

The Effect of Oral Administration of *Pistacia Atlantica Kurdica* Gum on the Eradication of *Helicobacter Pylori* in Patients with Dyspepsia: A Randomized Clinical Trial

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Abstract

H. pylori infection is one of the most common infections in the world so that the aim of this study was to evaluate the antimicrobial *P. Atlantica Kurdica* gum in the eradication of *H. pylori*. This study is a randomized clinical trial; Patients with positive Urea Breath Test and symptoms of dyspepsia were entered. Patients were randomly divided into four groups. Group A: three drugs including 500 mg of Amoxicillin twice a day (bd), Clarithromycin 500 mg bd and Omeprazole 20 mg (bd) and Group B: Group A drugs plus the capsule containing 1 g of powdered *P. Atlantica Kurdica* gum (bd). In Group C: the capsule containing 1 g of powdered *P. Atlantica Kurdica* gum (bd) and Group D: this group took placebo-containing capsule (bd) for 14 days respectively. Dyspeptic symptoms before and after healing period and the UBT results two days before the start of treatment and 30 days after the completion were compared in 4 groups. Patients were not statistically significant difference from each other in the four groups regarding the demographic situation. Moreover, *H. pylori* eradication rate was 19/24 in Group A, 18/24 in Group B, 10/23 in Group C and 2/24 in Group D. Relieving symptoms of dyspepsia in Groups B and C were significantly higher than in Group D (P=0.025 and p=0.006 respectively). *P. Atlantica Kurdica* significantly led to the treatment of dyspepsia symptoms and *H. pylori* eradication.

Keywords: *H. pylori*, dyspepsia, *pistacia atlantica kurdica*, traditional medicine, complementary medicine

1. Introduction

H. pylori are motile, non-spore-forming, curved (comma-shaped) or s-shaped gram-negative bacilli that their original position is human gastric mucosa (Shimomura et al., 2004). *H. pylori* infection is the most common infection in the world. There are two general different epidemiological patterns associated with *H. pylori* infection in the world. In the first pattern that can be seen in developing countries, infection affects 50 to 60% of children under one year and almost 90% of adults in different age groups. The second pattern has seen in developed countries where infection increases from the age of 20 and affects about 40% of the adult population (Perez-Perez et al., 2004). In different regions of Iran, the prevalence of *H. pylori* in adults older than 35 years have been reported nearly 90% (Malekzadeh et al., 2000). However, it seems that the prevalence of *H. pylori* infection is declining in recent decades and is expected to decrease up to 25% in European countries (Magalhães Queiroz & Lizza, 2006), since *H. pylori* are the main cause of a wide range of gastric pathologies such as ulcer, gastric lymphoma, and adenocarcinoma, treating the infections caused by it are considered as a major problem (Ernst & Gold, 2000). *H. pylori* infection can occur in the form of dyspepsia (Bercik & Collins, 2000). This upper gastrointestinal syndrome includes symptoms such as pain, epigastric discomfort, fullness, early satiety, and nausea, vomiting and belching (Tack & Lee, 2005). Dyspepsia can be functional or structural, but the functional type is more common and occurs in 20% to 30% of patients (Tack & Lee, 2005; Zagari et al., 2010). About the treatment of *H. pylori* infections, four main issues were raised. As following; first of all, you need to take two or three antibiotics concurrently along with a proton pump inhibitor drug. Next one is the side effects of

