randomization was done with fixed-size blocks. The random numbers were used to select the blocks. Therefore, 105 eligible volunteers were randomized into three groups. Randomization was performed by using a random number table. As all capsules were similar in color, weight, size, shape, and container in three groups, all patients and researchers, physicians, evaluator, and data analysts were blinded to the type of drug and the allocation of arms.

3.9. Ethical Review

Patients studied informed consent forms and signed them before inclusion to trial. This study was carried out according to the Ethical Guidelines for Clinical trials and approved by the Ethics Committee of Tabriz University of Medical Sciences (code: IR.TBZMED.REC.1396.968).

In addition, this clinical trial was registered at the Iranian Registry of Clinical trials database (<http://www.irct.ir>) with IRCT20180127038524N1.

3.10. Statistical Analysis

We used the F-test to compare background factors, including height, age, BMI, and weight. The chi-test was used for other variables measured on the nominal scale. The Kruskal-Wallis test was applied to distinguish differences between the three groups in VAS, FSSG, RS, and GERD-HRQL scores before and at the end of the treatment. Using the following formula, the improvement rates were calculated based on the VAS, FSSG, RS, and GERD-HRQL scores, and then the Kruskal-Wallis test was performed.

Improvement rate (%) = $\frac{([\text{pre-score}] - [\text{post-score}])}{[\text{pre-score}]} \times 100$

The Wilcoxon signed ranked test was used to evaluate the effectiveness of intervention after four weeks in three groups for heartburn, rubbing of the chest, burning after meals, unusual burning, heartburn in bending, stuck something, the acid in the throat, and other symptoms. The Kruskal Wallis test was used to compare the FSSG scores before and after the intervention between the three groups. We also performed the Wilcoxon signed ranked test for analyzing the differences before and after the intervention within each group for the FSSG scores. The statistical analysis was performed with IBM SPSS ver. 25, and the data were reported as percentages or percentiles.

4. Results

4.1. Patients Enrollment

From 29/09/2018 to 22/12/2019, 167 participants were evaluated for eligibility. All patients received healthy lifestyle modifications, as follows: masticating food well, diet, weight loss, using antioxidants, vitamin C, avoiding acidic foods, avoiding drinking water or cola with the meal, fast eating, and smoking, correct sleep position, avoiding meals within three hours of bedtime, using the tonic, and strengthening of digestion. By modifying the lifestyle, the symptoms of GERD improved in 20 patients, and they were not included in the trial. According to the inclusion criteria, 105 patients were included in the study, and they signed informed consent forms. They were divided into three groups. Thirty-five patients were assigned to each group (A, B, and C). [Figure 1](#) shows the flow diagram of the study and presents the participants and excluded cases. Data were analyzed in the ITT population.

As shown in [Table 1](#), the mean age of the patients was 42.48 ± 15.07 , 33.65 ± 11.81 , and 41.96 ± 10.07 in the A, B,

and C groups, respectively. Additional demographic information is presented in [Table 1](#). In the beginning, no significant differences were observed between the groups in the background characteristics.

The Kruskal-Wallis test results showed no significant differences in the VAS, FSSG, RS, and GERD-HRQL scores before and after the intervention between the three groups ([Table 2](#)). In all groups, the total FSSG ($Z = -4.200$, $P = 0.000$), VAS ($Z = -4.222$, $P = 0.000$), RS ($Z = -4.218$, $P = 0.000$), and GERD-HRQL ($Z = -4.199$, $P = 0.000$) scores significantly decreased and improved after four weeks of intervention. We found no significant differences in the improvement rate of GERD-HRQL, RS, FSSG, and VAS between the three intervention groups ([Table 3](#)).

The FSSG questionnaire scores with eight items were compared before and after the intervention. However, there was no significant difference in the FSSG scores before and at the end of the treatment between the three groups.

The Wilcoxon signed-rank test results showed heartburn ($Z = -6.929$, $P = 0.000$), rubbing of the chest ($Z = -4.864$, $P = 0.000$), burning after meals ($Z = -6.640$, $P = 0.000$), unusual burning ($Z = -6.227$, $P = 0.000$), heartburn in bending ($Z = -4.779$, $P = 0.000$), stuck something ($Z = -6.462$, $P = 0.000$), the acid in the throat ($Z = -5.956$, $P = 0.000$), and other symptoms ($Z = -4.268$, $P = 0.000$) scores significantly decreased in all groups after four weeks of the intervention ([Figure 2](#)).

