Iran Red Crescent Med J. 2018 July; 20(7):e63822. doi: 10.5812/ircmj.63822.

Published online 2018 May 31. **Research Article**

Effect of "*Pistacia atlantica*" Resin (Baneh) on Functional Dyspepsia: A Double-Blind, Randomized Clinical Study

Mahdiyehsadat Eftekharafzali,[1] Mitra Mehrabani,[2] Haleh Tajadini,[1,3] Bijan Ahmadi,[4] and Mohammad Javad Zahedi[4,*]

[1]Department of Traditional Medicine, School of Traditional Medicine, Kerman University of Medical Sciences, Kerman, Iran
[2]Herbal and Traditional Medicines Center, Kerman University of Medical Sciences, Kerman, Iran
[3]Neuroscience Research Center, Institute of Neuropharmacology, Kerman University of Medical Sciences, Kerman, Iran
[4]Gastroenterology and Hepatology Research Center, Kerman University of Medical Sciences, Kerman, Iran

[*]*Corresponding author*: Mohammad Javad Zahedi, Gastroenterology and Hepatology Research Center, Kerman Medical University of Sciences, Jomhuri Blvd, Kerman, Iran. Tel: +98-3433222250-1, E-mail: zahedi@yahoo.com

Received 2017 November 06; **Revised** 2018 January 19; **Accepted** 2018 February 24.

Abstract

Background: Functional dyspepsia (FD) is one of the most common problems around the world. *Pistacia atlantica* has beneficial effects in gastrointestinal disorders and is used for treating functional dyspepsia in Persian Medicine.
Objectives: The aim of this study was to assess the effect of "*Pistacia atlantica*" (Baneh) on functional dyspepsia.
Methods: This randomized, double-blind, placebo-controlled trial was carried out on 119 patients (18 to 60 years old) with functional dyspepsia based on Rome III criteria. Subjects were randomly divided to intervention (n = 61) and placebo (n = 58) groups. Participants received capsules twice daily (500 mg capsules containing 350 mg *Pistacia atlantica* resin plus 150 mg sugar in the intervention group, and 500 mg capsules containing 350 mg starch powder plus 150 mg sugar in the placebo group) for four weeks and they were followed up for one month. The intensity and frequency of gastrointestinal symptoms, such as fullness, bloating, nausea, pain, and burning were assessed using the questionnaire on arrival, two and four weeks, and one month after the intervention.
Results: Fifty-three patients in the *Pistacia atlantica* group and 48 patients in the placebo group completed the study. The severity and frequency of gastrointestinal symptoms, such as early satiation nausea, pain, and burning were significantly decreased in the *Pistacia atlantica* group. For example, severity of early satiation was 1.67 ± 0.13 in pistacia and 2.54 ± 0.17 in placebo groups in eight weeks ($P > 0.001$) and frequency of this symptom was 2.39 ± 0.27 and 4.41 ± 0.34 in *Pistacia* and placebo groups, respectively, in eight weeks ($P > 0.001$), which was significantly decreased in the *Pistacia* group. No serious adverse effects were reported.
Conclusions: This study revealed that *Pistacia atlantica* is significantly effective in functional dyspepsia symptoms.

Keywords: Dyspepsia, Medicinal, Medicine, *Pistacia*, Plant, Traditional

Archive of SID

1. Background

Functional dyspepsia (FD) with an approximate prevalence of 20% is one of the most common problems around the world (1-3). The prevalence of FD in Iran ranges from 2.2% to 29.9% (4-6). However, FD is not life-threatening and it generally persists lifelong, resulting in significant personal and economic costs and influences quality of life (2, 7-10). Pharmacological treatment includes acid inhibitory drugs or prokinetics, anxiolytics, and antidepressants (11). According to the Rome III criteria, functional dyspepsia is defined as the presence of early satiation, postprandial fullness, epigastric pain, or epigastric burning for the last three months, with symptom onset at least six months prior to diagnosis and in the absence of organic or structural evidence (including in upper endoscopy) (12, 13). Functional dyspepsia is subdivided to epigastric pain syndrome (EPS), which is characterized by epigastric pain or burning, and postprandial distress syndrome (PDS), which is characterized by postprandial fullness and early satiation (3, 13, 14). The pathophysiology of FD is poorly understood (15, 16). However, several treatments are recommended for FD yet therapeutic options remain limited and provided in most cases just as symptomatic (3). Therefore, other treatment methods, such as complementary and alternative medications, such as herbal medicine, are suggested (17-21). In Persian Medicine, stomach and its disorders are very important (22-25). Several herbal remedies, such as *Apium graveolens*, *Trachyspermum copticom* (26), and *Pistacia atlan*tica have been introduced as a treatment for FD in Persian Medicine (27, 28). The genus Pistacia belongs

Copyright © 2018, Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, provided the original work is properly cited

www.SID.ir

to the family Anacardiaceae (29). *Pistacia atlantica* (from *Pistacia* species) is called Baneh in Iran and its resin has beneficial effects in gastrointestinal disorders (27, 30-32).

