



Frequency of using complementary herbal medicines among *Helicobacter pylori*-infected patients in the North of Iran

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ABSTRACT

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Helicobacter pylori is a prevalent infection and one of the most critical factors that result in gastric cancer. Besides antibiotic therapy, some plants are suitable as an alternative treatment against *H. pylori* infection due to their role in protecting the gastric mucosa. This study investigated the frequency of using complementary herbal medicines among *H. pylori*-infected patients in the North of Iran. This cross-sectional study was conducted on 390 patients with *H. pylori* infection undergoing treatment in Rasht, Iran, 2022. The demographic data, clinical characteristics, and consumption of complementary herbals were recorded. The mean age of the patients was 40 years, and 63.6% were female. The majority of the patients were educated. About 55.9% of patients consumed at least one herbal product, and the most consumed herbal product was mint extract. Most patients purchased herbal products from the grocery (93.1%); none referred to the pharmacy. About 89.2% of the patients recovered completely, and 10.8% had a disease recurrence. No particular complications were observed in most patients (97.7%). However, no significant association between the consumption of herbal products and patients' recovery was reported ($P>0.05$). According to our results, consuming herbal products results in no specific improvement in patients with *H. pylori* infection.

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1. Introduction

Cancer is responsible for 13% of all annual deaths worldwide, and gastric cancer is one of the most common ones, especially in Japan and South America, where the incidence is between 10 and 70 per 100 individuals per year [1]. Gastric cancer happens due to genetic and epigenetic factors and the individual's lifestyle effect on presenting this malignancy. On the other hand, *Helicobacter pylori* is considered one of the most critical factors in causing gastric cancer [2]. About 70% of global deaths from cancer occur in developing countries such as Iran. The annual incidence of gastric cancer among Iranian population is around 7300 cases per year, and is the most common type of cancer in men [3]. *H. pylori*, a Gram-negative and microaerophilic bacteria, can colonize the stomach and withstand its inhospitable conditions using acid resistance mechanisms and colonization factors [4]. Given its high prevalence, infecting over 50% of the global population, *H. pylori* is a widespread human infection [5]. Several modes of transmission of *H. pylori* have been reported, including direct contact via contaminated water sources and food (7), iatrogenic transmission, and zoonotic transmission [6-8].

To treat *H. pylori* infection, besides choosing the regimen, antibiotics therapy should be considered. In patients who have not been previously exposed to macrolides and reside in regions with low clarithromycin resistance, the triple therapy regimen containing clarithromycin is commonly prescribed. Alternatively, the bismuth quadruple therapy or non-bismuth quadruple therapy is selected as the treatment regimen [9, 10]. In cases where the first-line therapy for *H. pylori* infection fails, second-line and even third-line therapies are necessary. However, the effectiveness of these subsequent therapies is hindered by potential microbial resistance to antibiotics [11, 12]. Phytotherapy or herbal therapy uses plants or plant extracts for medicinal purposes as a complementary therapy for *H. pylori* infection [13]. Some herbs have the most significant effect against *H. pylori* infection [14]. The antibacterial effects of herbal therapy were mainly examined in vitro conditions, and more clinical trials are required to investigate these herbs' effectiveness on *H. pylori* infection [15].

Given the significant impact of *H. pylori* infection on global health, including its widespread prevalence and the rising issue of antibiotic resistance, it becomes imperative to explore alternative treatment options. Some plants are suitable treatment options against *H.*

pylori infection because they protect the gastric mucosa. However, their use in humans requires more clinical studies. In this regard, we aimed to investigate the frequency of use of complementary herbal medicines among *H. pylori* infected patients in the North of Iran.

2. Materials and Methods

2.1 Study design

In this cross-sectional study, the demographical data and clinical characteristics of 390 patients with *H. pylori* infection who were undergoing treatment were collected in Rasht, Iran, in 2022. Pathological examination was used to confirm the *H. pylori* infection. The patients with incomplete data and patient who not completing antibiotic treatment were excluded from the study. The data included age, gender, educational status, types of herbal medicine (mint extract (*Mentha piperita* L.), thyme (*Thymus vulgaris* L.), oregano (*Origanum vulgare* L.), and borage flower (*Borago officinalis* L.), etc.), antibiotic treatment outcome, how herbal products were purchased, and side effects of herbal products.

