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ORIGINAL ARTICLE

Used of Probiotic Production of *Saccharomyces boulardii* to Eradication Triple Therapy of *Helicobacter pylori* Infection

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ABSTRACT

Objectives: Detection of the *H. pylori* infection by demonstrating BabA gene and expression level of this gene during mice infection, with study the effect of probiotics extract and histopathological study on mice tissue change after infection and treatment.

Methods: Out of 112 patients suffering from dyspepsia attending Al- Husain medical city / digestive system diseases center, Karbala city. Detection of *Helicobacter pylori* and also used probiotics yeast cell of *Saccharomyces boulardii* to eradicate antibiotic treatment of *H. pylori* infection. Study histological study on infected Lab animals with *H.pylori* treated with *S. boulardii*.

Results: This study used probiotics yeast cell of Saccharomyces boulardii to eradicate antibiotic treatment of Helicobacter pylori infection. This appears through expression level *BabA* gene from a clinical isolate of these bacteria, and histological study on infected Lab animals with *H.pylori* treated with *S. boulardii.* The probiotic role was shown in the results to the eradication of antibiotic therapeutic *Helicobacter* infection. This appeared through an expression study of *BabA* gene in mice after infection with *H. pylori* bacteria and comparison between the expression level of this gene after therapy with antibiotic alone and treatment with antibiotics with probiotic. The expression level of the normal *BabA* gene of *H. pylori* in infected mice was 32.31. This was reduced to the 4.038 after treatment with antibiotics. This level of expression of gene was reduced to 0.504 after treatment with antibiotics probiotics. The role of probiotics also appeared in a histopathological study in mice biopsy when compared tissues after treatment with antibiotics and after treatment with antibiotics with probiotics. The present study proves

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that the probiotic yeast cell used for eradication role to the increase the effective treatment of *H. pylori* by antibiotics as the result mention.

Conclusion: The present study proves the probiotic yeast *S. boulardii* used for eradication role of the increase the effective treatment of *H. pylori* by antibiotics. There were many methods used to diagnosis *H. pylori* infection, PCR sensitive one and especially when used more than one gene duplex PCR.

INTRODUCTION

Helicobacter pylori (*H. pylori*) was world distribution Gram's negative, had flagellum bacteria, infection human stomach, and both non-gastric tumor and gastric tumor sickness.[1-3] The therapy for *H. pylori*[2] depends on the integration of antibiotics. As well as, despite many treatment ways had suggested, for method direction treatment administration still un disband matter.[4]

Triple therapy (established a proton pump preventer, clarithromycin and amoxicillin) unto near time ago, deemed as the criterion first-line ardor.[6-9] Because of antibiotic resistance, the failure range has increased; lately, H. pylori genome mutations were mainly caused [5]. Due to these causes, alternate first-line ardor had been suggested (with and without bismuth, and hybrid).[7]

The live organisms were production material that are orally taken and could had a beneficial influence to the host named Probiotics.[8] Probiotics specifically affected *H. pylori* by main mechanisms that produce anti-bacterial material; representing as first line to defense against pathogenic bacteria, they strongly non-immunological obstacle along with stabilization stomach mucosal obstacle.[10,11]

Moreover, probiotics can intervene with prospective pathogens which might grow in the gastric region.[12] In addition, *Saccharomyces boulardii* (S. *boulardii*) may contend with *H. pylori* to combined with host surface receptors and, lead to, prevent adhesion to epithelial cells.[13] Moreover, when pretending that S. *boulardii* may inhibit *H. pylori* urease action *in vitro*.[14] At final, *Saccharomyces* production acetic acid and lactic acid can frustrate *H. pylori*-induced hypochlorhydria and consider bactericidal influence itself.[15]

MATERIALS AND METHODS

Patients and Samples: A total of 112 patients who received endoscopy examination in Al- Hussany general hospital (GIT) center patient had symptoms of gastrointestinal disorders and dyspepsia for 58 men and 54 women and their ages between 10-80 years old. The infection of *H. pylori* was diagnosis by rapid urease test (RUT), Bacterial culturing polymerase chain reaction (PCR).