drugs are another factor that should be taken into account. The last problem is regarded to the cost of the drugs should be considered, and the final challenge is the drug resistance that is growing rapidly (Longo et al., 2012). Genus *Pistacia* includes 11 species including *P. Atlantica*. Thus, this species as short trees or shrubs is one of the most important *Pistacia* species with three subspecies of *Cabulica*, *Mutica* and *Kurdica*. *P. Atlantica* is distributed from the Canary Islands and the coastal countries of the Mediterranean to Asia Minor, Syria, Caucasus, Iran, Afghanistan, and Pakistan. It can be massively observed in Iran between Fars and Khuzestan provinces and sporadically in other parts of the country (Saffarzadeh et al., 1999; Taran et al., 2010; Daryaei et al., 2012). In previous studies, *Pistacia* species resin has shown the bactericidal effect on different bacteria including *Streptococcus* mutants, *Staphylococcus aureus*, *Salmonella enteritidis*, *Bacillus cereus*, *E. coli* and *H. pylori* (Daifas et al., 2004). Alpha-pinene, which is a very strong antimicrobial compound, has been reported in *Pistacia* species with very high concentration (Douissa et al., 2005). The impact of this species has been proposed in previous studies on healing the peptic ulcers (Al-Habbal et al., 1984; Dimas et al., 2012) and *H. pylori* infections (Huwez et al., 1998). Previously, the role of *P. Atlantica Kurdica* has been mentioned in Traditional Medicine in the treatment of gastrointestinal pains, dyspepsia and stomach ulcers (Sharifi, 2014). Moreover, the antimicrobial effect of *P. Atlantica Kurdica* natural gum against *H. pylori* has been reported more than *P. lentiscus* in-vitro study (Sharifi et al., 2011). Given the problems with *H. pylori* infection drug therapy mentioned already, and the lack of clinical studies on the benefits of treating the mentioned infection using natural gum of *P. Atlantica Kurdica*.

2. Methods

2.1 Study Design

This study is a randomized clinical trial, carried out from June 2015 to February 2016 on patients referred to Shahid Motahari Subspecialty gastrointestinal clinic affiliated with Namazi Hospital of Shiraz Medical University in Iran.

2.2 Study Population

Inclusion criteria are dyspepsia symptoms; positive urea breathes test (UBT) and the patient's informed consent to participate in the study. The following participants were excluded from the survey, for instance pregnant or breastfeeding patients, the known cases of gastric ulcer or duodenal ulcer any malignancy or those taking NSAIDs, anticoagulants, antibiotics (4 weeks before UBT), any combination of bismuth (2 weeks before the UBT), proton pump inhibitors, and antacids (three days before the UBT). If complications are preventing the continuation of treatment occurred (nausea, vomiting, abdominal pain, and headache) or in cases such as not a proper use of drugs, lack of follow-up or unwillingness to continue cooperation with the research, the patient will exclude from the study.

2.3 Sample Determination

During the study period, 180 patients were referred to the Gastroenterology Center, 111 cases were positive UBT. 11 patients were excluded due to lack of follow-up, and then the sample size of 100 patients (25 patients per group) was selected as shown in Figure 1.

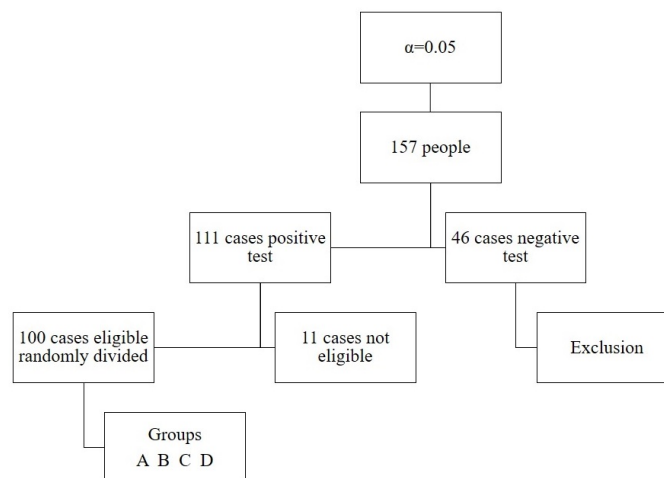


Figure 1. Patients randomly selected and divided into four groups according ninety-five percent confidence ($\alpha=.05$)

2.4 *P. Atlantica Kurdica Gum Capsule Preparation*

The gum from *P. Atlantica var. Kurdica* tree was obtained in late September and early autumn in the trunk with creating a 3-5 cm incision. The mentioned gum contains essential oil and acidic, neutral, and polymeric compounds. To obtain gum powder, the essential oil of gum was separated from it under the supervision of a Pharmaceutical Specialist (Model Number xy-1 China juneng Brand) using the steam distillation process. Then the solid residue was powdered using pulverizer (TianFeng china-model 130 D) and poured into one-gram capsules (1 g ±0.003 g) by Capsule Filling Machine (Karasnt Iran Model CF 800).