2.2 Statistical analysis

The qualitative variables were reported as percentages and numbers; the quantitative variables were reported as mean \pm standard deviation (SD). The Kolmogorov-Smirnov and Chi-Square tests were used to compare the variables. The data was analyzed using SPSS version 16 software with a significance level of less than 0.05.

3. Results

The mean age of patients was 40.4 ± 12.7 years (15-67 years) with a median of 38 years old. About 36.4% of cases were male, and the frequency of *H. pylori* infection significantly differed among genders ($P < 0.001$). Most patients had diplomas (42.3%), and about 218 consumed herbal products (55.9%). The most frequent herbal product was mint extract (36.9%), and patients purchased herbal products from the grocery (93.1%). Most patients recovered (89.2%) after their prescribed antibiotic treatment. Also, only in 2.3% of the patients, the side effects of herbal products were observed (Table 1). According to Table 2, no statistically significant association was seen due to the effectiveness of herbal products on the patients' recovery status ($P > 0.05$).

Table 1. The frequency of demographical data and clinical characteristics among patients with *H. pylori* infection who are undergoing treatment.

Basic data	Variables	Number	Percentage
Gender	Male	142	36.4
	Female	248	63.6
	Illiterate	67	17.2
Educational level	Diploma	165	42.3
	Bachelor	123	31.5
	Master	10	2.6

	PhD	25	6.4
Consuming herbal products	Yes	218	55.9
	No	172	44.1
	Mint extract	144	36.9
Types of herbal products	Thyme	32	8.2
	Borage flower	11	2.8
	Oregano	27	6.9
How herbal products were purchased	Grocery	203	93.1
	Pharmacy	0	0.0
	Homemade	15	100.0
Recovery	Yes	348	89.2
	No	42	10.8
Side effects of consumed herbal products	Yes	5	2.3
	No	213	97.7

Table 2. The association between types of herbal medicine and the improvements of the clinical condition of patients with *H. pylori* infection who are undergoing treatment

Variables		Recovery n (%)		P value
		Yes	No	
Consuming herbal products	Yes	199 (51.0)	19 (4.9)	0.096
	No	149 (38.2)	23 (5.9)	
Consuming mint extract	Yes	133 (34.1)	11 (2.8)	0.086
	No	215 (55.1)	31 (7.9)	
Consuming thyme	Yes	30 (7.7)	2 (0.5)	0.304
	No	318 (81.5)	40 (10.3)	
Consuming borage flower	Yes	11 (2.8)	0 (0.0)	0.281
	No	337 (86.4)	42 (10.8)	
Consuming oregano	Yes	26 (6.7)	1 (0.3)	0.186
	No	322 (82.6)	41 (10.5)	

4. Discussion

Due to the importance of controlling *H. pylori* infection and its resistance to antimicrobial therapy, patients usually follow alternative remedies, including some unwanted side effects besides their supplementary role. The majority of patients in the current study were females and middle-aged individuals. Regarding the frequency of *H. pylori* infection among genders, women have a rate of 42.7%, and men have a rate of 46.3% infection. The highest gender gap has been observed in Africa (male/female ratio equal to 1.16) and the lowest in Latin America and the Caribbean (male/female ratio equal to 1.03). Although the predominance of men for *H. pylori* infection is evident in all continents, none have shown statistically significant differences [13, 16, 17].

Similar to our results, it was demonstrated that individuals with older age had a significantly higher prevalence of *H. pylori* infection than younger individuals because the risk of exposure increases with age [18]. Regarding education, most patients had a diploma or bachelor's degree, which can be related to using more ready meals and fast food in these age groups. *H. pylori* infection is more common in developing countries (50.8%) compared to developed countries (34.7%) [18]. Socio-economic status is associated with the prevalence of *H. pylori* infection [19, 20]. The hypothesis that food is the transmission route of *H. pylori* infection is supported by epidemiological studies that have observed a higher prevalence of *H. pylori* infection in areas with poor sanitary conditions [21, 22].