2. Objectives

The aim of this study was to assess the effect of "*Pistacia atlantica mutica*" (Baneh) on functional dyspepsia.

3. Methods

3.1. Setting

This single center, randomized, double-blind, placebo-controlled trial was carried out from May 2016 to September 2016 on patients referred to the research center of gastroenterology and hepatology of Afzalipour Hospital, affiliated with Kerman University of Medical Sciences of Iran. This hospital was a governmental and referral center.

3.2. Study Participants

Patients (18 to 60 years old) with functional dyspepsia based on Rome III criteria were enrolled and randomly divided to intervention and placebo groups. This study was registered at Iranian Registry of Clinical Trials with code IRCT2016031327033N1.

3.3. Inclusion Criteria

Inclusion criteria for this trial were as follows: The presence of early satiation, postprandial fullness, epigastric pain, or epigastric burning for the last three months with symptom onset at least six months prior to diagnosis. Participants stopped taking herbal or chemical drugs for two weeks before the intervention (washout period).

3.4. Exclusion Criteria

The exclusion criteria for this study were as follows: Organic or structural evidence (including upper endoscopy), history of peptic ulcer or reflux, underlying disease, including heart failure, renal failure, cirrhosis, diabetes, hypothyroidism, and history of abdominal surgeries after evaluation of a gastroenterologist. It is noteworthy to mention that participants using herbal, and chemical drugs, and those drinking alcohol, and abusing opiates were also excluded. Furthermore, pregnant and lactating females were also excluded.

3.5. Preparation of Pistacia atlantica mutica Capsules

The drug used in this study was the resin of *Pistacia atlantica mutica* that was obtained from Rabor county of Kerman Province in Iran with herbarium code KF1136-3. *Pistacia atlantica mutica* resin after drying and microbial cultures and standardization was powdered and prepared as 500-mg capsules (containing 350 mg *Pistacia atlantica mutica* resin plus 150 mg sugar). Also, 500-mg capsules containing 350 mg starch powder plus 150 mg sugar (as a placebo) with taste and flavor similar to the target group was prepared.

3.6. Randomization and Intervention

In this clinical trial, treatment assignment was done with simple randomization using random numbers (Random digit number).

Participants received capsules twice daily (one after lunch, and one after dinner) for four weeks and they were followed up for one month. Primary and secondary symptoms of patients were assessed on arrival, 4-weeks, and 1-month after the intervention.

3.7. Safety Evaluation

Patients were assessed for possible side effects in each visit, and if present, symptoms were documented in a form. Routine physical examinations were also done at every visit.

3.8. Statistical Analyses

Both demographic characteristics and symptom scores were normally distributed, so we have presented them using symptoms mean $\pm$ SE. Independent t-test and Chi-square were used to compare quantitative and qualitative variables between two groups respectively. In order to compare DSS score, the two-way repeated measures ANOVA test was used for three consecutive 0, 2nd and 4th week. Independent t-test after Bonferroni correction was used to compare the DSS score in each of the above time intervals, We used the Per Protocol method for data analysis, therefore, had no missing values during statistical analyses.

In this study the software, SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA) were utilized and P values < 0.05 were considered statistically significant.

3.9. Sample Size

The sample size was calculated based on a 30% decreased in mean symptom score in the treatment group and considerably a = 0.05 and power of 80% to be 47 in each group.

Archive of SID

www.SID.ir

3.10. Measurement Tools

In this study, the Rome III diagnostic questionnaire was used to evaluate the symptom score of patients (33). Dyspeptic symptoms, such as postprandial fullness, early satiation, epigastric pain, epigastric burning, belching, nausea, vomiting, and bloating was graded and scored on a Likert scale, according to its severity as follows: Absent = 0, mild = 1, moderate = 2 (diverting from but not urging modifications in daily activities), and severe = 3 (influencing daily activities markedly enough to urge modifications). The frequency of each symptom was also graded as follows: 1, occurring < 1 day (d)/month (m); 2, occurring 1 d/m; 3, occurring 2 - 3 d/m; 4, occurring 1 d/week; 5, occurring > 1 d/week; and 6, occurring every day. The score for a single dyspeptic symptom was an aggregate of frequency and severity ratings, ranging from 0 to 9. Dyspeptic symptoms score (DSS) was assessed by summing the score of eight dyspepsia symptoms (33). Validity and reliability of the questionnaire was confirmed in the Persian language (26, 34, 35).

3.11. Ethics

The ethics committee of Kerman University of Medical Sciences approved this study (IR.KMU.AH.REC.1395.10). All patients were fully aware of the objectives and details of the study through an information form, and a signed written consent form was obtained.