2.5 *Interventions*

Patients were randomly classified into four groups as following; Group A: three different drugs involved of 500 mg of Amoxicillin bd, Clarithromycin 500 mg bd and Omeprazole 20 mg bd for 14 days. Group B: Drugs Group A plus the capsule containing 1 g of powdered *P. Atlantica Kurdica* gum bd for 14 days. Group C: the capsule containing 1 g of powdered *P. Atlantica Kurdica* gum bd for 14 days, Group D: placebo-containing capsule (bd), for 14 days.

2.6 *Studied Variables*

Sex and age of the patients before interventions, dyspepsia symptoms based on the criteria Rome III)Drossman and Dumitrascu 2006() before and after the intervention, the results of UBT two days before and 30 days after the completion of their interventions as well as treatment-related complication in all four groups during and after the intervention were recorded.

2.7 *Urea Breath Test*

To take UBT test, the ¹³C-containing capsule and carbon analyzer B (Fisher Analyzer Instrument GmbH, Germany) were used. Once before taking the capsule and half hours later, the exhale sample is entered into the device, and the amount of CO₂ in the breath is measured. The increased ¹³C amounts indicate the presence of *H. Pylori* in the stomach and infection rate in this device is expressed in Delta over Baseline as Equation (1).

$$(\text{DOB} = \Delta_{(\text{after trace intake})} - \Delta_{(\text{baseline})}) \quad (1)$$

Accordingly, natural DOB ≤4% and greater than 4% are considered as *H. pylori* infection. In this study, DOB values were divided into four ranges from 4 to 10, 10 to 20, and 20 to 30 and above 30, for evaluating its relationship with response to treatment and dyspeptic symptoms.

2.8 *Ethics*

The Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.REC.1394.48) approved this study. All patients were fully aware of the objectives and details of the study through the information form, and the signed written consent forms were taken from them. This study has been recorded at Iranian Registry of Clinical Trials with the code of IRCT2016042527599N1.

2.9 *Statistical Analysis*

Statistical analysis was carried out using SPSS 18 (SPSS Inc, Chicago, IL, USA). Basic demographic information, dyspepsia symptoms, and UBT results were analyzed in the aforementioned four groups using chi-square and K square tests. In this study, 95% confidence interval and the level of significance of 0.05 were chosen.

3. Results

3.1 *Baseline Characteristics*

In this study, 5 subjects who did not return for the second UBT were excluded from the study and ultimately 95 patients (45 men/50 women) with a mean who have age of 33 years were enrolled (Group A: 24 patients, Group B: 24 patients, Group C: 23 patient and Group D: 24 patients). Patients were not statistically significantly different from each other in the four groups regarding age, gender (P=0.503).

3.2 *Urea Breath Test*

Average DOB was not significantly different (P=0.98) in the groups under study before the intervention (Table 1) Before the therapeutic interventions, DOB was between 10 to 20 in 42.5% of samples, between 20 and 30 in 42.5%, higher than 30 in 8.5% and, finally, between 4 and 10 in 6.5%. There was no significant association regarding the severity of symptoms with the DOB rate at the four mentioned times (P=0.793). Average DOB in the groups under study had a significant difference 30 days after the intervention (P=0.00) (Table 1). As expected, the highest DOB rate 30 days after the treatment period was observed in the placebo group (D) and, apart from

this group, DOB significantly decreased in other three groups (for all three groups A, B, and C, $P=0.000$). A significant difference in the secondary DOB among the four groups was because of the significant difference between Groups A, B, and C with the placebo group (for the three groups A, B and C, $P=0.000$). Some cases of *H. pylori* eradication are 19/24 in Group A (=79.2%), 18/24 in Group B (=75%), 10/23 in Group C (=43.5%) and 2/24 in Group D (=8.3%). Further eradication in Groups A, B and C was significantly higher than in Group D (Placebo) (For A, $P=0.000$ and C $P=0.025$) It can be said that the triple drug regimens including the capsule with the gum from *P. Atlantica Kurdica* were effective in the eradication of *H. pylori*. It should be noted that treatment regimens in both Groups A and B, have significantly led to more eradication than C ($P=0.022$ and $P=0.041$). However, treatment of Group A was more successful for the eradication of *H. pylori*, but the difference was not significant between the two Groups A and B ($P=0.986$).

