Life Sciences Student Journal

2024, Vol2, No1
DOI:10.22034/LSSJ.2024.109

The Role of Probiotics in Treatment of Helicobacter pylori Infections

Haniye Fayezi [1], Negar Jamshidi[1], Saghar Zarrin Tarazian[1],Nazanin Jamshidi[1*],Amir Hossein Ghasemi [1], Alireza Zardar[2]

[1] Kimia Andisheh Teb Medical and Molecular Laboratory Research Co., Tehran, Iran .
[2]Department of Veterinary Medicine. Islamic Azad University. Karaj Branch . Iran.

Haniye Fayezi
M.sc of Pathogenic microbes

Article Type:
Review Article

Received: 28 April. 2024
Revised: 10 may . 2024
Accepted: 12 May . 2024
ePublished: 16 May. 2024

Abstract

The term "probiotics" refers to organisms that, when administered in sufficient quantities, confer health benefits on the host and have a variety of effects, including inhibition of pathogens, stimulation of organ function, and activation of the immune response in the human body. Studies have demonstrated that probiotics can inhibit Helicobacter pylori in both experimental and clinical settings. Competition for nutrients, production of bactericidal substances, competition to inhibit adherence and stimulation of host functions, and immunity are the mechanisms by which probiotics reduce H. pylori infections. In addition, probiotics are used clinically to eradicate H. pylori infection, and the effects of probiotics as a single therapy and in combination with other drugs, including proton pump inhibitors and anti-H. Pylori antibiotics have been reported. Studies have shown that probiotics are increasing the eradication rate and preventing side effects such as diarrhea, nausea, vomiting, or a taste disorder. Some probiotics may be helpful for the eradication of H. pylori and their efficacy in reducing side effects of treatment with antibiotics, but more research is necessary to answer several questions relating to the mechanism of action of Probiotics. Moreover, in future studies, it is necessary to clarify the strain specificity, dose, and duration of probiotic therapy for eradication of H. pylori infection.

Keywords: Helicobacter pylori, Treatment, Probiotics, Microbiota, Lactobacillus

1. Introduction

About half of the world's population is infected with Helicobacter pylori, which is more frequently found in developing countries where it can affect up to 80 % of people (1). H. pylori has been linked to the development of several GI disorders, including gastritis, peptic ulcer, and gastric adenocarcinoma (2). H. pylori has also been involved in the development of other extra gastric disorders, such as associated lymphoid mucosa lymphoma MALT Idiopathic Thrombocytopenic purpura, vitamin B12 deficiency and iron deficiency; In the management of these H. pylori related disorders, eradication of H. pylori can be helpful (2). The standard triple therapy (3), consisting of a proton pump inhibitor or ranitidine bismuth citrate, together with clarithromycin and amoxicillin or metronidazole, has been recommended for eradication of H. pylori for the past two decades. However, some studies have begun to focus on probiotics as a therapeutic approach due to the increased incidence of antibiotic resistance. Probiotics are the living microbial species that may include anti-inflammatory and antioxidative mechanisms which can improve gastrointestinal health (4).Probiotics are live microbes that have a health benefit for the host when administered in an appropriate amount. Lactobacillus and Bifidobacteria are the most commonly used probiotic bacteria (5). During treatment, probiotics could improve eradication of H. pylori and decrease adverse reactions (6).

2. Helicobacter Pylori

Helicobacter pylori is a Gram negative microorganism. More than 20 species have been formally identified since the genus Helicobacter was first discovered (7). In case of bacterial infection, the mucosa of the stomach is well protected. H. pylori must survive the bactericidal activity of its gastric lumen after ingestion, enter a mucous layer. H. pylori is very good at adapting to certain stomach conditions (8).