5. Discussion

In this study, we evaluated the effects of *Pistacia lentiscus*, Coriander Triphala, and omeprazole on the improvement of gastroesophageal reflux disease (GERD) symptoms in a double-blinded, randomized clinical trial. The results showed that regurgitation and heartburn frequency, quality of life, visual analog scale, and reflux scores in GERD patients significantly decreased in the three intervention groups. Lifestyle and diet modification, weight loss (to reach appropriate weight), use of proper foods and drinks, raising the head before sleeping, etc. are the first steps to reduce GERD symptoms. According to Persian traditional medicine (PTM), consideration and observation of healthy lifestyle recommendations help to maintain body health, especially the stomach and digestive system.

Coriander Triphala used as the intervention in group B has multi-ingredient compositions, including *Coriander sativum* (Coriander), *Phyllanthus emblica* L. (Amla), *Terminalia chebula* Retz., and *Terminalia bellerica* Retz. Coriander Triphala is an astringent medicine. These herbal remedies are assigned to dry and cold temperaments (Mizaj)

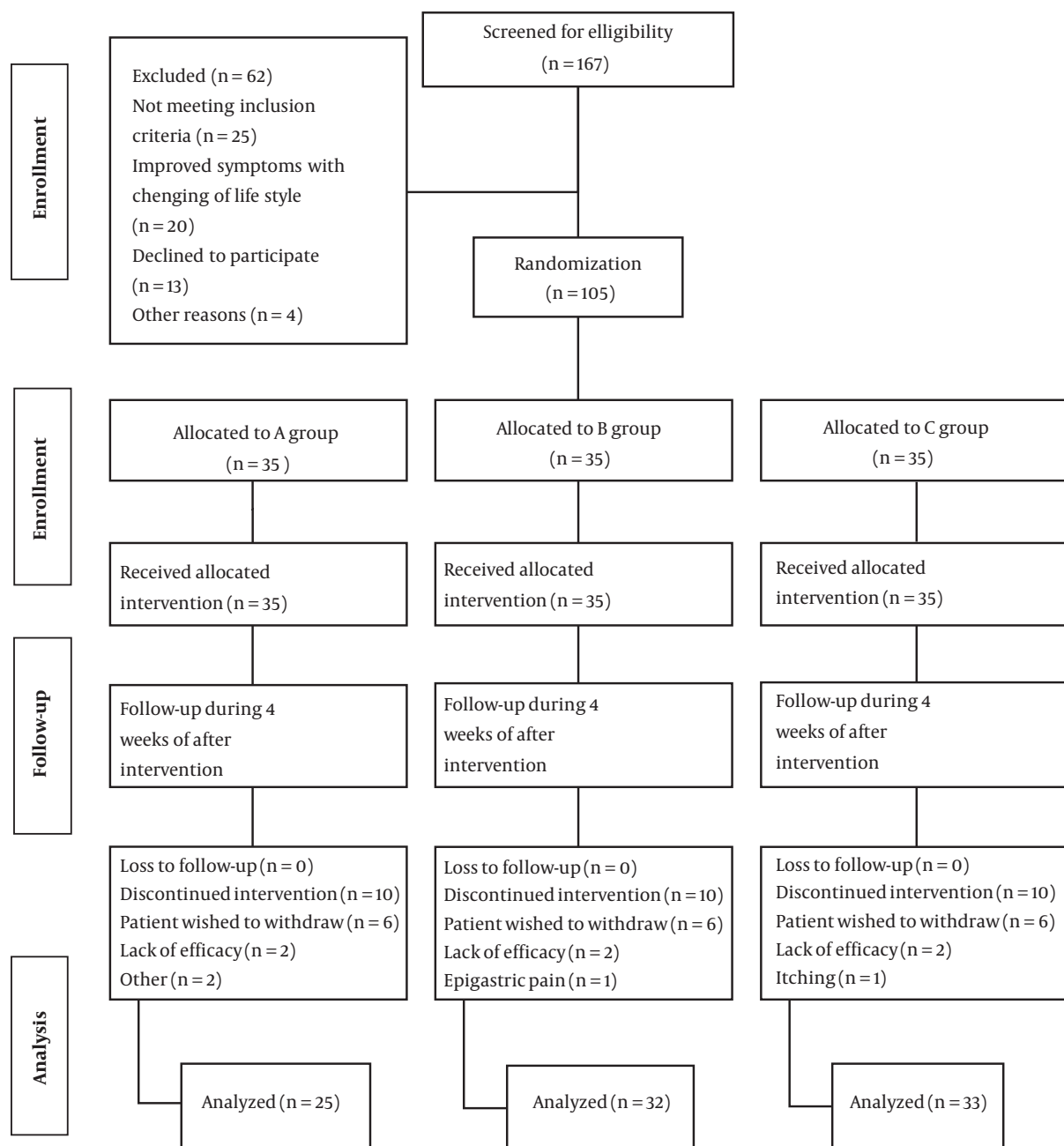


Figure 1. The flow of participants in the study

and are great sources of phenolic agents. The major components of Triphala are gallic acid, tannins, ellagic acid, and chebulinic acid, which have been reported to have antioxidant and immunomodulatory activities. They have tonic, antispasmodic, carminative, astringent, digestive, and laxative effects. A study in rats demonstrated that colitis was significantly reduced by Triphala (300 mg/kg) due