Culturing of Bacteria and Condition of Growth: Bacteria was cultured from biopsy after collected on Columbia agar and brain heart infusion media (Oxiod prepare condition) adding *H. pylori* supplement (vancomycin, 2.5 units/mL polymyxin B 5 µ g/mL trimethoprim, 10 µ g/mL and 2.5 µ g/mL amphotericin B) before sterilize and add 5 to 7% lysed blood horse after cooling media then culturing bacteria and incubation in condition nitrogen 90%, carbon dioxide7.6%, oxygen5%.[18]

Biochemical test: The biochemical test had done after bacterial culturing like urease test, oxidase, catalase for detection *H. pylori* infection.[16,17]

Molecular Diagnosis: RNA was extracted from all specimen by RNA extraction kit (Geneaid, Sengapure). Specific primers for virulence factors *BabA* and *16S rRNA* (housekeeping gene) of *H. pylori* amplification to the cDNA by used standard condition. *BabA* gene expression level measurement by real-time PCR using the Applied Biosystems 7500 detection system, Specific primers, and house-keeping gene 16SrRNA were designed with the aid of Primer Express. Real-time PCR was performed in a 20 µL reaction volume containing 3 µL of cDNA, 2 µL of oligo primer, 10 µL real-time PCR master mix, and nuclease-free water up to 20 µL, these performed in standard condition.[19,20]

Animal Models: Animal models of *Helicobacter* infected both sexes mice in weighing range 25–35 g the animal gained of pharmacy collage, University of Kerbala. At short notes, after overnight without eat, animal was given 0.25 mL liquid of substance 0.2 M NaHCO3 through oral by sterilized gavage needle for acidic equalization. Similarly, 108 CFUs from every bacterial isolation of 0.15 mL of sterilized saline were injected to every mice. Oneself treated were reiterated within 3 and 5 days. The same amount of saline give to the control groups.[17]

The Efficacy and Safety of Adding the Probiotic Treatment

They are randomized into two treatment regimens: mice in Group A were given amoxicillin (1000 mg), clarithromycin (500 mg), omeprazole 20 mg only, mice in Group B were given *S. boulardii* probiotic (250 mg) for 14 days, and mice in Group C were given amoxicillin (1000 mg), clarithromycin (500 mg) and omeprazole (20 mg) plus probiotics extract for 3 to 5 days.[21]

Histology Study

Mice have died through overdose from anesthesia at the end of the tests, and stomach tissue sample approximate "one-fifth," involving fundic mucosa and oxyntic, were takeoff, buffering formalin 4% fix, and embed within paraffin stained with hematoxylin and eosin after sections 5–7 mm was the standard method.[22]

RESULTS AND DISCUSSION

Expression of *BabA* gene:

In the expression study of *BabA* gene, results in Table 1 shows that the through 2^-ΔΔct value represented expression range of the gene in mice after being infected with *H. pylori* was

32.31059 (as control without treatment), this value decreased to the 4.038824 after treatment of mice with antibiotic triple therapeutic for two weeks only and the value also decreased to 0.504853 after treatment with antibiotic with probiotic product. The results improved the probiotic extraction eradication the antibiotic treatment of *H. pylori* infection.

The results of the current study, in Figure 1, show the expression level of *BabA* gene in mice after infection and comparison expression level with infection progression during the beginning of infection *H. pylori* needed *BabA* gene expression to adhesion and colonization to make infection. These results agree with,[23] after that, the expression level remains constant because the bacteria needed adhesion after entry.

Expression of *BabA* Gene after Treated with Probiotic

To this time, many therapeutic systems have been an endeavor to eradicate *H. pylori*; however, the comfort area is far from intellect, ranging from 50% in the developing countries to 75% in the developing improving world. The most widely passable first-line treatment regimen includes the incorporation of the proton pump preventing and two antibiotics (Amoxicillin and Clarithromycin). Antibiotic-resistant of some *H. pylori* isolate, result in treatment failed, the beneficent of an alternative non-antibiotic method to treatment *H. pylori* and appear necessary for other pathogenic bacteria.[24] The probiotics adjuvant used to treatment *H. pylori* eradication has lately been widely used.