4. Results

Initially, 142 patients were enrolled, 23 subjects, who did not have the inclusion criteria were excluded and 119 patients were recruited and randomized to two groups. 18 patients were lost to follow-up: Eight in the *Pistacia* group and ten in the placebo group. The main reason was due to lack of regular drug use or concurrent use of herbal medicine or other chemicals (six patients in the drug and eight in the placebo group). Four patients had side effects and discontinued medication (in *Pistacia atlantica* group, one was due to severe bloating and irritation, and was one due to bloating and constipation, and in the placebo group one because of severe diarrhea and one due to severe pain). 53 patients in the *Pistacia atlantica* group and 48 patients in the placebo group completed the study (Figure 1). The mean age for subjects in the *Pistacia atlantica* group was 38.30 $\pm$ 12.57 and for subjects in the placebo group was 44.85 $\pm$ 13.08 years. There was no significant difference between the study groups in terms of age (P = 0.66). In both groups, females dominated males (34 females and 19 males in the *Pistacia atlantica* group and 35 females and 13 males in the placebo group) and there was no significant difference between them (P = 0.34).

The baseline characteristics regarding chief complaint and provocation factors of these patients are shown in Tables 1 and 2. There were no relevant differences between the groups. The severity of FD in some symptoms, such as early satiation, nausea, pain, and burning had significantly decreased in the *Pistacia atlantica* group (Table 3). There were significant differences in the mean score of the frequency of dyspeptic symptoms (except vomiting) during the second and fourth week's trial period and also one-month follow-up in *Pistacia atlantica* and placebo groups (P $\leq$ 0.001) (Table 4). Epigastric pain or burning (EPS) diminished in 43 subjects (81.1%) of the *Pistacia atlantica* group yet only 21 patients (43.8%) with EPS had been improved in the placebo group in the fourth week (P $\leq$ 0.001). Postprandial fullness and early satiation (PDS) was improved in 41 (77.4%) patients in the *Pistacia atlantica* group yet only 18 patients (37.5%) with PDS improved in the placebo group by the fourth week (P $\leq$ 0.001). Mean symptom score during the 2nd and 4th week trial and one month follow-up period significantly decreased in the *Pistacia atl*antica group (Figure 2).

5. Discussion

Nowadays, functional dyspepsia is a common disorder (1, 2) with unsatisfactory treatments (2). The current study showed that *Pistacia atlantica* improved gastrointestinal symptoms in patients with functional dyspepsia and it had no significant side effects. Only a short paper was found about the effect of *Pistacia atlantica* on functional dyspepsia. In a clinical study, Afrasiabian et al. assessed the effect of *Pistacia atlantica kurdica* gum on the eradication of *Helicobacter pylori* in patients with dyspepsia. Their study showed that *Pistacia atlantica kurdica* significantly led to the treatment of dyspepsia symptoms and *H. pylori* eradication (36). Their results, similar to that of the current study, showed medicinal plants improved FD symptoms. However, their intervention period was shorter than the current study, as two weeks. In another clinical trial, Dabos et al. investigated the effect of Chios mastic gum capsule on functional dyspepsia for three weeks. Patients were assessed one month later for adverse effects. This herb significantly improved symptoms of functional dyspepsia (37). The intervention period of this trial was shorter than that of the current study, yet the follow-up period was similar. Both studies showed an significant efficacy of medicinal plants on FD. In another study, the efficacy of *Ocimum basilicum* was studied. Their results showed that *Ocimum basilicum* could relieve symptoms of functional dyspepsia, especially in female and young patients with dysmotility