Moreover, the bacteria produce enzyme urease, which hydrolyzes urea into carbon dioxide and ammonia and elevates pH in the surroundings of the bacteria. The enzyme activity is highest at low pH (9). Due to a complex balance between host factors and bacterial virulence factors, H. pylori bacteria most often cause chronic infection. One of the main factors driving Th17 inflammation is secreted peptidyl-prolyl cis, trans-isomerase, among several bacterial factors (10). H. pylori infection continues to be one of the most common bacterial infections in the world. Eastern Europe, Africa and the majority of Asian countries have very high rates of H. pylori infection; The prevalence has fallen and is less than 10 % in children and under 30 % in adults in advanced parts of the world (11). Twenty percent of infected individuals develop symptomatic gastritis, gastric or duodenal ulcer, gastric adenocarcinoma, and non-Hodgkin's gastric lymphoma (12). Irondeficiency anemia, idiopathic thrombocytopenic purpura, and vitamin B12 deficiency are also associated with H. pylori (13). To identify the clinical outcome of H. pylori infection, a number of bacteria, hosts and environment factors have been investigated. The most important bacterial factors are virulence genes, and the severity of H. pylori related diseases is correlated with CAgA, VAC A s1m1 and BAbA2 genotype (14,15). Chronic active gastritis can proceed to precancerous lesions such as gastric mucosal atrophy and intestinal metaplasia, and finally to the development of gastric adenocarcinoma. Recent studies have shown that eradication of H. pylori has a beneficial effect on the prevention of gastric cancer and on the reversal of mucosal atrophy and intestinal metaplasia of the gastric mucosa (16). Therefore, rapid detection of H. pylori and eradication of the bacteria are needed to treat precancerous gastric lesions.

Two antibiotics and a proton pump inhibitor that lasts for 7 to 14 days are used as an ordinary eradication treatment. The rate of treatment failure is increasing, mainly due to the rise in bacterial resistance to commonly prescribed antibiotics. A high rate of resistance to clarithromycin has been observed in H. pylori due to the frequent use of clarithromycin for respiratory tract infections (17). There is a smaller clinical impact of resistance to metronidazole. Increasing the dose and duration of treatment may partly overcome resistance to metronidazole. There have been reports of resistance to metronidazole between 30% and 40% in H. pylori (18). The eradication rate in standard triple treatment is between 60% and 80%, the last being considered to be a minimal acceptable level according to

Maastricht criteria (19).

Therefore, it is important to develop new options such as quadruple or sequential treatment for eradication. An additional medicinal product may also be added to the standard treatment protocol. Several studies have examined the potential influence of probiotics as adjuncts to standard therapy on H. pylori eradication rate. Moreover, in view of the fact that adverse events related to H. pylori treatment are an important factor affecting compliance, probiotics have been investigated for reducing the occurrence of side effects. In a multicenter study, the overall incidence of side effects was 53.3% (20). The most commonly reported side effects are diarrhea, nausea, and vomiting, which have significant physical and social effects, and side effects have been shown to be significantly associated with decreased compliance and treatment failure (21).

2. Porotbiotic

According to the FAO and WHO definition, probiotics are organisms of a living nature that when administered in sufficient quantities offer health benefits for hosts (22). Bacteria from genera *Bififobacterium*, *Lactobacillus*, *Saccharomyces* and *Bacillus* are the most commonly used probiotics in humans (23). They are used as a single-species or multispecies preparation. The beneficial effects of probiotics seem to be strain-specific and dose-dependent. There is a rapid increase in clinical studies on probiotics in humans. In diseases like acute diarrhea, antibiotic-related diarrhea, function disorder in the gastrointestinal tract, inflammation of the colon, and so on, the beneficial effects of probiotics have been known to exist (24).

3. Probiotic'smicroorganim

Probiotics are defined as live microorganisms that, when administered in sufficient quantities, can improve intestinal microbial balance and have a positive effect on the health of the host, including beneficial effects on the prevention of intestinal infections, cardiovascular disease, cancer, and anti-allergy (25).

Probiotics are a group of microorganisms that can be identified as bacteria or yeasts. However, most of probiotics are bacteria, including lactic acid bacteria, which are commonly found in the human digestive tract and are the most commonly used (26).

Two of the most frequently utilized probiotic species, Lactobacillus and Bifidobacterium, are the Gram (+) cocci and rod species that have been extensively studied for their beneficial effects on the host, of gut

maturation and integrity, antagonism against pathogens, and modulation of the immune system and tumor -promoting agents. The ability to anaerobically digest saccharides and to produce lactic acid is a common feature of these bacteria. The resistance to pH and tolerance at a variety of temperatures are characteristic of these organisms. The digestive tract, mucous membrane of the mouth, and genital tract of humans and animals are the natural ecosystems of lactic acid bacteria (27).