to its flavonoid components that have antioxidant properties (31). Baliga et al. (21) reported that the components of Triphala were effective in colic pain, constipation, hemorrhoids, indigestion, anorexia, liver disorders, gastritis, vomiting, abdominal ailments, and belching. Peterson et al. (32) reported that mucous, abdominal pain, constipation, hyperacidity, and distention were decreased by using

Table 1. Background Factors in the Three Groups^a

Characteristics	Intervention			Total Mean	Test
	A	B	C		
Age	42.48 ± 15.07	33.65 ± 11.81	41.96 ± 10.07	40.93 ± 12.22	F = 0.872, P = 0.422
Height	166.52 ± 8.54	167.31 ± 9.39	168.63 ± 8.80	167.57 ± 8.89	F = 0.419, P = 0.659
Weight	74.94 ± 12.03	73.32 ± 13.75	73.72 ± 15.76	73.92 ± 13.95	F = 0.099, P = 0.906
BMI	26.96 ± 3.20	26.32 ± 4.96	25.78 ± 4.56	26.30 ± 4.36	F = 0.512, P = 0.601
Smoking habits					
Yes	0	3 (9.4)	5 (15.2)	8 (8.9)	$\chi^2 = 4.046, P = 0.132$
No	25 (100)	29 (90.6)	28 (84.8)	82 (91.1)	
Gender					
Female	14 (56)	15 (46.1)	14 (42.4)	43 (47.8)	$\chi^2 = 1.067, P = 0.587$
Male	11 (44)	17 (53.1)	19 (57.6)	47 (52.2)	
Marital status					
Single	22 (88)	27 (84.4)	31 (96.9)	80 (89.9)	$\chi^2 = 5.671, P = 0.225$
Married	2 (8)	5 (11.5)	1 (3.1)	8 (9.0)	
Other	1 (4)	0	0	1 (1.1)	
Coffee					
Yes	1 (4)	1 (3.3)	0	2 (2.3)	$\chi^2 = 1.225, P = 0.534$
No	24 (96)	31 (96.7)	33 (100)	88 (97.7)	
Chocolate					
Yes	4 (16)	6 (18.8)	1 (3.0)	11 (12.2)	$\chi^2 = 4.202, P = 0.122$
No	21 (84)	26 (81.3)	32 (97.0)	79 (87.8)	
Soft drink					
Yes	9 (36)	7 (21.9)	1 (3.0)	17 (18.9)	$\chi^2 = 4.320, P = 0.126$
No	16 (64)	25 (78.1)	32 (97.0)	73 (81.1)	
Spice					
Yes	12 (48)	10 (31.3)	9 (27.3)	31 (34.4)	$\chi^2 = 2.931, P = 0.231$
No	13 (52)	20 (68.8)	24 (72.7)	59 (56.6)	
Pickle					
Yes	10 (40)	9 (28.1)	7 (21.2)	26 (28.9)	$\chi^2 = 2.458, P = 0.293$
No	15 (60)	23 (71.9)	26 (78.8)	64 (71.1)	

^aValues are expressed as mean ± SD or No. (%).