In this study, more than half of the patients used at

least one herbal product. This amount is almost double that in the USA (25%) [23]. Plants are a complex mixture of organic chemicals, and the risks and benefits of herbal products are complex and confusing. The side effects of using herbal products are less than the side effects of antibiotics. Salem et al. reported that the side effects in patients who consumed *N. sativa* were minor compared to patients who consumed antibiotics [24]. Another study illustrated that the side effects of using cinnamon were also minor [25]. However, biologically active compounds of plants need to be examined and detoxicated to decrease the unwilling side effects. Moreover, many patients do not inform their doctor about the use of herbal products, which can cause worse results and more side effects in patients. Several studies have shown that although more than 17% of Americans use supplements, only one-third inform their doctor [26]. In the current study, mint extract was the most consumed herbal product, similar to other studies [27, 28]. Conversely, popular beliefs about improving gastric pain after consuming mint will increase its consumption rate. Most of the herbal products were purchased from groceries. Pharmacies usually do not offer these products due to the clinical interactions between herbal supplements and drugs, which appear as pharmacokinetic interactions that affect the drug's blood concentration and pharmacological action. The risk of a pharmacokinetic interaction occurs when herbal supplements have the same absorption, distribution, metabolism, or excretion mechanism as a concomitant drug and may result in changes in the drug concentration at the site of action [23].

The frequency of recovery was 89.2% among the

patients, which is consistent with other studies [29, 30]. Treatment failure poses a significant challenge in the management of *H. pylori* infection. Antibiotic resistance is crucial in this problem as the bacteria can persist in protective environments like the gastric mucosa and epithelial layers [31]. Among the antibiotics employed in treating *H. pylori* infection, clarithromycin is highly recommended due to its effectiveness. However, when the strain develops resistance to clarithromycin, the success rate of standard treatment drops to 20%, as opposed to 90% when the strain remains susceptible [32]. Despite our results on the effectiveness of herbal products on patients' recovery from *H. pylori* infection, some studies demonstrated improvements in patients' clinical condition by consuming various herbal products that were eliminated with *H. pylori* infection [28, 33, 34]. However, these studies have been conducted in vitro, and few studies have been conducted on the effectiveness of these herbal extracts at the bedside. No trials have been registered to analyze the activity of herbal products except for Cranberry to be effective against *H. pylori* infection [35]. The results of the present study also show no significant association between the consumption of herbal products and the recovery of patients with *H. pylori* infection. Since a history of consumption of herbal products and their side effects was self-reported, the recall bias is considered one of the study's limitations. On the other hand, some symptoms or side effects are not identifiable by patients, and the reported side effects might be less than what they were.

According to our results, most patients with *H. pylori* infection were women and middle-aged. Most patients consumed at least one herbal product along with the medicine prescribed by the doctor, with a high recovery rate. However, no significant difference was found between the consumption of herbal products and the frequency of recovery among patients.

Authors' contributions

Concept development (provided the idea for the research): HB, MA and KD. Design (planned the methods to generate the results): HB, MA and KD. Supervision (provided oversight, responsible for organization and implementation): HK, SS and SZ. Data collection/processing (responsible for experiments, patient management, organization, or reporting data) and data analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): HK, SS and SZ. Literature search (performed the literature search and writing of the manuscript): HB, MA and KD. All authors contributed to the article and approved the final version of manuscript.

Conflict of interest

No potential conflict of interest was reported by the authors.

Ethical declarations

All the patients gave their informed consent to participate in this current study. This study design was approved by the ethical committee of Guilan University of Medical Sciences (IR.GUMS.REC.1401.209).