Archive of SID

www.SID.ir

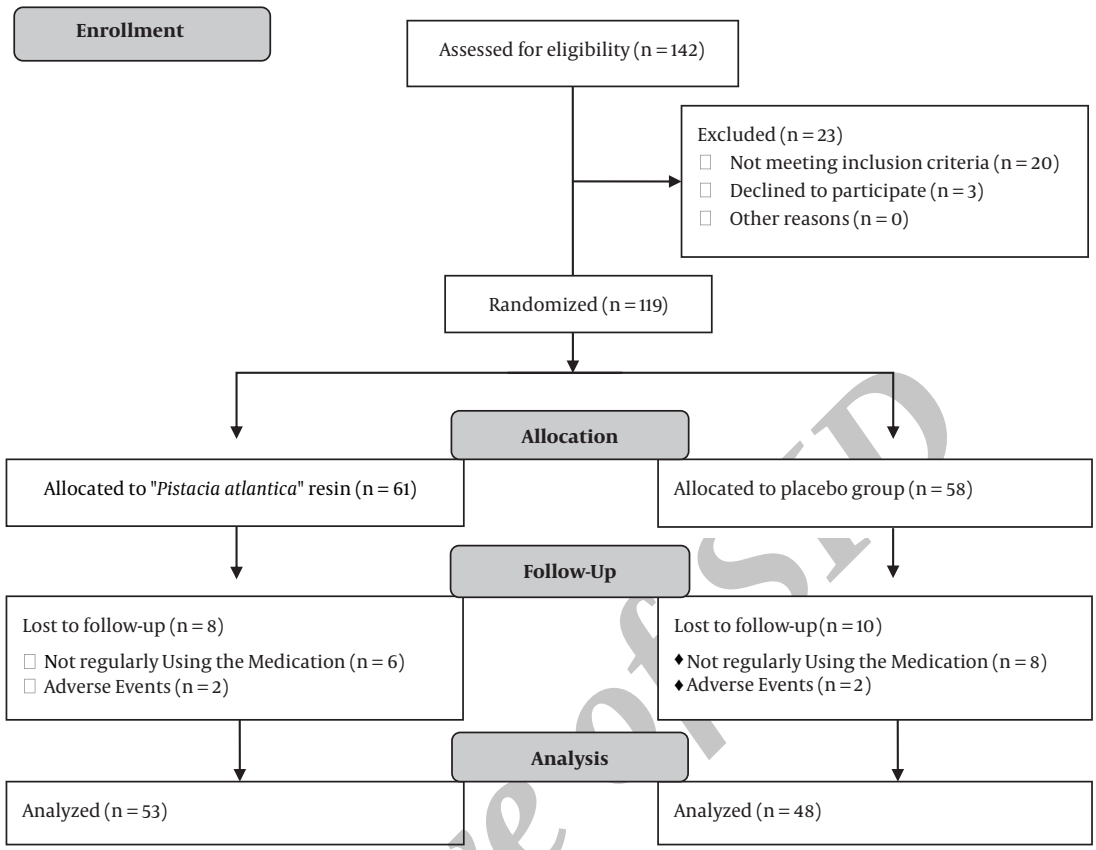

Figure 1. Distribution of patients

Table 1. Demographic Characteristics of Patients[a]

Demographic Characteristics	"*Pistacia atlantica*" (Baneh) Group, 53	Placebo Group, 48	P Value
Age	38.30 ± 12.57	44.85 ± 13.08	0.66
Sex			
Female	34 (64.2)	35 (72.9)	0.34
Male	19 (35.8)	13 (27.1)	
Marital status	9 (17.0)		0.09
Single		2 (4.2)	
Married	42 (79.2)	45 (93.8)	
Divorced	2 (3.8)	1 (2.1)	
BMI	24.67 ± 4.75	27.04 ± 24.69	0.49

[a]Values are expressed as No. (%).

(38). This study and the current trial both showed the significant efficacy of medicinal herbs without any serious adverse events. However, in the current study, there were no differences in efficacy of *Pistacia atlantica* based on age or genus. Mohtashami et al. assessed the efficacy and safety of honey-based formulation of *Nigella sativa* seed oil in functional dyspepsia. Their Results showed that sativa could cause significant symptomatic improvement in patients with functional dyspepsia no serious adverse event was reported (39). Their intervention period was longer than that of the current study at eight weeks. Both studies had no serious adverse effects. Babaeian et al. investigated the efficacy of Mentha longifolia in patients with postprandial distress syndrome. Their results showed a significant im-

www.SID.ir

Table 2. Baseline Clinical Characteristics and Confounding Factor[a]

Variables	"*Pistacia atlantica*" (Baneh) Group, 53	Placebo Group, 48	P Value
Chief complaint			0.491
Postprandial fullness	1 (1.9)	3 (6.3)	
Bloating	16 (30.2)	15 (31.3)	
Nausea	1 (1.9)	3 (6.3)	
Pain	33 (62.3)	24 (50.0)	
Burning	2 (3.8)	3 (6.3)	
Provocation factors			0.142
Fasting	4 (7.5)	8 (16.7)	
Stress	30 (56.6)	22 (45.8)	
Eating	16 (30.2)	18 (37.5)	
Other cases	3 (5.7)	0 (0.0)	

[a]Values are expressed as No. (%).

Table 3. Comparison of Mean (Standard Error) Scores of Severity of FD Between Baneh and Placebo Group Across the Study Period

Symptom	Baneh				Placebo				
	Baseline	2 Week	4 Week	8 Week	Baseline	2 Week	4 Week	8 Week	P Value
Early satiation	3.09 (0.17)	2.01 (0.15)	1.41 (0.13)	1.67 (0.13)	3.10 (0.20)	2.41 (0.17)	2.45 (0.17)	2.54 (0.17)	> 0.001
Bloating	3.45 (0.12)	2.28 (0.14)	1.52 (0.10)	2.00 (0.11)	3.33 (0.14)	2.52 (0.14)	2.43 (0.13)	2.56 (0.13)	0.321
Fullness	3.03 (0.14)	2.18 (0.12)	1.64 (0.09)	1.60 (0.09)	2.35 (0.14)	2.04 (0.13)	2.04 (0.13)	2.20 (0.13)	0.505
Belching	2.07 (0.16)	1.47 (0.09)	1.16 (0.05)	1.28 (0.07)	2.39 (0.16)	1.87 (0.13)	1.91 (0.13)	1.91 (0.13)	0.107
Nausea	2.15 (0.15)	1.43 (0.10)	1.09 (0.04)	1.15 (0.07)	1.83 (0.15)	1.41 (0.09)	1.50 (0.12)	1.50 (0.11)	> 0.001
Vomiting	1.26 (0.93)	1.11 (0.05)	1.00 (0.00)	1.11 (0.06)	1.33 (0.10)	1.18 (0.08)	1.29 (0.11)	1.16 (0.06)	0.055
Pain	3.26 (0.13)	2.28 (0.13)	1.64 (0.11)	1.98 (0.14)	3.00 (0.14)	2.56 (0.14)	2.47 (0.15)	2.54 (0.13)	> 0.001
Burning	2.45 (0.16)	1.90 (0.12)	1.47 (0.09)	1.50 (0.09)	2.14 (0.17)	1.66 (0.13)	1.79 (0.14)	1.93 (0.14)	> 0.001