Table 1. Average DOB and eradication rates in the studied groups, before and 30 days after the intervention.

	Eradication	DOB pre (mean)	DOB post (mean)	P value (pre and post)
Group A	19.24 (79.16%)	20.788±9.1788	4.14±3.7418	0.000
Group B	18.24 (75%)	20.338±9.3877	5.09±4.5903	0.000
Group C	10.23 (43.47%)	21.330±7.8172	7.07±5.7584	0.000
Group D	2.23 (8.3%)	21.142±7.7418	17.12±8.5799	0.790
P value (between groups)	0.000	0.980	0.000	

3.3 Dyspepsia

In this study, the criteria for early satiety and anorexia, bloating, epigastric pain, fullness, halitosis, and nausea were evaluated to examine dyspepsia can be seen from Figure 2. In general, dyspeptic symptoms in 41.7% of samples in Group A, 62.5% of samples in Group B, 56.5% of samples in Group C and, ultimately, 16.7% of samples in Group D were eliminated at the end of the interventions. Relieving dyspepsia in Groups B and C compared with Group D (placebo) was significantly higher ($P=0.006$ and $P=0.025$ respectively) But the Group A was not significantly different from Group D ($P=0.267$). Therefore, *P. Atlantica Kurdica* alone also affects to eliminate these symptoms. Relieving the symptoms in Group B was significantly higher than in Groups A and C ($P=0.023$ and $P=0.039$ respectively). It should be noted that there was no significant difference between Groups A and C from this perspective ($P=0.672$).

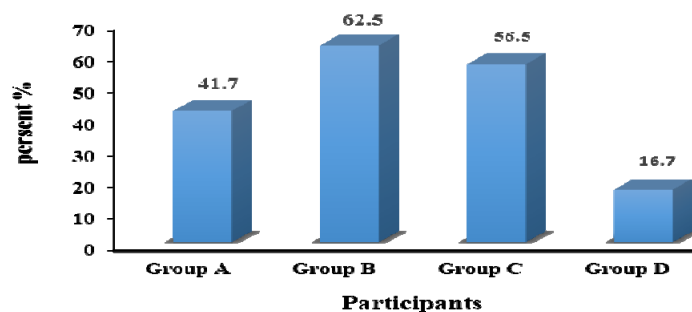


Figure 2. The chart of dyspepsia disposal amount after completion of treatment in four groups

3.4 Side effects

In Group A besides existed two cases of abdominal pain, one case of nausea, a case of palpitation, and a case of diarrhea, while in Group B was two cases of abdominal pain, one case of nausea and a case of joints pain. Moreover, in Group C happened just two cases of mild diarrhea and ultimately in Group D only one case of mild abdominal pain was observed. In none of the above cases, complications did not impede treatment process.

4. Discussion

Despite the reduction in the prevalence of *H. pylori* infection in recent decades (Magalhães Queiroz & Luzza, 2006), the treatment of infections caused by it, still is considered as a major medical problem because *H. pylori*