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References

- Choi JJ, Kim CG, Lee JY, Kim YI, Kook MC, Park B, et al. Family History of Gastric Cancer and Helicobacter pylori Treatment. *N Engl J Med.* 2020;382(5):427-36. DOI: [10.1056/NEJMoa1909666](https://doi.org/10.1056/NEJMoa1909666) PMID: [31995688](https://pubmed.ncbi.nlm.nih.gov/31995688/)
- Salvatori S, Marafini I, Laudisi F, Monteleone G, Stolfi C. Helicobacter pylori and Gastric Cancer: Pathogenetic Mechanisms. *Int J Mol Sci.* 2023;24(3). DOI: [10.3390/ijms24032895](https://doi.org/10.3390/ijms24032895) PMID: [36769214](https://pubmed.ncbi.nlm.nih.gov/36769214/)
- Movahedi M, Afsharfard A, Moradi A, Nasermoaddeli A, Khoshnevis J, Fattahi F, et al. Survival rate of gastric cancer in Iran. *J Res Med Sci.* 2009;14(6):367-73. PMID: [21772910](https://pubmed.ncbi.nlm.nih.gov/21772910/)
- Mladenova I. Clinical Relevance of Helicobacter pylori Infection. *J Clin Med.* 2021;10(16). DOI: [10.3390/jcm10163473](https://doi.org/10.3390/jcm10163473) PMID: [34441769](https://pubmed.ncbi.nlm.nih.gov/34441769/)
- Salih BA. Helicobacter pylori infection in developing countries: the burden for how long? *Saudi J Gastroenterol.* 2009;15(3):201-7. DOI: [10.4103/1319-3767.54743](https://doi.org/10.4103/1319-3767.54743) PMID: [19636185](https://pubmed.ncbi.nlm.nih.gov/19636185/)
- Farrell S, Doherty GM, Milliken I, Shield MD, McCallion WA. Risk factors for Helicobacter pylori infection in children: an examination of the role played by intrafamilial bed sharing. *Pediatr Infect Dis J.* 2005;24(2):149-52. DOI: [10.1097/01.inf.0000151104.14058.70](https://doi.org/10.1097/01.inf.0000151104.14058.70) PMID: [15702044](https://pubmed.ncbi.nlm.nih.gov/15702044/)
- Brown LM. Helicobacter pylori: epidemiology and routes of transmission. *Epidemiol Rev.* 2000;22(2):283-97. DOI: [10.1093/oxfordjournals.epirev.a018040](https://doi.org/10.1093/oxfordjournals.epirev.a018040) PMID: [11218379](https://pubmed.ncbi.nlm.nih.gov/11218379/)
- Goodman KJ, Correa P, Tenganá Aux HJ, Ramírez H, DeLany JP, Guerrero Pepinosa O, et al. Helicobacter pylori infection in the Colombian Andes: a population-based study of transmission pathways. *Am J Epidemiol.* 1996;144(3):290-9. DOI: [10.1093/oxfordjournals.aje.a008924](https://doi.org/10.1093/oxfordjournals.aje.a008924) PMID: [8686698](https://pubmed.ncbi.nlm.nih.gov/8686698/)
- Pellicano R, Zagari RM, Zhang S, Saracco GM, Moss SF. Pharmacological considerations and step-by-step proposal for the treatment of Helicobacter pylori infection in the year 2018. *Minerva Gastroenterol Dietol.* 2018;64(3):310-21. DOI: [10.23736/S1121-421X.18.02492-3](https://doi.org/10.23736/S1121-421X.18.02492-3) PMID: [29600697](https://pubmed.ncbi.nlm.nih.gov/29600697/)
- Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. *Am J Gastroenterol.* 2017;112(2):212-39. DOI: [10.1038/ajg.2016.563](https://doi.org/10.1038/ajg.2016.563) PMID: [28071659](https://pubmed.ncbi.nlm.nih.gov/28071659/)
- Lin TF, Hsu PI. Second-line rescue treatment of Helicobacter pylori infection: Where are we now? *World J Gastroenterol.* 2018;24(40):4548-53. DOI: [10.3748/wjg.v24.i40.4548](https://doi.org/10.3748/wjg.v24.i40.4548) PMID: [30386104](https://pubmed.ncbi.nlm.nih.gov/30386104/)
- Puig I, López-Góngora S, Calvet X, Villoria A, Baylina M, Sanchez-Delgado J, et al. Systematic review: third-line susceptibility-guided treatment for Helicobacter pylori infection. *Therap Adv Gastroenterol.* 2016;9(4):437-48. DOI: [10.1177/1756283X15621229](https://doi.org/10.1177/1756283X15621229) PMID: [27366212](https://pubmed.ncbi.nlm.nih.gov/27366212/)
- Vitor JM, Vale FF. Alternative therapies for Helicobacter pylori: probiotics and phytomedicine. *FEMS Immunol Med Microbiol.* 2011;63(2):153-64. DOI: [10.1111/j.1574-695X.2011.00865.x](https://doi.org/10.1111/j.1574-695X.2011.00865.x) PMID: [22077218](https://pubmed.ncbi.nlm.nih.gov/22077218/)
- Aliramaei MR, Rabbani khorasgani M, Rahmani MR, Zarkesh Esfahani SH. The effect of Iranian native medicinal plants on