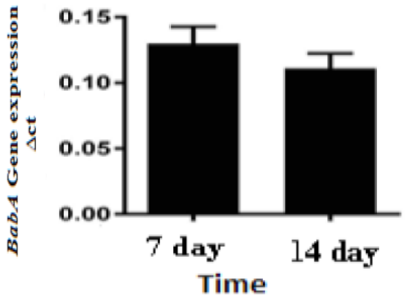

Figure 1. **mRNA expression of *BabA* gene in mice. Expression of *BabA* after 7 and 14 days of mice infection, measuring ΔCt related to *16S rRNA* as a housekeeping gene.**

Table 1. ***BabA* Gene expression fold change (2^-ΔΔct) value for mice infected with *H. pylori* (control), value after treated with antibiotic only, and value after treated with antibiotic with probiotic.**

	Gene expression fold value for mice		
Mean	**infected (control)**	**treatment with antibiotic only**	**treatment with antibiotic with probiotic**
ct *16S rRNA*	8.755	8.933	9.537
ct *BabA*	14.05	16.55	18.05
Δct	6.68	7.795	9.295
ΔΔct	-2.505	-9.005	4.95
Fold change (2^-ΔΔct)	32.31059	4.038824	0.504853

Managed different strains by various research and doses of probiotics and yielded inconsistent outcomes.

In Figure 2, results show minimized *H. pylori BabA* gene expression when treated with the probiotic of *S. boulardii* compared to the group treated with antibiotics alone. The probiotic reduction of the level of expression of BabA gene leads to the prevention of these bacteria and colonization, then reduces the risk of infection. These results agree with Skoog E.C. et al.[23,] who found expression level reduce after treatment with antibiotics and more reduce after used probiotic.

The *BabA* gene showed subordinate bounding for *Helicobacter* to Leb-glycoconjugates prevent the propagation of the bacteria result of aggregates formation, gastric mucins had a similar effect to the human carrying Leb *ArsS* have regulated these events. Moreover, Leb decreases binding to *BabA* gene expression and articulates a negative feedback loop.[25]

By binding an additional way mucin caused of growth determine accumulation for pathogen numbers control supply for the host alongside combined facilitate irrigation away of pathogen together with mucus shedding. Mucins caused Jiang has reported aggregates of H. pylori in liquid cultures, and Doyle,[23,27] appears that *Helicobacter* accumulation might be protected for the outer condition. The beneficial of aggregation to *Helicobacter* safeguard stomach acidity, antibiotics, and other hurtful agent to the environment. Damaging accumulate created within stomach mucosal through eradicate treatment may be driving to slow development of resistance and a high sensitivity to antibiotics.[26]

Aggregate-causing *H. pylori* was life after culturing with glycoconjugates and mucins, as showed through stained, they showed indirect anti-bacterial or little effect result to combined. Formation of aggregates was explicated for the binding causes slowly down the proliferation, resulting in physical impediment or inter-bacterial connection.[28,29]

Studies showed the techniques of labor of *S. boulardii* in the treatment of diarrhea could involve the following 4 aspects: (i) immunomodulatory effects such as an increase in IgA. (ii) increase of short-chain fatty acids concentrations. (iii) direct or indirect inhibition of growth of intestinal

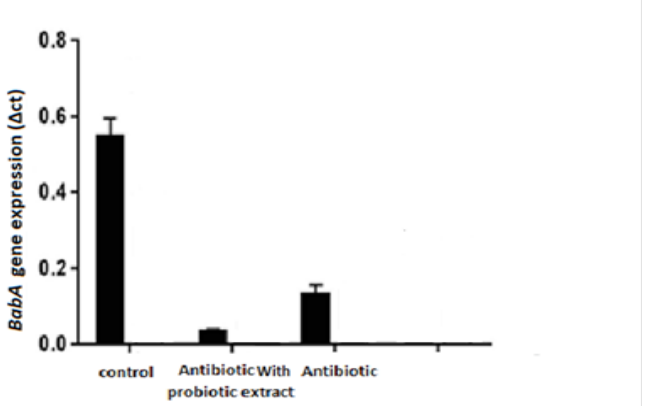

Figure 2. **Expression of *BabA* gene, with antibiotic and antibiotic with probiotic product.**

pathogens. (iv) effects of anti-bacterial toxins. Host immune response by up-regulation for the *H. pylori* reacts with the of many cytokines, such as interferon-γ, tumor necrosis factor-α, interleukin (IL-8), IL-1, and IL-6.[31]

Histopathological Study

Figure 3 shows dissecting mice after 14 day from the first dose of *H. pylori* and infected with gastritis leading to the swelled stomach of this mice compared with normal mice stomach.