Triphala. Tarasiuk et al. (33) and Karkon et al. (34) reported Triphala as an anti-*H. pylori* agent. Karkon Varnosfaderani et al. (26) reported that *Embllica officinalis* L. probably could inhibit refluxate diffusion into the intercellular spaces and decrease intracellular space volume and suppress brain-gut interactions. *Coriander sativum* L. is a medicinal herb that belongs to the Apiaceae family (35). It has anti-*H. pylori* (27), anti-inflammatory, antioxidant (36), antispasmodic, and carminative (86) activities. In PTM, it is used for dyspepsia (37). Its antiulcer activity might be attributed to the

formation of a protective layer (37). It seems that the synergistic effects of Triphala and Coriander have made them great, high-potential agents for improving GI diseases.

In our study, we observed 80% and 83.33% improvements in RS and FFSG scores, respectively, in group B, which received Coriander Triphala as an intervention (Table 3). Patients in this group showed a significant decrease in GI symptoms such as heartburn, burning after meals, unusual burning sensation, dysphagia, and acid in the throat after treatment with Coriander Triphala (Figure 2). The im-

Table 2. Comparison of Symptom Scores Before and After Intervention in Three Groups

Group	GERD-HRQL Before Intervention	GERD-HRQL After Intervention	Reflux syndrome Before Intervention	Reflux syndrome After Intervention	FSSG Before Intervention	FSSG After Intervention	VAS Before Intervention	VAS After Intervention
A								
Median	15.00	1.00	5.00	1.00	14.00	4.00	7.00	2.00
Per-centiles								
25	11.000	1.00	3.00	0.00	12.50	2.00	5.50	1.00
75	22.50	3.0	7.00	2.00	15.50	5.00	8.50	3.00
B								
Median	17.00	1.00	5.00	1.00	15.00	2.00	6.00	1.50
Per-centiles								
25	12.00	0.00	4.00	0.00	11.25	1.00	5.00	0.00
75	24.25	4.50	6.00	2.00	18.00	5.00	7.75	3.00
C								
Median	20.00	4.00	5.00	1.00	13.50	4.00	7.00	3.00
Per-centiles								
25	13.00	1.00	3.00	.00	10.00	1.00	5.00	1.50
75	25.00	7.00	7.50	3.00	16.00	6.00	8.00	4.00
Kruskal-Wallis	0.675	3.832	0.068	0.579	1.683	3.077	2.955	4.485
P	0.713	0.147	0.667	0.749	0.431	0.215	0.228	0.106

²Abbreviations: FSSG, Frequency scale for the symptoms of GERD; GERD-HRQL, GERD-health-related quality of life; RS, reflux syndrome; VAS, Visual Analog scale.

provement of the FSSG score in our trial (83.33% in group B) was more than what Karkon Varnosfaderani et al. (26) reported (50%), and it seems to be because of a synergistic interaction between Coriander Triphala components.

Our results also showed a 75% improvement in the VAS score in group B (Table 3), in which patients reported significantly less pain after receiving Coriander Triphala (Figure 2). Besides, a 91.28% improvement was observed in the GERD-HRQL score in group B (Table 3). Patients in this group had significantly less heartburn and regurgitation in the lying and standing positions, regurgitation affecting their quality of life, dysphagia, and odynophagia; overall, after the intervention, they were more satisfied than before (Figure 2).

Pistacia lentiscus L. (Mastic) from the Anacardiaceae family has been reported to have many therapeutic effects, especially in the management of GI disorders (15). It preserves the innate heat of the stomach. About 55% of mastic weight is of the acid fraction (38). Triterpenoid acids seem to have antioxidant and antimicrobial properties

(39). Oleanolic acid, oleanonic acid, and gallic acid seem to have Peroxisome proliferator-activated Receptor (PPAR) modulator activity. Peroxisome proliferator-activated receptor is a nuclear receptor that acts as a transcription factor and controls cellular functions in gene expression (40). The phenolic compounds of mastic play important roles by regulating gastric acid secretion and improving gastric blood flow (41).