- Helicobacter pylori*: review study. *J Microb Biol.* 2019;8(31):1-18. [In Persian] DOI: [10.22108/bjm.2019.113830.1169](https://doi.org/10.22108/bjm.2019.113830.1169)
15. Ayala G, Escobedo-Hinojosa WI, de la Cruz-Herrera CF, Romero I. Exploring alternative treatments for *Helicobacter pylori* infection. *World J Gastroenterol.* 2014;20(6):1450-69. DOI: [10.3748/wjg.v20.i6.1450](https://doi.org/10.3748/wjg.v20.i6.1450) PMID: [24587621](https://pubmed.ncbi.nlm.nih.gov/24587621/)
 16. Akeel M, Elmakki E, Shehata A, Elhafey A, Aboshouk T, Ageely H, et al. Prevalence and factors associated with *H. pylori* infection in Saudi patients with dyspepsia. *Electron Physician.* 2018;10(9):7279-86. DOI: [10.19082/7279](https://doi.org/10.19082/7279) PMID: [30258561](https://pubmed.ncbi.nlm.nih.gov/30258561/)
 17. Bravo D, Hoare A, Soto C, Valenzuela MA, Quest AF. *Helicobacter pylori* in human health and disease: Mechanisms for local gastric and systemic effects. *World J Gastroenterol.* 2018;24(28):3071-89. DOI: [10.3748/wjg.v24.i28.3071](https://doi.org/10.3748/wjg.v24.i28.3071) PMID: [30065554](https://pubmed.ncbi.nlm.nih.gov/30065554/)
 18. Zamani M, Ebrahimitabar F, Zamani V, Miller WH, Alizadeh-Navaei R, Shokri-Shirvani J, et al. Systematic review with meta-analysis: the worldwide prevalence of *Helicobacter pylori* infection. *Aliment Pharmacol Ther.* 2018;47(7):868-76. DOI: [10.1111/apt.14561](https://doi.org/10.1111/apt.14561) PMID: [29430669](https://pubmed.ncbi.nlm.nih.gov/29430669/)
 19. Bastos J, Peleteiro B, Barros R, Alves L, Severo M, de Fátima Pina M, et al. Sociodemographic determinants of prevalence and incidence of *Helicobacter pylori* infection in Portuguese adults. *Helicobacter.* 2013;18(6):413-22. DOI: [10.1111/hel.12061](https://doi.org/10.1111/hel.12061) PMID: [23725608](https://pubmed.ncbi.nlm.nih.gov/23725608/)
 20. Zamani M, Vahedi A, Maghdouri Z, Shokri-Shirvani J. Role of food in environmental transmission of *Helicobacter pylori*. *Caspian J Intern Med.* 2017;8(3):146-52. DOI: [10.22088/cjim.8.3.146](https://doi.org/10.22088/cjim.8.3.146) PMID: [28932364](https://pubmed.ncbi.nlm.nih.gov/28932364/)
 21. Vale FF, Vitor JM. Transmission pathway of *Helicobacter pylori*: does food play a role in rural and urban areas? *Int J Food Microbiol.* 2010;138(1-2):1-12. DOI: [10.1016/j.ijfoodmicro.2010.01.016](https://doi.org/10.1016/j.ijfoodmicro.2010.01.016) PMID: [20122750](https://pubmed.ncbi.nlm.nih.gov/20122750/)
 22. Nurgalieva ZZ, Malaty HM, Graham DY, Almuchambetova R, Machmudova A, Kapsultanova D, et al. *Helicobacter pylori* infection in Kazakhstan: effect of water source and household hygiene. *Am J Trop Med Hyg.* 2002;67(2):201-6. DOI: [10.4269/ajtmh.2002.67.201](https://doi.org/10.4269/ajtmh.2002.67.201) PMID: [12389948](https://pubmed.ncbi.nlm.nih.gov/12389948/)
 23. Asher GN, Corbett AH, Hawke RL. Common Herbal Dietary Supplement-Drug Interactions. *Am Fam Physician.* 2017;96(2):101-7. PMID: [28762712](https://pubmed.ncbi.nlm.nih.gov/28762712/)
 24. Salem EM, Yar T, Bamosa AO, Al-Quorain A, Yasawy MI, Alsulaiman RM, et al. Comparative study of *Nigella Sativa* and triple therapy in eradication of *Helicobacter Pylori* in patients with non-ulcer dyspepsia. *Saudi J Gastroenterol.* 2010;16(3):207-14. DOI: [10.4103/1319-3767.65201](https://doi.org/10.4103/1319-3767.65201) PMID: [20616418](https://pubmed.ncbi.nlm.nih.gov/20616418/)