Table 4. Comparison of Mean (Standard Error) Scores of Frequency of FD Between Baneh and Placebo Group During the Study Period

Symptom	Baneh				Placebo				
	Baseline	2 Week	4 Week	8 Week	Baseline	2 Week	4 Week	8 Week	P Value
Early satiation	4.90 (0.29)	3.52 (0.29)	1.96 (0.24)	2.39 (0.27)	4.79 (0.35)	4.25 (0.33)	4.33 (0.33)	4.41 (0.34)	> 0.001
Bloating	5.26 (0.17)	3.81 (0.26)	2.20 (0.22)	2.77 (0.22)	5.00 (0.21)	4.39 (0.23)	4.25 (0.23)	4.45 (0.21)	> 0.001
Fullness	4.35 (0.23)	3.52 (0.27)	2.24 (0.21)	2.58 (0.22)	3.43 (0.23)	3.33 (0.24)	3.14 (0.22)	3.12 (0.22)	> 0.001
Belching	3.33 (0.31)	2.30 (0.25)	1.66 (0.19)	1.67 (0.19)	3.91 (0.30)	3.20 (0.29)	3.08 (0.27)	3.41 (0.28)	> 0.001
Nausea	3.16 (0.29)	1.83 (0.20)	1.28 (0.11)	1.35 (0.14)	2.91 (0.30)	2.43 (0.27)	2.12 (0.24)	2.16 (0.23)	> 0.001
Vomiting	1.67 (0.22)	1.05 (0.05)	1.07 (0.05)	1.20 (0.11)	1.60 (0.20)	1.31 (0.15)	1.39 (0.15)	1.37 (0.14)	0.031
Pain	5.01 (0.18)	3.58 (0.25)	2.16 (0.20)	2.60 (0.23)	4.75 (0.25)	4.10 (0.25)	3.79 (0.27)	4.14 (0.24)	> 0.001
Burning	4.00 (0.27)	2.75 (0.26)	1.86 (0.20)	2.32 (0.24)	3.18 (0.30)	2.68 (0.27)	2.75 (0.28)	3.06 (0.26)	> 0.001

provement in the mean severity scales of FD symptoms (P < 0.001) (40). Compared with the current study, their follow up period was longer. Pasalar et al. in a clinical trial study showed that *jollab* (a mixture of rose water, saffron, white rock candy, and water) was effective on FD without any complicated side effects (41). This natural compound was effective and had no serious side effects, similar to the current study. This study had several strengths and limitations. One of the strengths of this trial was the use of domestic and safe medication. The authors did not find any clinical study about the effect of the *Pistacia atlantica* on FD, thus it seems the present study was the first clinical trial to evaluate the effect of *Pistacia atlantica* in FD. The current study had some limitations, such as short follow-up period, single-center study, and small sample size. Due to the fact that standard treatment for this disease has not been documented, as well as the complications of chemical drugs, based on the sources of Iranian medicine, a new drug was selected, which, in addition to the patient's complexity and therapeutic properties, was less complicated and more stable than other drugs. The authors suggest another clinical study with longer follow-up period.