is the main cause of a wide range of pathologies such as gastric ulcer, gastric lymphoma, and adenocarcinoma, (Ernst & Gold, 2000). *H. pylori* infection can occur in the form of dyspepsia (Bercik & Collins, 2000) and show symptoms such as pain, epigastric discomfort, fullness, and early satiety, nausea, vomiting and belching (Tack & Lee, 2005). Regardless of current drug therapies for *H. pylori* infection, the antimicrobial effect of natural gum from *P. Atlantica Kurdica* against *H. pylori* has been proved (Sharifi et al., 2011). Moreover, in Iranian Traditional Medicine, *P. Atlantica Kurdica* role has been mentioned in the treatment of gastrointestinal pains, dyspepsia, and peptic ulcers (Sharifi, 2014). In this clinical trial, the effect of oral administration of *Pistacia Atlantica Kurdica* was investigated on the eradication of *H. pylori* in patients with symptoms of dyspepsia through capsules containing the powder of this material. For this purpose, 100 patients with positive UBT and dyspepsia diagnosis based on Rome III criteria, were divided into four groups with different treatments. Secondary UBT results were analyzed and compared 30 days after the end of interventions and improvement of dyspepsia symptoms immediately after the interventions. This study is the first clinical trial of its kind. Before this, no human study to examine the antimicrobial activity against *H. pylori* *P. Atlantica Kurdica* gum or dyspepsia symptoms have been reported. According to the results of this study, all three regimens significantly reduced the secondary DOB compared to the DOB before the start of the interventions. In 79% of samples in Group A, 75% of samples in Group B, 43.5% of samples in Group C and 8.3% of samples in Group D, *H. pylori* eradication were reported according to the results of UBT. The elimination of all groups was significantly higher than in placebo group. Treatment in both Groups A and B with three drugs including 500 mg. of Amoxicillin twice a day bd, Clarithromycin 500 mg bd and omeprazole 20 mg bd with or without *P. Atlantica Kurdica* capsules showed the greatest antimicrobial effect. In fact, adding the mentioned capsules (in Group B) resulted in an insignificant reduction of eradication rate (79% vs. 75%). The mechanism of this decrease is not known and is probably associated with the interaction among the antibiotics and gum components. Because treatment with *P. Atlantica Kurdica* has alone significantly increased the amount of eradication compared with the placebo group, the antimicrobial activity of the gums can be proved. Sharifi et al. have proven the antimicrobial effect of monomer and Polymeric Fractions *P. Atlantica Kurdica* gum against *H. pylori* in-vitro study. These researchers also stated that from among the gum from different species of *Pistacia*, *H. pylori* are most susceptible to *Kurdica* species, and they have raised this antimicrobial property associated with Beta-myrcene (Sharifi et al., 2011). In another in-vitro study, Sharifi has raised 3-O-acetoxy-3-epiisomasticadienolic acid, as the most active chemical substance isolated from an acidic fraction of *P. Atlantica Kurdica* gum (Sharifi & Hazell, 2011). The Alpha-pinene available in the resin of different species of *Pistacia* can also justify their antimicrobial activity (Douissa, Hayder, et al. 2005). In a similar study, Dabos et al. evaluated the antimicrobial effect of mastic gum (*Pistacia. Lentiscus*) against *H. pylori* in patients with positive UBT. According to the results of this study, the highest eradication rate of the bacterium was observed in the use of triple therapy regimen, which is similar to findings of this study. Although mastic gum significantly reduced DOB and the bacterial eradication (30 to 40%), the effect of the Triple therapy regimen was much more (Dabos et al., 2010). Although the genus *Pistacia* used in this study and the current study were different, the eradication amount of *H. pylori* is consistent with the *Pistacia* gum in the exclusive treatment. The triple therapy regimens in Dabos's study and this study have eradicated the *Helicobacter* in a similar level (77% and 79%). In the mentioned study, the presence of PPI with gum mastic has inhibited the antimicrobial activity of this gum. Also, in the concurrent treatment with mastic gum and pantoprazole not only no eradication was reported, but also DOB was not reduced significantly. These results are also consistent with the results of this study. *Pistacia* gum requires an acidic environment for activity, and this can explain the declination of its antimicrobial effect in the presence of PPIs. Elimination of dyspepsia in Groups B (62.5%) and C (56.5%) was significantly higher than the placebo group (16.7%), but no difference was observed between Groups A (41.7%) and D in this regard. Although *P. Atlantica Kurdica* gum (Group C) was more successful in treating the symptoms of dyspepsia patients compared with triple therapy regimen (group A), this difference was not statistically significant. On the other hand, concurrent treatment with Triple therapy regimen and *P. Atlantica Kurdica* (Treatment Group B) was significantly more effective than treating the other groups. It should be noted that the eradication of *H. pylori* does not eliminate the symptoms of dyspepsia). Accordingly, although in Group A, a significant eradication of infection was observed as shown in Figure 2, relieving symptoms of dyspepsia was not satisfactory. As far as researches have been shown the impact mechanism of *P. Atlantica Kurdica* Gum on relieving the symptoms of dyspepsia and the mechanism of its possible synergistic activity in combination with a triple therapy regimen were unknown and required further laboratory studies. The only similar study on the impact of *Pistacia* species on symptoms of dyspepsia is Dabos et al. study in which the health effects of *Pistacia Lentiscus* var. chia in patients with functional dyspepsia were investigated compared with placebo. The results of this study were similar to that of the present study and were satisfactory results (Dabos et al., 2010). In the present study, no serious complication preventing the continuation