Figure 4 shows mice stomach walls' gastrointestinal tubules to compose serosa, external, muscularis outer mucosa, and inner submucosa. The lamina propria composed gastric mucosa of the stomach "consist of loose connective tissue" and the epithelium, smooth muscle as a little layer of called (mucosae muscularis) detach it consist submucosa under. The fibrous connective tissue consists of the submucosa layer under the mucosa, "Meissner's plexus" detach layer of the mucosa in this layer. Beneath submucosa muscularis external layer and

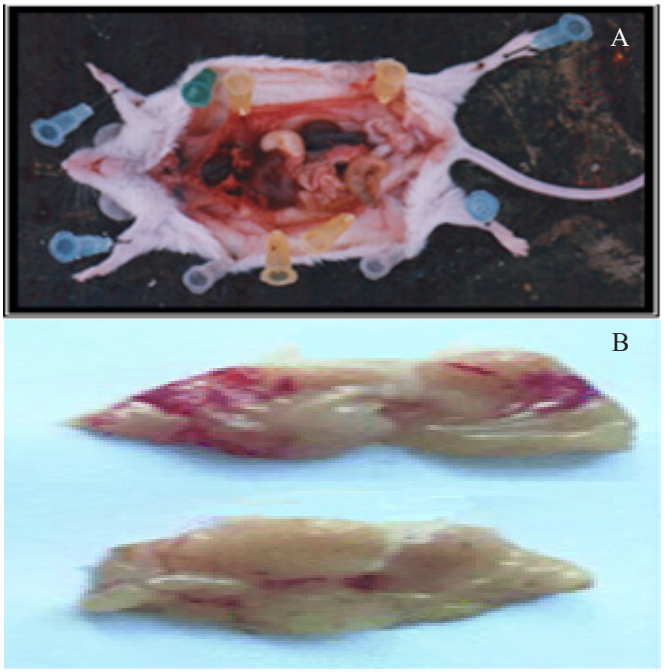

Figure 3. **Swollen stomach of mice after 14 days from first Dose of *H. pylori* in (A) and normal stomach in (B).**

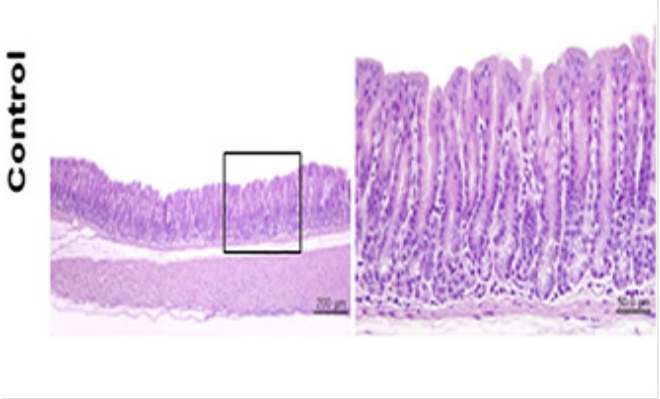

Figure 4. **Normal tissue of the mice stomach, 4X left and 40X on right (H &E stain).**

was unrivaled of other organs with gastrointestinal tubules, involving three layers.[32]

The second layer is a middle circular layer. A thicker circular muscular dike in this layer, the pylorus is encompassed by contractions normally tonically, pyloric sphincter if not anatomically discrete (forming a functional), in the duodenum the chyme controls by motion.[31]

Figure 5 shows the gastritis infection of the gastrointestinal tract of mice stomach. Very few inflammatory cells number in healthy gastric mucosa. Moreover, while *Helicobacter* colonizes in the gastric region, neutrophils and polymorphonuclear cells emigrate to the region to produce severe inflammatory responses.