Archive of SID

www.SID.ir

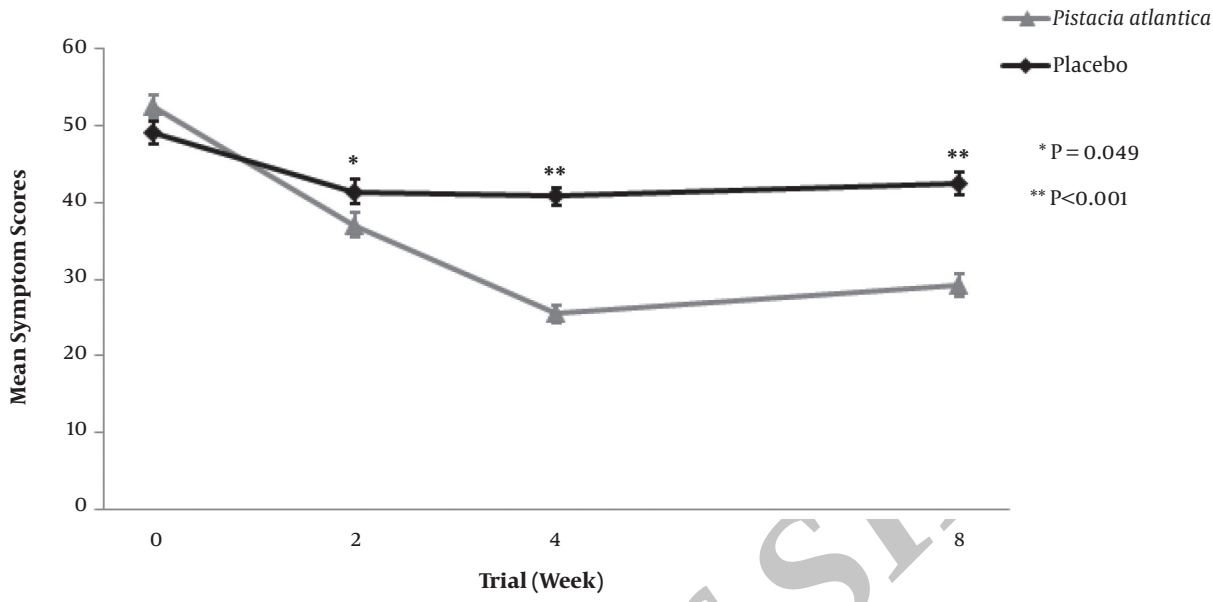

Figure 2. Mean symptom Score during the second and fourth week of trial and one month follow-up period in *Pistacia atlantica mutica* and placebo groups

5.1. Conclusion

This study showed that *Pistacia atlantica* is significantly effective on functional dyspepsia in comparison with the placebo. The authors suggest another clinical study with longer follow-up period in the future.

Acknowledgments

The authors appreciate Professor Nouzar Nakhaee for his contribution to this study and valuable statistical comments.

Footnotes

Authors' Contribution: The work presented here was carried out through collaboration between all authors. Mahdiyehsadat Eftekharafzali collected data. Haleh Tajadini, Mohammad Javad Zahedi and Mitra Mehrabani designed methods; and Bijan Ahmadi and Mitra Mehrabani analyzed the data and interpreted the results. All authors have contributed to, seen, and approved the article

Conflict of Interests: There was no conflict of interest.

References

1. Mehboob M. Functional dyspepsia: An unresolved issue. *Intern Med*. 2015;**5**(3). doi: 10.4172/2165-8048.1000192.
2. Napthali K, Koloski N, Walker MM, Talley NJ. Women and functional dyspepsia. *Womens Health (Lond)*. 2016;**12**(2):241–50. doi: 10.2217/whe.15.88. [PubMed: 26901578]. [PubMed Central: PMC5375052].
3. Talley NJ. Functional dyspepsia: advances in diagnosis and therapy. *Gut Liver*. 2017;**11**(3):349–57. doi: 10.5009/gnl16055. [PubMed: 28452210]. [PubMed Central: PMC5417776].
4. Amini E, Keshteli AH, Jazi MS, Jahangiri P, Adibi P. Dyspepsia in Iran: SEPAHAN systematic review No. 3. *Int J Prev Med*. 2012;**3**(Suppl 1):S18–25. [PubMed: 22826763]. [PubMed Central: PMC3399299].
5. Khademolhosseini F, Mehrabani D, Zare N, Salehi M, Heydari S, Beheshti M, et al. Prevalence of dyspepsia and its correlation with demographic factors and lifestyle in shiraz, southern iran. *Middle East J Dig Dis*. 2010;**2**(1):24–30. [PubMed: 25197509]. [PubMed Central: PMC4154903].
6. Seyedmirzaei SM, Haghdoost AA, Afshari M, Dehghani A. Prevalence of dyspepsia and its associated factors among the adult population in southeast of iran in 2010. *Iran Red Crescent Med J*. 2014;**16**(11). e14757. doi: 10.5812/ircmj.14757. [PubMed: 25763207]. [PubMed Central: PMC4329955].
7. Aro P, Talley NJ, Agreus L, Johansson SE, Bolling-Sternevald E, Storskrubb T, et al. Functional dyspepsia impairs quality of life in the adult population. *Aliment Pharmacol Ther*. 2011;**33**(11):1215–24. doi: 10.1111/j.1365-2036.2011.04640.x. [PubMed: 21443537].
8. Voiosu TA, Giurcan R, Voiosu AM, Voiosu MR. Functional dyspepsia today. *Maedica (Buchar)*. 2013;**8**(1):68–74. [PubMed: 24023602]. [PubMed Central: PMC3749766].
9. Filipovic BF, Randjelovic T, Ille T, Markovic O, Milovanovic B, Kovacevic N, et al. Anxiety, personality traits and quality of life in functional dyspepsia-suffering patients. *Eur J Intern Med*. 2013;**24**(1):83–6. doi: 10.1016/j.ejim.2012.06.017. [PubMed: 22857883].
10. Miwa H, Ghoshal UC, Fock KM, Gonlachanvit S, Gwee KA, Ang TL, et al. Asian consensus report on functional dyspepsia. *J Gastroenterol Hepatol*. 2012;**27**(4):626–41. doi: 10.1111/j.1440-1746.2011.07037.x. [PubMed: 22142407].
11. Miwa H, Kusano M, Arisawa T, Oshima T, Kato M, Joh T, et al. Evidence-based clinical practice guidelines for functional dyspepsia. *J Gastroenterol*. 2015;**50**(2):125–39. doi: 10.1007/s00535-014-1022-3. [PubMed: 25586651].