of treatment was observed, and special effects have not been reported in previous studies too (Kang et al., 2007; Dabos et al., 2010).

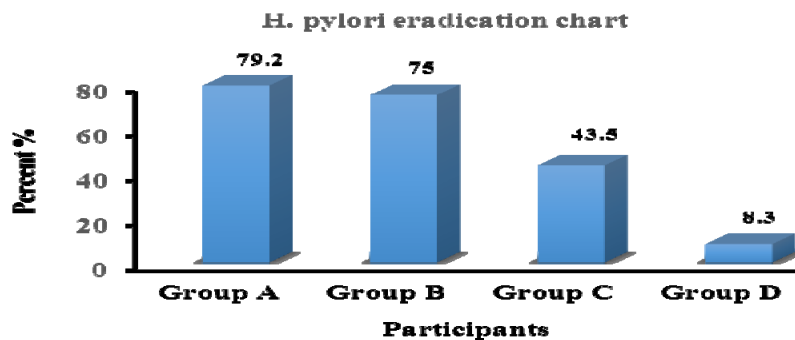


Figure 3. The percentage of *H. pylori* eradication in whole groups after treatment

Thus, considering the significant increase in improving the symptoms of dyspepsia in the quadruple therapy regimen (Amoxicillin, Clarithromycin, Omeprazole and *P. Atlantica Kurdica* gum) this treatment can be an alternative to the conventional triple-therapy regimen while lack of significant decrease in eradication of bacterium. The main limitations of this study include the use of raw gum, while in case of separating active acidic fraction of gum; its antimicrobial properties will be much more. However its role in improving the symptoms of dyspepsia may be impacted, these hypotheses require further studies with larger sample sizes. In this study, only the UBT was used to evaluate the activity of *H. pylori* yet in future studies adding endoscopy can help accurate diagnosis and reduces laboratory errors. Although, investigating the effect of concurrent administration of the mentioned gum with amoxicillin and clarithromycin in the absence of PPI can provide us with useful information, due to reduced activity of *P. Atlantica Kurdica* gum in the presence of PPIs. In conclusion a course of treatment with PPIs is likely to be required before starting antimicrobial therapy.

5. Conclusion

In the group of A has been used three drugs including Amoxicillin, Clarithromycin, Omeprazole with therapeutic efficiency was maximum (=79.2%). Whereas through the group B was employed four drugs comprising Amoxicillin, Clarithromycin, Omeprazole as well as Kurdika gum so that efficacy treatment decreased slightly (Cheer et al., 2003). To conclude in the group of A Omeprazole has acted as a complementary therapy that by reducing gastric acidity psychological effect of antibiotics against microbes is rather significant. However in the group B excited four effective therapeutic agents, the rate of final efficiency treatment has fallen. Since Kurdika gum is activated through an acidic environment in stomach, in this group Omeprazole not only reduces gastric acidity but also has interference in the functioning of the Kurdika gum (Dabos et al., 2010).