Due to the fact that H. pylori is considered to be a difficult to treat infection mainly due to acquired resistance to commonly used antibiotics, there is a growing interest in the use of probiotics in combination with antibiotic regimens to eradicate H. pylori. In addition to the benefit of probiotic bacteria in the intestines, certain positive effects on the stomach have been observed; it is also shown that probiotics are useful for the treatment of several gastrointestinal disorders including diarrhea (28).

Probiotics can also help to improve the symptoms of H. pylori, too. Several factors, including the type of H. pylori strain, level of inflammation, and density of H. pylori colonization are important in determining the clinical outcome of H. pylori infection. In addition, the use of probiotics in improving H. pylori infections can be beneficial. Several factors such as the type of H. pylori strain, extent of inflammation and density of colonization are involved in determining clinical outcome for H. pylori infection. The risk of peptic ulcer disease and stomach cancer has been reported to increase with increasing infections. Therefore, permanent or long-term suppression of H. pylori can reduce the risk of developing H. pylori-related diseases (3).

Several studies have been conducted to show the favorable effect of different probiotics against H. pylori and have clarified the mechanism of action of probiotics against H. pylori, including strength of mucosal barrier, competition for adhesion, and immunomodulatory mechanisms (22).

4. Therapeutic mechanism of probiotic in *H. pylori*

Probiotics are commonly employed for the treatment of H. pylori infection during bacterial therapy. By colonizing a person's body and altering the composition of their flora in some part of it, probiotics are types of biological organisms that can contribute to host health. In the case of H. pylori infection in the gastrointestinal tract, because they grow in acidic conditions at pH 4 to 6, probiotics, in particular lactic acid, can be used. For the treatment of certain gastrointestinal disorders, bacteria have safety, immunomodulatory and antibacterial properties, so they are often given alone or in combination with medicinal products (29). By regulating the balance of the intestinal flora, they can regulate the function of the host's immune system or maintain intestinal health. In a randomized controlled trial, a probiotic (Lactobacillus Acidophilus LA-5, Lactiplantibacillus plantarum, Bifidobacterium lactis BB-12, and Saccharomyces boulardii) combined with four antibiotics (omeprazole, amoxycillin, clarithromycin, and metronidazole) was used to treat H. pylori infection. The results show that the control group with no probiotics had a cure rate of 86.8 percent for H. pylori, while the experimental group was at 92 % (30). Aiba et al. used L. johnsonii No. 1088 to treat a model mouse infected with H. pylori. The study showed that L. johnsonii No. 1088 significantly blocked the growth of H. pylori in the stomachs of mice. For this reason, the treatment of H. pylori infection with probiotics is also an excellent alternative (31).

Various strains of bacteria inhibit H. pylori via various pathways, and the flora that can be used to heal H. pylori are listed Table 1.

Probiotics not only inhibit the activity of urease, but also inhibit the adhesion of H. pylori to host cells, which is the key to probiotics in treating H. pylori infection (38). Thus, for the prevention of H. pylori infection, probiotics could be very important. The results indicate that diet can be used for treating H. pylori infection. In the treatment of H. pylori, probiotics have been an important tool and it should be possible to use them more often as a result of developments in medicine (32).

5. Treatment mechanism of probiotics

There are, in particular, two possible mechanisms for the inhibition of H. pylori infection by probiotics.

5.1 Non-immune pathways

1) Probiotics can inhibit H. pylori by produce antibacterial substances. Studies have shown that probiotics can produce various antibacterial substances that affect the growth of H. pylori, such as hydrogen peroxide, organic acids and bactericin. Antibiotics are capable of inhibiting H. pylori through the production of antimicrobial substances. . Studies have shown that, in addition to hydrogen peroxide, organic acids and bactericin, probiotics can produce a variety of antibacterial substances that affect the growth of H. pylori (41). The Bulgarian strain has been found to produce an antibacterial substance with a strong anti H. pylori effect activity, inhibiting more than 81% of H. pylori (42). H. pylori was reduced by 62.5 and 100%, respectively, when treated with L. . reuteri ATCC 23272 and its superna-

Table 1. The type of probiotic that inhibits Helicobacter pylori (32).