Roe et al. (42) reported that the use of mastic was effective in limiting the concentration of *H. pylori*, as well as gastritis. The results of Huwez et al. (43) and Afrasiabian et al. (44) studies showed that *Pistacia* spp. eradicated *H. pylori* and improved the symptoms of dyspepsia. Kottakis et al. (45) study suggested that the Arabinogalactan proteins/Chios mastic gum (AGPs/CMG) inhibited neutrophil activation in the presence of *H. pylori*-neutrophil activating protein (HP-NAP), playing a critical part in *H. pylori*-associated pathologies in gastric mucosa. Similar to our results, Dabos et al. (46) showed 77% of patients who received mastic gum had significant improvements

Table 3. Comparison of the Effect of Mastic, Coriander Triphala, and Omeprazole on the Improvement (%) of GERD-HRQL, Reflux Syndrome, FSSG, and VAS

Group	GERD-HRQL	Reflux	FSSG	VAS
A				
Median	90.00	66.66	73.68	66.66
Percentiles				
25	84.61	50.00	69.23	50.00
75	96.29	100.00	85.71	80.00
B				
Median	91.28	80.00	83.33	75.00
Percentiles				
25	80.38	50.00	71.47	57.50
75	100.00	100.00	92.36	100.00
C				
Median	82.00	66.66	68.62	62.50
Percentiles				
25	63.79	50.00	51.13	41.42
75	96.11	100.00	92.50	79.44
Kruskal-Wallis	0.593	3.748	0.244	
P	0.743	0.154	0.197	

in GERD symptoms. Another study by Dabos et al. (20) in patients with functional dyspepsia proved that *Pistacia* improved the symptoms compared to a placebo. Similar to what we concluded, Eftekharaizali et al. (47) also showed that an eight-week treatment with *Pistacia* spp. reduced the GI symptoms such as pain and burning compared to the placebo group. Our trial results showed that the intervention with *Pistacia lentiscus* (group C) made statistically significant improvements by 66.66% and 68.62% in the RS and FFSG scores, respectively (Table 3). Patients who received *Pistacia lentiscus* as an intervention had fewer GI complaints such as retrosternal burning, epigastric pain, regurgitation to the throat or mouth, and burning sensation when bending (Figure 2). We also observed a 62.50% improvement in the VAS score that was statistically significant (Table 3). Our data analysis also showed statistically significant improvement by 82% in the GERD-HRQL score (Table 3). Considering several factors such as the quality of life being affected by regurgitation, drug consumption, wakeups during the night due to regurgitation, etc., patients in this group reported a significant improvement in their quality of life after treatment (Figure 2).

It should be noted that in seven placebo-controlled trials of PPI therapy, the therapeutic gain for regurgitation response averaged 17% compared to placebo; this effect was more than 20% lower than that observed for heartburn (48). Yamashita et al. (14) reported that adding gastric acid

inhibitors to acotiamide could reduce the total reflux, liquid reflux, and proximal reflux episodes. The combination of omeprazole (20 mg/day) and baclofen showed high improvement in burning and reflux (34). Lu et al. (49) reported that 71.7% of patients responded to PPIs, similar to what we observed in group A. Our data analysis showed that the intervention with omeprazole (A group) made statistically significant improvements by 73.68%, 66.66%, 66.66%, and 90% in the FFSG, RS, VAS, and GERD-HRQL scores, respectively. In summation, we concluded that *Pistacia lentiscus* and Coriander Triphala are as effective as omeprazole in the treatment of GERD but with fewer adverse effects.

5.1. Adverse Events

Previous studies reported allergic contact dermatitis due to mastic gum (Mastisol) medical adhesive bandages (50). There was a patient among the participants of our study who reported itching and erythema as the adverse events of mastic oral, which led to the termination of the intervention. Another participant in group B reported epigastric pain, and thus, treatment discontinued.

5.2. Limitation of Study

The treatment duration and the follow-up period were short. The number of capsules as the intervention was high, which seemed to lead to less intention of the patients