In conclusion, the results of this study indicated that consuming 1g of powdered *P. Atlantica Kurdica* gum twice daily for two weeks significantly led to *H. pylori* eradication and improvement of dyspepsia symptoms compared with placebo. Additionally, the most efficient treatment for *H. pylori* eradication was the conventional triple therapy regimen, whereas about the treatment of dyspepsia, adding *P. Atlantica Kurdica* gum to triple therapy regimen leads to better the results.

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Competing Interests Statement

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

- Al-Habbal, M. J., Al-Habbal, Z., & Huwez, F. U. (1984). A Double-Blind Controlled Clinical Trial of Mastic and Placebo in the Treatment of Duodenal Ulcer. *Clinical and experimental pharmacology and physiology*, 11(5), 541-544. <http://dx.doi.org/10.1111/j.1440-1681.1984.tb00864.x>

- Bercik, P., & Collins, S. (2000). Current concepts of dyspepsia: The role of the nervous system. *Helicobacter pylori*, 411-420. http://dx.doi.org/10.1007/978-94-011-3927-4_43
- Cheer, S., Prakash, A., & Faulds, D. (2003). Pantoprazole: An update of its pharmacological properties and therapeutic use in the among the proton pump inhibitors in terms of management of acid-related disorders. *Drugs*, 63, 101-132. <http://dx.doi.org/10.2165/00003495-200363010-00006>
- Dabos, K. J., Sfika, E., Vlatta, L. J., Frantzi, D., Amygdalos, G. I., & Giannikopoulos, G. (2010). Is Chios mastic gum effective in the treatment of functional dyspepsia? A prospective randomised double-blind placebo controlled trial. *Journal of ethnopharmacology*, 127(2), 205-209. <http://dx.doi.org/10.1016/j.jep.2009.11.021>
- Dabos, K., Sfika, E., Vlatta, L., & Giannikopoulos, G. (2010). The effect of mastic gum on Helicobacter pylori: A randomized pilot study. *Phytomedicine*, 17(3), 296-299. <http://dx.doi.org/10.1016/j.phymed.2009.09.010>
- Daifas, D. P., Smith, J. P., Blanchfield, B., Sanders, G., Austin, J. W., & Koukoutisis, J. (2004). Effects of mastic resin and its essential oil on the growth of proteolytic Clostridium botulinum. *International Journal of Food Microbiology*, 94(3), 313-322. <http://dx.doi.org/10.1016/j.ijfoodmicro.2004.01.017>
- Daryaei, M., Hoseiny, S., Taheri, K., Mirzaei, J., & Mzbani, A. (2012). *Effect of morphological variables of Pistacia atlantica on gum and seed Production*.
- Dimas, K. S., Pantazis, P., & Ramanujam, R. (2012). Chios mastic gum: A plant-produced resin exhibiting numerous diverse pharmaceutical and biomedical properties. *In vivo*, 26(5), 777-785.
- Douissa, F. B., Hayder, N., Chekir-Ghedira, L., Hammami, M., Ghedira, K., Mariotte, A. M., & Dijoux-Franca, M. G. (2005). New study of the essential oil from leaves of Pistacia lentiscus L. (Anacardiaceae) from Tunisia. *Flavour and Fragrance Journal*, 20(4), 410-414. <http://dx.doi.org/10.1002/ffj.1445>
- Drossman, D. A., & Dumitrascu, D. L. (2006). Rome III: New standard for functional gastrointestinal disorders. *Journal of Gastrointestinal and Liver Diseases*, 15(3), 237.
- Ernst, P. B., & Gold, B. D. (2000). The disease spectrum of Helicobacter pylori: The immunopathogenesis of gastroduodenal ulcer and gastric cancer. *Annual Reviews in Microbiology*, 54(1), 615-640. <http://dx.doi.org/10.1146/annurev.micro.54.1.615>
- Huwez, F. U., Thirlwell, D., Cockayne, A., & Ala'Aldeen, D. A. (1998). Mastic gum kills Helicobacter pylori. *New England Journal of Medicine*, 339(26), 1946-1946. <http://dx.doi.org/10.1056/NEJM199812243392618>
- Kang, J. S., Wanibuchi, H., Salim, E. I., Kinoshita, A., & Fukushima, S. (2007). Evaluation of the toxicity of mastic gum with 13 weeks dietary administration to F344 rats. *Food and chemical toxicology*, 45(3), 494-501. <http://dx.doi.org/10.1016/j.fct.2006.09.013>
- Longo, D. L., Fauci, A. S., Kasper, D. L., Hauser, S. L., Jameson, J. L., & Loscalzo, J. (2012). *Harrison's Principles of Internal Medicine*, 18E(2), 1262. McGraw Hill Professional.
- Magalhães Queiroz, D. M., & Luzza, F. (2006). Epidemiology of Helicobacter pylori infection. *Helicobacter*, 11(s1), 1-5. <http://dx.doi.org/10.1111/j.1478-405X.2006.00429.x>
- Malekzadeh, R., Ansari, R., Vahedi, H., Siavoshi, F., Alizadeh, B., Eshraghian, M., ... Massarrat, S. (2000). Furazolidone versus metronidazole in quadruple therapy for eradication of Helicobacter pylori in duodenal ulcer disease. *Alimentary Pharmacology and Therapeutics*, 14(3), 299-304. <http://dx.doi.org/10.1046/j.1365-2036.2000.00709.x>
- Perez-Perez, G. I., Rothenbacher, D., & Brenner, H. (2004). Epidemiology of Helicobacter pylori infection. *Helicobacter*, 9(s1), 1-6. <http://dx.doi.org/10.1111/j.1083-4389.2004.00248.x>
- Saffarzadeh, A., Vincze, L., & Csapo, J. (1999). Determination of the chemical composition of acorn (Quercus branti), Pistacia atlantica and Pistacia Khinjik seeds as non-conventional feedstuffs. *Acta Agr Kapos*, 3(3), 59-69.
- Sharifi, M. S. (2014). Chapter Five Pistacia Atlantica Kurdica. *Perspectives on Kurdistan's Economy and Society in Transition*, 2, 64.
- Sharifi, M. S., & Hazell, S. L. (2011). Isolation, analysis and antimicrobial activity of the acidic fractions of Mastic, Kurdica, Mutica and Cabolica gums from genus Pistacia. *Global journal of health science*, 4(1), 217. <http://dx.doi.org/10.5539/gjhs.v4n1p217>
- Sharifi, M. S., Ebrahimi, D., Hibbert, D. B., Hook, J., & Hazell, S. L. (2011). Bio-activity of natural polymers