Probiotics	Source	Effect
***Lactobacillus reuteri* DSM 17648**	Probiotic capsule	The probiotic group had an eradication rate of 91.1% compared to the placebo group (68.9%)
	Function	**Ref.**
	eradication rate of Improving the and reducing symptoms *H. pylori* discomfort such as abdominal	[33]
Probiotics	**Source**	**Effect**
***Lactobacillus johnsonii* No. 1088**	Gastric juice	When co-cultured with *L. johnsonii* No.1088, the level of *H.pylori* decreased to about 1/3,000
	Function	**Ref.**
	Have the strongest acid resistance; inhibit the growth of *H. pylori*	[27]
Probiotics	**Source**	**Effect**
***Lactobacillus salivarius* LN12**	---	After probiotic treatment, the morphology of the *H. pylori* biofilm changes from a helical arrangement to a loose, broken and cracked one
	Function	**Ref.**
	Destroy the biofilm of *H. pylori* and inhibit the growth of *H. pylori*	[34]
Probiotics	**Source**	**Effect**
***Lactobacillus acidophilus* NCFM**	Compound *Lactobacillus* Tablets	The mRNA and protein expression levels of pro- inflammatory cytokines (IL-8 and TNF-α, etc.) in probiotic group were significantly inhibited. The urease activity (urea A and urea B) in the treatment group decreased significantly
	Function	**Ref.**
	Reduce the adhesion of *H. pylori* to AGS cells and reduce the occurrence of stomach inflammation	[35]
Probiotics	**Source**	**Effect**
***Lactobacillus plantarum* ZJ316**	Fresh fecal samples from children	*L. plantarum* ZJ316 could inhibit the urease activity of *H. pylori* with an inhibitory rate of 67.47%±2.36%
	Function	**Ref.**
	Reduce the secretion of interleukin -6 (IL-6), promote the release of IL-10, and repair mucosa damage	[36]
Probiotics	**Source**	**Effect**
***Lacticaseibacillus casei* T1**	---	The expression levels of pro- inflammatory cytokines, such as IL -6 and TNF-α, were significantly decreased in the probiotic group
	Function	**Ref.**
	Reduce the oxidative stress caused by *H. pylori*, improve the inflammatory reaction and reduce the damage of gastric mucosa.	[37]
Probiotics	**Source**	**Effect**
***Lactiplantibacillus pentosus* SLC13**	Mustard pickles	The cell-free supernatant of *L. pentosus* SLC13 inhibited the growth of 78% of *H. pylori*
	Function	**Ref.**
	Modulat inflammatory response, reduce urease activity and attachment on the cells	[38]

-atant. The activity of ureas may also be inhibited by the bacterium, but this inhibition is removed in a neutral environment. Therefore, it is assumed that there are acids in the supernatant. In order to validate that assumption, Rezaee et al. culture H. pylori in the same environment with lactic acid and found an inhibition of urease levels comparable to those of supernatants. Therefore, there is further evidence that L. reuteri ATCC 23272 may be producing antimicrobial acid [43].

2)Some probiotics are preventing H. pylori from attaching to cells in the host's gastrointestinal tract [44]. Probiotics can prevent H. pylori infection by synthesizing antimicrobial agents. Furthermore, at the junction with the host cell, probiotics may compete with H. pylori, reducing its adhesion to the host cell. Organic acids are antibacterial substances that can enter H. pylori's body and reduce the pH, causing the death of the bacteria [45]. The combination of H. pylori and host cells can be blocked by Saccharomyces boulardii CNCM I745, mainly with duodenal cells. The reason may be that the probiotic contains an amidase which regulates H. pylori's attachment to its host cells [46]. Therefore, Saccharomyces boulardii has a great potential to treat H. pylori. L. plantarum Z316J has been shown to inhibit the adhesion of H. pylori and reduce its association with AGS cells by 70.14% [47]. When Shen et al. cultured L. acidophilus NCFM and L. plantarum Lp-115 with AGS cells (H. pylori positive), it was found that probiotics hinder the adhesion of H. pylori to host cells [35].

3) Urease is one of the indispensable factors of H. pylori colonization in the digestive system, which is composed of Ure subunits (A, B, C). The enzyme is capable of breaking down urea to ammonia, neutralizing the stomach's environment. The expression of the Ure gene is blocked by L. plantarum ZJ316, thereby inhibiting the synthesis of urea [47].