Stomach acidity reduction or hypochlorhydria come of severe illness. Whether the first response failure for obvious illness, macrophages and T cells, B cells neutrophils, aggregate at stomach mucosal Atherton J.[33] which is a distinctive histopathological image of chronic active gastritis. Many strains of *H. pylori* continue permanently cause gastric inflammation if not eradicated with antibiotics.[34,35]

The results in Figure 6 shows that peptic ulcer infection in mice stomach gastric ulceration (GU) was related a basin-stomatic inflammation manner and acid product normal or decreased and this agreement with Atherton J.[34] The GU improvement most generally with transitive area among antrum and the body on the minimal gastric convolution. Colonization

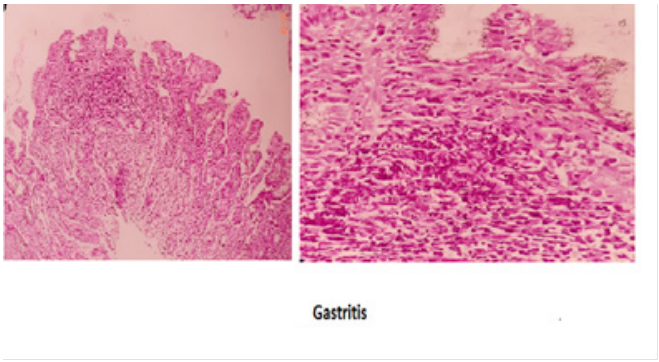

Figure 5. ***Helicobacter pylori* infection by increase inflammatory cell number gastritis in dissecting section to mice stomach, 4X left and 40X on the right (H &E stain).**

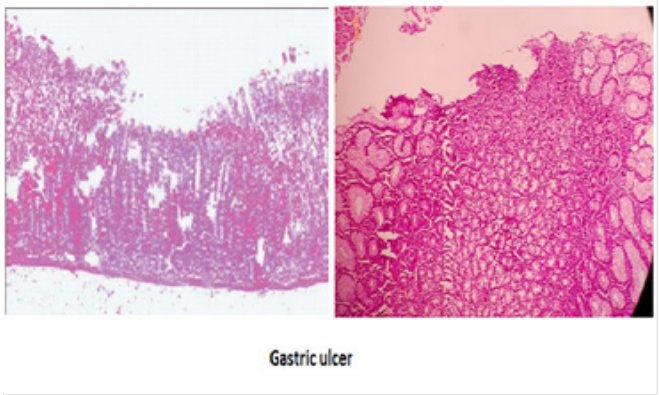

Figure 6. **High severity pathogenesis of *H. pylori* infection by converted to the gastric ulcer in dissecting section to mice stomach, 4X on left and 40X on right (H &E stain).**