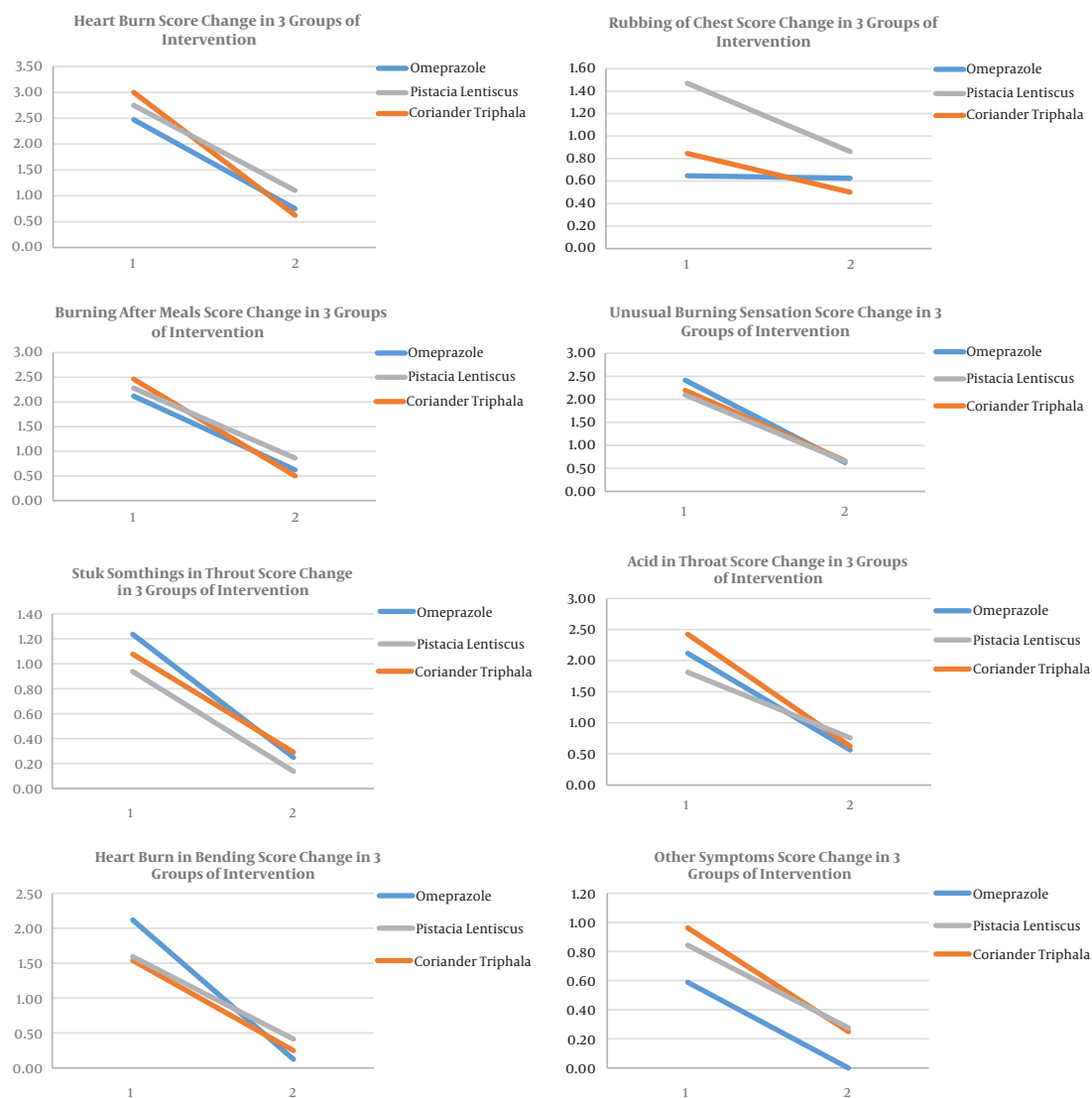


Figure 2. The Frequency scale for the symptoms of gastroesophageal reflux disease (FSSG) total scores before and after the intervention in each group. A, Omeprazole; B, Coriander Triphala; C, *Pistacia lentiscus*.

to participate. Carrying out further research with larger sample size and longer treatment and follow-up periods and applying other forms of medication such as syrups or topical oils are proposed.

5.3. Conclusions

To the best of our knowledge, this study is the first clinical trial that assessed the effects of Coriander Triphala on adults' GERD. We studied the effects of Mastic and Coriander Triphala on the GERD symptoms and quality of life of patients and compared them with conventional therapy. Herbal preparations had several components and pharma-

cological effects, and they were as effective as conventional medications but with fewer side effects.

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Footnotes

Authors' Contribution: Study concept and design: Seyed Mohammad Bagher Fazljou and Hassan Monorifar. Analysis and interpretation of data: Fariba Sadeghi and Bita Sepehri. Diagnosis and follow-up: Bita Sepehri, Seyed Mohammad Bagher Fazljou, and Fariba Sadeghi. Drafting of the manuscript: Hassan Monorifar, Fariba Sadeghi, and Seyed Mohammad Bagher Fazljou. Administrative, technical, and material support: Laleh Khodaie. Statistical analysis: Hassan Monirifar.

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