5.2 Immune pathways

1) The effect of different probiotics on the immune system is different. (1) Some probiotics also induce the production of anti-inflammatory cytokine (IL-10) and inhibit the secretion of pro-inflammatory cytokine (IL-6, IL-1β, INF-γ), which mediates the inflammatory response in vivo [38,48]. L. rhamnosus LGG 18 and L. acidophilus Chen-08 have been administered to mice infected with H. pylori infection. The results showed that probiotics could significantly hinder the expression of pro-inflammatory factors related genes (NF—kappa B, TNF signaling pathway [49]. Forooghi Nia et al. treated mice positive for H. pylori with limosilactobacillus reuteri 2892. After 5 weeks, the results showed that the secretion of cytokines such as IL-6, IL-1β, and INF-γ decreased significantly, while the secretion of IL-10 was significantly increased [48].

2) By modulating phagocytes and lymphocytes, probiotics can stimulate both the humoral and cellular immune response of the host [50]. Moreover, the combination of probiotics and herbs is not only beneficial for the fermentation of live bacteria, but also for the treatment of H. pylori infection and for the improvement of human gastrointestinal health. Hasna et al. treated H. pylori with fenugreek extract and Bifidobacterium breve alone, and the highest IZD (inhibition zone diameter) was 16.00 ± 0.00 mm and 20.33 ± 0.58 mm, respectively. However, when the two drugs were combined to treat H. pylori, the IZD was 28.67 ± 0.58 mm [51]. As a result, the combination has begun to be taken seriously. However, in order to verify the effectiveness and cure rate of probiotic therapy, specific clinical data are needed so that further validation is required.

6.CONCLUSION

Both in vitro and in vivo studies provide evidence that probiotics may represent a novel approach to the management of H. pylori infection. Despite the fact that there is no conclusive evidence to suggest an increase in eradication rates when probiotics are added to eradication therapy, this appears to be effective at preventing antibiotic associated adverse reactions. Moreover, the persistent strains specific ability, although weak in some cases, of some probiotics to decrease H. pylori density and gastritis could be of help in reducing the risk of H. pylori-associated complication later in life. Finally, the hypothesis that probiotics may inhibit H. pylori adhesion to gastric epithelium cells and thereby prevent H. pylori colonization in patients at increased risk of infection is fascinating as an overall perspective. The results so far are encouraging and further clinical studies should be carried out. The purpose of the studies should be to identify which probiotic strains are appropriate, in what form, at what dose and for a given duration.

Refrence

1. Moayyedi P and Hunt RH. Helicobacter pylori public health implications. Helicobacter 2004; 9: 67–72.
2. Kuipers EJ. Helicobacter pylori and the risk and management of associated diseases: gastritis, ulcer disease, atrophic gastritis and gastric cancer. Aliment Pharmacol Ther 1997; 11: 71–88.
3. Papastergiou V, Georgopoulos SD, and Karatapanis S. Treatment of Helicobacter pylori infection: Past, present and future. World J Gas-

4. Lu C, Sang J, He H, Wan X, Lin Y, Li L, et al. Probiotic supplementation does not improve eradication rate of Helicobacter pylori infection compared to placebo based on standard therapy: a meta-analysis. Sci Rep 2016; 6: 23522.

5. Ruggiero P. Use of probiotics in the fight against Helicobacter pylori. World J Gastrointest Pathophysiol 2014; 5: 384.

6. Kim MN, Kim N, Lee SH, Park YS, Hwang J, Kim J, et al. The effects of probiotics on PPI-triple therapy for Helicobacter pylori eradication. Helicobacter 2008; 13: 261–8.

7. Solnick J V and Schauer DB. Emergence of diverse Helicobacter species in the pathogenesis of gastric and enterohepatic diseases. Clin Microbiol Rev 2001; 14: 59–97.

8. Josenhans C and Suerbaum S. The role of motility as a virulence factor in bacteria. Int J Med Microbiol 2002; 291: 605–14.

9. Weeks DL, Eskandari S, Scott DR, and Sachs G. A H+-gated urea channel: the link between Helicobacter pylori urease and gastric colonization. Science (80-) 2000; 287: 482–5.

10. D'Elios MM and Czinn SJ. Immunity, Inflammation, and Vaccines for H elicobacter pylori. Helicobacter 2014; 19: 19–26.

11. Elitsur Y, Dementieva Y, Rewalt M, and Lawrence Z. Helicobacter pylori infection rate decreases in symptomatic children: a retrospective analysis of 13 years (1993-2005) from a gastroenterology clinic in West Virginia. J Clin Gastroenterol 2009; 43: 147–51.