 25. Nir Y, Potasman I, Stermer E, Tabak M, Neeman I. Controlled trial of the effect of cinnamon extract on *Helicobacter pylori*. *Helicobacter.* 2000;5(2):94-7. DOI: [10.1046/j.1523-5378.2000.00014.x](https://doi.org/10.1046/j.1523-5378.2000.00014.x) PMID: [10849058](https://pubmed.ncbi.nlm.nih.gov/10849058/)
 26. Clarke TC, Black LI, Stussman BJ, Barnes PM, Nahin RL. Trends in the use of complementary health approaches among adults: United States, 2002-2012. *Natl Health Stat Report.* 2015;(79):1-16. PMID: [25671660](https://pubmed.ncbi.nlm.nih.gov/25671660/)
 27. Mishra LK, Sarkar D, Mentreddy R, Shetty K. Evaluation of phenolic bioactive-linked anti-hyperglycemic and *Helicobacter pylori* inhibitory activities of Asian Basil (*Ocimum spp.*) varieties. *J Herb Med.* 2020;20:100310. DOI: [10.1016/j.hermed.2019.100310](https://doi.org/10.1016/j.hermed.2019.100310)
 28. Ghannadi A, Sajjadi S-E, Abedi D, Yousefi J, Daraei-Ardekani R. The in vitro activity of seven Iranian plants of the Lamiaceae family against *Helicobacter pylori*. *Niger J Nat Prod Med.* 2004;8:40-2. DOI: [10.4314/njnp.v8i1.11812](https://doi.org/10.4314/njnp.v8i1.11812)
 29. Laine L, Hunt R, El-Zimaity H, Nguyen B, Osato M, Spénard J. Bismuth-based quadruple therapy using a single capsule of bismuth biscalcitrate, metronidazole, and tetracycline given with omeprazole versus omeprazole, amoxicillin, and clarithromycin for eradication of *Helicobacter pylori* in duodenal ulcer patients: a prospective, randomized, multicenter, North American trial. *Am J Gastroenterol.* 2003;98(3):562-7. DOI: [10.1111/j.1572-0241.2003.t01-1-07288.x](https://doi.org/10.1111/j.1572-0241.2003.t01-1-07288.x) PMID: [12650788](https://pubmed.ncbi.nlm.nih.gov/12650788/)
 30. Venerito M, Krieger T, Ecker T, Leandro G, Malfertheiner P. Meta-analysis of bismuth quadruple therapy versus clarithromycin triple therapy for empiric primary treatment of *Helicobacter pylori* infection. *Digestion.* 2013;88(1):33-45. DOI: [10.1159/000350719](https://doi.org/10.1159/000350719) PMID: [23880479](https://pubmed.ncbi.nlm.nih.gov/23880479/)
 31. Dubois A, Borén T. *Helicobacter pylori* is invasive and it may be a facultative intracellular organism. *Cell Microbiol.* 2007;9(5):1108-16. DOI: [10.1111/j.1462-5822.2007.00921.x](https://doi.org/10.1111/j.1462-5822.2007.00921.x) PMID: [17388791](https://pubmed.ncbi.nlm.nih.gov/17388791/)
 32. Mégraud F. *H. pylori* antibiotic resistance: prevalence, importance, and advances in testing. *Gut.* 2004;53(9):1374-84. DOI: [10.1136/gut.2003.022111](https://doi.org/10.1136/gut.2003.022111) PMID: [15306603](https://pubmed.ncbi.nlm.nih.gov/15306603/)
 33. Abachi S, Khademi F, Fatemi H, Malekzadeh F. Study of antibacterial activity of selected Iranian plant extracts on *Helicobacter pylori*. *IOSR J Dental Med Sci.* 2013;5:155-9. URL: <https://www.iosrjournals.org/iosr-jdms/papers/Vol5-issue1/O0515559.pdf>
 34. Moghaddam MN. In vitro inhibition of *Helicobacter pylori* by some spices and medicinal plants used in Iran. *Glob J Pharmacol.* 2011;5(3):176-80. URL: [https://idosi.org/gjp/5\(3\)11/11.pdf](https://idosi.org/gjp/5(3)11/11.pdf)
 35. Murali MR, Naveen SV, Son CG, Raghavendran HRB. Current knowledge on alleviating *Helicobacter pylori* infections through the use of some commonly known natural products: bench to bedside. *Integr Med Res.* 2014;3(3):111-8. DOI: [10.1016/j.imr.2014.04.001](https://doi.org/10.1016/j.imr.2014.04.001) PMID: [28664086](https://pubmed.ncbi.nlm.nih.gov/28664086/)