Archive of SID

www.SID.ir

12. Talley NJ. Functional dyspepsia: new insights into pathogenesis and therapy. *Korean J Intern Med*. 2016;**31**(3):444–56. doi: 10.3904/kjim.2016.091. [PubMed: 27048251]. [PubMed Central: PMC4855108].
13. Feldman M, Friedman LS, Brandt LJ. *Sleisenger and Fordtran's gastrointestinal and liver disease: pathophysiology, diagnosis, management*. Elsevier Health Sciences; 2016.
14. Carbone F, Holvoet L, Vanuytsel T, Tack J. Rome III functional dyspepsia symptoms classification: Severity vs frequency. *Neurogastroenterol Motil*. 2017;**29**(6). doi: 10.1111/nmo.13024. [PubMed: 28295895].
15. Talley NJ, Holtmann G, Walker MM. Therapeutic strategies for functional dyspepsia and irritable bowel syndrome based on pathophysiology. *J Gastroenterol*. 2015;**50**(6):601–13. doi: 10.1007/s00535-015-1076-x. [PubMed: 25917563].
16. Ford AC. Aetiopathogenesis of functional dyspepsia. *Gut*. 2015;**64**(7):1182–3. doi: 10.1136/gutjnl-2014-308959. [PubMed: 25573418].
17. Lacy BE, Talley NJ, Locke G3, Bouras EP, DiBaise JK, El-Serag HB, et al. Review article: current treatment options and management of functional dyspepsia. *Aliment Pharmacol Ther*. 2012;**36**(1):3–15. doi: 10.1111/j.1365-2036.2012.05128.x. [PubMed: 22591037]. [PubMed Central: PMC3970847].
18. Pasalar M, Nimrouzi M, Choopani R, Mosaddegh M, Kamalinejad M, Mohagheghzadeh A, et al. Functional dyspepsia: A new approach from traditional Persian medicine. *Avicenna J Phytomed*. 2016;**6**(2):165–74. [PubMed: 27222829]. [PubMed Central: PMC4877961].
19. Rosch W, Liebregts T, Gundermann KJ, Vinson B, Holtmann G. Phytotherapy for functional dyspepsia: a review of the clinical evidence for the herbal preparation STW 5. *Phytomedicine*. 2006;**13 Suppl 5**:114–21. doi: 10.1016/j.phymed.2006.03.022. [PubMed: 16978851].
20. Melzer J, Rosch W, Reichling J, Brignoli R, Saller R. Meta-analysis: phytotherapy of functional dyspepsia with the herbal drug preparation STW 5 (Iberogast). *Aliment Pharmacol Ther*. 2004;**20**(11-12):1279–87. doi: 10.1111/j.1365-2036.2004.02275.x. [PubMed: 15606389].
21. Tafti LD, Shariatpanahi SM, Damghani MM, Javadi B. Traditional Persian topical medications for gastrointestinal diseases. *Iran J Basic Med Sci*. 2017;**20**(3):222–41. doi: 10.22038/ijbms.2017.8349. [PubMed: 28392893]. [PubMed Central: PMC5378958].
22. Guo Y, Zhu J, Su X, Yang J, Li Y, Wang Q, et al. Efficacy of Chinese herbal medicine in functional dyspepsia: A meta-analysis of randomized, double-blind, placebo-controlled trials. *Journal of Traditional Chinese Medical Sciences*. 2016;**3**(3):147–56. doi: 10.1016/j.jtcms.2016.09.006.
23. Alizadeh M, Khadem E, Aliasl J. Diagnosis protocol of stomach distemperament for clinical practice in Iranian traditional medicine: A narrative review. *Iran J Public Health*. 2017;**46**(7):877–81. [PubMed: 28845397]. [PubMed Central: PMC5563868].
24. Shirbeigi L, Halavati N, Abdi L, Aliasl J. Dietary and medicinal herbal recommendation for management of primary bile reflux gastritis in traditional Persian medicine. *Iran J Public Health*. 2015;**44**(8):1166–8. [PubMed: 26587489]. [PubMed Central: PMC4645745].
25. Rostami A, Minaii B, Rostamian A, Parsa Yekta Z, Aliasl J, Ahmadbegi S. Overview of avicenna (ibn sina) opinion on stomach swelling. *Iran Red Crescent Med J*. 2014;**16**(9). e21350. doi: 10.5812/ircmj.21350. [PubMed: 25593735]. [PubMed Central: PMC4270677].
26. Azimi M, Zahedi MJ, Mehrabani M, Tajadini H, Zolala F, Baneshi MR, et al. Effect of Apium graveolens and Trachyspermum copticom on clinical symptoms of patients with functional dyspepsia. *Avicenna J Phytomed*. 2017;**7**(6):554–64. [PubMed: 29299438]. [PubMed Central: PMC5745539].
27. Babaeian M, Naseri M, Kamalinejad M, Ghaffari F, Emadi F, Feizi A, et al. Herbal remedies for functional dyspepsia and traditional Iranian medicine perspective. *Iran Red Crescent Med J*. 2015;**17**(11). e20741. doi: 10.5812/ircmj.20741. [PubMed: 26734483]. [PubMed Central: PMC4698144].