12. Parsonnet J, Hansen S, Rodriguez L, Gelb AB, Warnke RA, Jellum E, et al. Helicobacter pylori infection and gastric lymphoma. N Engl J Med 1994; 330: 1267–71.

13. Malfertheiner P, Megraud F, O'Morain CA, Atherton J, Axon ATR, Bazzoli F, et al. Management of Helicobacter pylori infection—the Maastricht IV/Florence consensus report. Gut 2012; 61: 646–64.

Homan M, Luzar B, Kocjan BJ, Mocilnik T, Shrestha M, Kveder M, et al. Prevalence and clinical relevance of cagA, vacA, and iceA genotypes of Helicobacter pylori isolated from Slovenian children. J Pediatr Gastroenterol Nutr 2009; 49: 289–96.

15. Homan M, Šterbenc A, Kocjan BJ, Luzar B, Zidar N, Orel R, et al. Prevalence of the Helicobacter pylori babA2 gene and correlation with the degree of gastritis in infected Slovenian children. Antonie Van Leeuwenhoek 2014; 106: 637–45.

16. Kodama M, Murakami K, Okimoto T, Abe T, Nakagawa Y, Mizukami K, et al. Helicobacter pylori eradication improves gastric atrophy and intestinal metaplasia in long-term observation. Digestion 1956; 85: 126–30.

17. Megraud F. H pylori antibiotic resistance: prevalence, importance, and advances in testing. Gut 2004; 53: 1374–84.

18. Saracino IM, Zullo A, Holton J, Castelli V, Fiorini G, Zaccaro C, et al. High prevalence of primary antibiotic resistance in Helicobacter pylori isolates in Italy. J Gastrointest Liver Dis 2012; 21.

19. Sasaki M, Ogasawara N, Utsumi K, Kawamura N, Kamiya T, Kataoka H, et al. Changes in 12-year first-line eradication rate of Helicobacter pylori based on triple therapy with proton pump inhibitor, amoxicillin and clarithromycin. J Clin Biochem Nutr 2010; 47: 53–8.

20. Misiewicz JJ. Management ofHelicobacter pylori-related disorders. Eur J Gastroenterol Hepatol 2012; 9: S17–21.

21. Henry A and Batey RG. Enhancing Compliance Not A Prerequisite for Effective Eradication ofHelicobacter Pylori: The Help Study. Off J Am Coll Gastroenterol ACG 1999; 94: 811–5.

22. Organization WH. Food and agriculture organization of the United Nations. Vitam Miner Requir Hum Nutr 2004; 2: 17–299.

23. Sullivan Å and Nord CE. Probiotics and gastrointestinal diseases. J Intern Med 2005; 257: 78–92.

24. Gill HS and Guarner F. Probiotics and human health: a clinical perspective. Postgrad Med J 2004; 80: 516–26.

25. Rodes L, Coussa-Charley M, Marinescu D, Paul A, Fakhoury M, Abbasi S, et al. Design of a novel gut bacterial adhesion model for probiotic applications. Artif Cells, Nanomedicine, Biotechnol 2013; 41: 116–24.

26. Rodes L, Khan A, Paul A, Coussa-Charley M, Marinescu D, Tomaro-Duchesneau C, et al. Effect of probiotics Lactobacillus and Bifidobacterium on gut-derived lipopolysaccharides and inflammatory cytokines: an in vitro study using a human colonic microbiota model. J Microbiol Biotechnol 2013; 23: 518–26.

27. Moayyedi P and Hunt RH. Helicobacter pylori public health implications. Helicobacter 2004; 9: 67–72.

28. Kuipers EJ. Helicobacter pylori and the risk and management of associated diseases: gastritis, ulcer disease, atrophic gastritis and gastric cancer. Aliment Pharmacol Ther 1997; 11: 71–88.

29. Papastergiou V, Georgopoulos SD, and Karatapanis S. Treatment of Helicobacter pylori infection: Past, present and future. World J Gastrointest Pathophysiol 2014; 5: 392.

30. Lu C, Sang J, He H, Wan X, Lin Y, Li L, et al. Probiotic supplementation does not improve eradication rate of Helicobacter pylori infection compared to placebo based on standard therapy: a meta-analysis. Sci Rep 2016; 6: 23522.

31. Ruggiero P. Use of probiotics in the fight against Helicobacter pylori. World J Gastrointest Pathophysiol 2014; 5: 384.