- from the genus pistacia: A validated model for their antimicrobial action. *Global journal of health science*, 4(1), 149. <http://dx.doi.org/10.5539/gjhs.v4n1p149>
- Shimomura, H., Hayashi, S., Yokota, K., Oguma, K., & Hirai, Y. (2004). Alteration in the composition of cholesteryl glucosides and other lipids in *Helicobacter pylori* undergoing morphological change from spiral to coccoid form. *FEMS microbiology letters*, 237(2), 407-413. <http://dx.doi.org/10.1111/j.1574-6968.2004.tb09724.x>
- Tack, J., & Lee, K. (2005). Pathophysiology and treatment of functional dyspepsia. *Journal of clinical gastroenterology*, 39(5), S211-S216. <http://dx.doi.org/10.1097/01.mcg.0000156109.97999.d1>
- Taran, M., Sharifi, M., Azizi, E., & Khanahmadi, M. (2010). Antimicrobial activity of the leaves of *Pistacia khinjuk*. *Journal of Medicinal Plants*, 1(33), 81-85.
- Zagari, R. M., Law, G. R., Fuccio, L., Cennamo, V., Gilthorpe, M. S., Forman, D., & Bazzoli, F. (2010). Epidemiology of functional dyspepsia and subgroups in the Italian general population: An endoscopic study. *Gastroenterology*, 138(4), 1302-1311. <http://dx.doi.org/10.1053/j.gastro.2009.12.057>

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