28. Sina IE. *Al-Qanun fi al-Tibb (The Canon of Medicine)*. Lebanon: Alamy leal-Matbooat institute; 2005.
29. Taran M, Mohebali M, Esmaeli J. In vivo efficacy of gum obtained pistacia atlantica in experimental treatment of cutaneous leishmaniasis. *Iran J Public Health*. 2010;**39**(1):36–41. [PubMed: 23112988]. [PubMed Central: PMC3468973].
30. Bozorgi M, Memariani Z, Mobli M, Salehi Surmaghi MH, Shams-Ardekani MR, Rahimi R. Five Pistacia species (P. vera, P. atlantica, P. terebinthus, P. khinjuk, and P. lentiscus): a review of their traditional uses, phytochemistry, and pharmacology. *ScientificWorldJournal*. 2013;**2013**:219815. doi: 10.1155/2013/219815. [PubMed: 24453812]. [PubMed Central: PMC3876903].
31. Borhani M, Khoshzaban Z, Jodeiri B, Naseri M, Kamlinejad M, Faghihzade S. Comparison between used herbs for treatment of gastroesophageal reflux disease [GERD] in Iranian Traditional of Medicine [ITM]. *Adv Environ Biol*. 2014;**8**(10):773–82. doi: 10.13140/rg.2.1.4751.2161.
32. Tanideh N, Masoumi S, Hosseinzadeh M, Safarpour AR, Erjaee H, Koohi-Hosseinabadi O, et al. Healing effect of pistacia atlantica fruit oil extract in acetic Acid-induced colitis in rats. *Iran J Med Sci*. 2014;**39**(6):522–8. [PubMed: 25429174]. [PubMed Central: PMC4242986].
33. Yu J, Liu S, Fang XC, Zhang J, Gao J, Xiao YL, et al. Gastrointestinal symptoms and associated factors in Chinese patients with functional dyspepsia. *World J Gastroenterol*. 2013;**19**(32):5357–64. doi: 10.3748/wjg.v19.i32.5357. [PubMed: 23983441]. [PubMed Central: PMC3752572].
34. Sorouri M, Pourhoseingholi MA, Vahedi M, Safaee A, Moghimi-Dehkordi B, Pourhoseingholi A, et al. Functional bowel disorders in Iranian population using Rome III criteria. *Saudi J Gastroenterol*. 2010;**16**(3):154–60. doi: 10.4103/1319-3767.65183. [PubMed: 20616409]. [PubMed Central: PMC3003223].
35. Toghiani A, Maleki I, Afshar H, Kazemian A. Translation and validation of the Farsi version of Rome III diagnostic questionnaire for the adult functional gastrointestinal disorders. *J Res Med Sci*. 2016;**21**:103. doi: 10.4103/1735-1995.193175. [PubMed: 28250780]. [PubMed Central: PMC5322693].
36. Afrasiabian H, Imanieh MH, Nejati MA, Salehi A. The effect of oral administration of pistacia atlantica kurdica gum on the eradication of helicobacter pylori in patients with dyspepsia: A randomized clinical trial. *Glob J Health Sci*. 2016;**9**(2):256. doi: 10.5539/gjhs.v9n2p256.
37. Dabos KJ, Sfika E, Vlatta LJ, Frantzi D, Amygdalos GI, Giannikopoulos G. Is Chios mastic gum effective in the treatment of functional dyspepsia? A prospective randomised double-blind placebo controlled trial. *J Ethnopharmacol*. 2010;**127**(2):205–9. doi: 10.1016/j.jep.2009.11.021. [PubMed: 19961914].
38. Rafieian-Kopaei M, Hosseini-Asl K. Effects of Ocimum basilicum on functional dyspepsia: a double-blind placebo-controlled study. *Iran J Med Sci*. 2015;**30**(3):134–7.
39. Mohtashami R, Huseini HF, Heydari M, Amini M, Sadeqhi Z, Ghaznavi H, et al. Efficacy and safety of honey based formulation of Nigella sativa seed oil in functional dyspepsia: A double blind randomized controlled clinical trial. *J Ethnopharmacol*. 2015;**175**:147–52. doi: 10.1016/j.jep.2015.09.022. [PubMed: 26386381].
40. Babaeian M, Naseri M, Kamalinejad M, Ghaffari F, Emadi F, Feizi A, et al. The efficacy of mentha longifolia in the treatment of patients with postprandial distress syndrome: A double-blind, randomized clinical trial. *Iran Red Crescent Med J*. 2016;**19**(2). doi: 10.5812/ircmj.34538.
41. Pasalar M, Choopani R, Mosaddegh M, Kamalinejad M, Mohagheghzadeh A, Fattahi MR, et al. Efficacy and safety of jollab to treat functional dyspepsia: a randomized placebo-controlled clinical trial. *Explore (NY)*. 2015;**11**(3):199–207. doi: 10.1016/j.explore.2015.02.007. [PubMed: 25777290].

Archive of SID

www.SID.ir