32. Kim MN, Kim N, Lee SH, Park YS, Hwang J, Kim J, et al. The effects of probiotics on PPI-triple therapy for Helicobacter pylori eradication. Helicobacter 2008; 13: 261–8.

33. Solnick J V and Schauer DB. Emergence of diverse Helicobacter species in the pathogenesis of gastric and enterohepatic diseases. Clin Microbiol Rev 2001; 14: 59–97.

34. Josenhans C and Suerbaum S. The role of motility as a virulence factor in bacteria. Int J Med Microbiol 2002; 291: 605–14.

35. Weeks DL, Eskandari S, Scott DR, and Sachs G. A H+-gated urea channel: the link between Helicobacter pylori urease and gastric colonization. Science (80-) 2000; 287: 482–5.

36. D'Elios MM and Czinn SJ. Immunity, Inflammation, and Vaccines for H elicobacter pylori. Helicobacter 2014; 19: 19–26.

37. Elitsur Y, Dementieva Y, Rewalt M, and Lawrence Z. Helicobacter pylori infection rate decreases in symptomatic children: a retrospective analysis of 13 years (1993-2005) from a gastroenterology clinic in West Virginia. J Clin Gastroenterol 2009; 43: 147–51.

38. Parsonnet J, Hansen S, Rodriguez L, Gelb AB, Warnke RA, Jellum E, et al. Helicobacter pylori infection and gastric lymphoma. N Engl J Med 1994; 330: 1267–71.

39. Malfertheiner P, Megraud F, O'Morain CA, Atherton J, Axon ATR, Bazzoli F, et al. Management of Helicobacter pylori infection—the Maastricht IV/Florence consensus report. Gut 2012; 61: 646–64.

40. Homan M, Luzar B, Kocjan BJ, Mocilnik T, Shrestha M, Kveder M, et al. Prevalence and clinical relevance of cagA, vacA, and iceA genotypes of Helicobacter pylori isolated from Slovenian children. J Pediatr Gastroenterol Nutr 2009; 49: 289–96.

41. Homan M, Šterbenc A, Kocjan BJ, Luzar B, Zidar N, Orel R, et al. Prevalence of the Helicobacter pylori babA2 gene and correlation with the degree of gastritis in infected Slovenian children. Antonie Van Leeuwenhoek 2014; 106: 637–45.

42. Kodama M, Murakami K, Okimoto T, Abe T, Nakagawa Y, Mizukami K, et al. Helicobacter pylori eradication improves gastric atrophy and intestinal metaplasia in long-term observation. Digestion 1956; 85: 126–30.

43. Megraud F. H pylori antibiotic resistance: prevalence, importance, and advances in testing. Gut 2004; 53: 1374–84.

44. Saracino IM, Zullo A, Holton J, Castelli V, Fiorini G, Zaccaro C, et al. High prevalence of primary antibiotic resistance in Helicobacter pylori isolates in Italy. J Gastrointest Liver Dis 2012; 21.

45. Sasaki M, Ogasawara N, Utsumi K, Kawamura N, Kamiya T, Kataoka H, et al. Changes in 12-year first-line eradication rate of Helicobacter pylori based on triple therapy with proton pump inhibitor, amoxicillin and clarithromycin. J Clin Biochem Nutr 2010; 47: 53–8.

46. Misiewicz JJ. Management ofHelicobacter pylori-related disorders. Eur J Gastroenterol Hepatol 2012; 9: S17–21.

47. Henry A and Batey RG. Enhancing Compliance Not A Prerequisite for Effective Eradication ofHelicobacter Pylori: The Help Study. Off J Am Coll Gastroenterol ACG 1999; 94: 811–5.

48. Organization WH. Food and agriculture organization of the United Nations. Vitam Miner Requir Hum Nutr 2004; 2: 17–299.

49. Sullivan Å and Nord CE. Probiotics and gastrointestinal diseases. J Intern Med 2005; 257: 78–92.

50. Gill HS and Guarner F. Probiotics and human health: a clinical perspective. Postgrad Med J 2004; 80: 516–26. WJG 2015; 21: 10644.

51. Hasna B, Houari H, Koula D, Marina S, Emilia U, and Assia B. In vitro and in vivo study of combined effect of some Algerian medicinal plants and probiotics against Helicobacter pylori. Microorganisms 2023; 11: 1242.