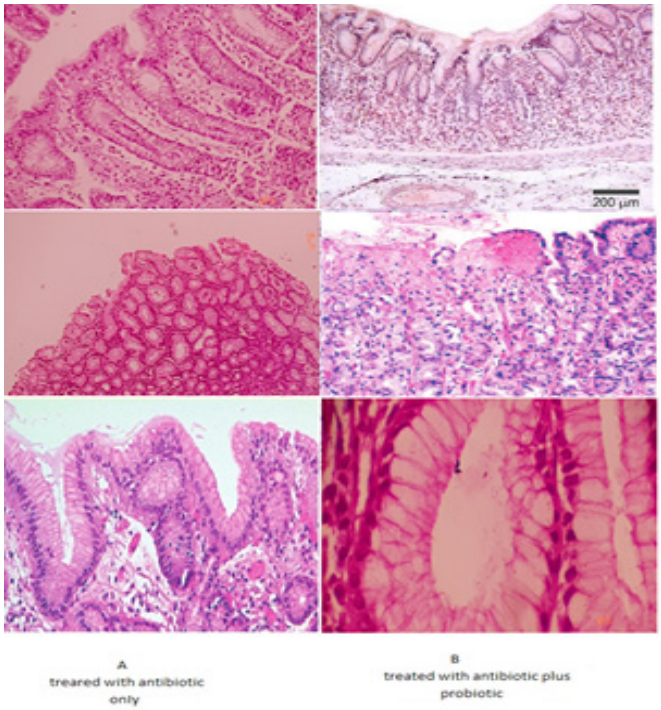

Figure 7. **Histology change after infection with *H pylori* and treatment with antibiotic only(A) 40X, and histology change after infection with *H. pylori* and treatment with antibiotic with probiotic in (B) 40X, (H &E stain).**

will be consistently spread throughout gastric mucosa when there is low acid secretion. The progressive inflammatory cell infiltration is caused by *H. pylori* colonization and epithelium cells increasing peeling. The modification produces bicarbonate production and inefficient mucin; the tissue becomes more susceptible to ulceration because of weakens the mucus barrier.[36]

In Figure 7, results show the stage of the infected stomach by *H.pylori* of mice and formation of gastritis by increasing filtration of polymorphic nucleated cell to the position of bacterial colonization after infected mice with bacteria. It also shows that the tissue after treatment with antibiotic triple therpautic for two weeks leads to killing the bacteria and reducing the inflammatory cell in gastric tissue with healing these tissue from infection in section A section of Figure.

While the Figure in section B shows the infection stage of *H.pylori* in the stomach of mice and in this section the infection treatment with antibiotic with probiotic extract to compare the two treatment methods. In this section of the Figure, the healing periods of ten days and re-irreagenment of the stomach epithelial tissue by probiotic extract result from infection and increased inflammatory cells. This tissue becomes nodular and irregular as it appear in the Figure 7.

The first-line of anti-*H. pylori* therapy generally 20–30% failure, and one of the clinical practice causes to the fail is the adverse effects of higher spread. In the current research, the aggregate of the probiotic was efficient in mitigating *H. pylori* eradication therapy adverse effects of the studies done.[37,31] For the probiotics group, the eradication range overriding 90%, is deemed higher. Moreover, because this outcome is in rates with preceding research of another probiotic, one firm inference does not permit one to appear because of teeny specimen size.[38]

H. pylori illness people reduced gastrin-17 levels by probiotic interference. *Helicobacter* infected was related to acid output and catalyzed plasma and increased basal gastrin concentricity, particularly with duodenal ulcers patients. Gastrin-17 rising range had been related to rising danger with gastric atrophy and cancer.[40]

The adherence of probiotics to gastric mucosa appears unlinked to the techniques back the reduced gastrin-17. Reduce in TNF-α and IL-8 relates many probiotic strains.[39] Current research, most logic to explain the reduce gastrin-17 after probiotics exhaustion can be the reduce *H. pylori* range within gastric region as particular through 13C-UBT measured, and that case can perhaps leaded to decrease produce cytokines pro-inflammatory in gastric region.[41]

Probiotics interference, *S. boulardii* attached little to the upper gastrointestinal mucosal patients, but through gastrointestinal tract crossing, most probiotics survive well. *H. pylori*-infected through technique unlinked to the capability to prevent bacteria attachment and probiotic influenced fence function.[40]

REFERENCES

1. Ierardi E, Goni E, Losurdo G, Di Mario F. Helicobacter pylori and nonmalignant diseases. Helicobacter. 2014; 19(Suppl. 1): 27-31. Available from: https://doi.org/10.1111/hel.12157.
2. Giuseppe L, Rossella C, Michele B, Mariabeatrice P, Gioacchino L, Ierardi E et. al. Probiotic monotherapy and Helicobacter pylori eradication: A systematic review with pooled-data analysis. World J. Gastroenterol. 2018; 24(1): 139-149. Available from: DOI: 10.3748/wjg.v24.i1.139.
3. Venerito M, Vasapolli R, Rokkas T, Malfertheiner P. Helicobacter pylori and Gastrointestinal Malignancies. Helicobacter. 2015; 20 (S1): 36-39. Available from: https://doi.org/10.1111/hel.12255.
4. Georgopoulos SD, Papastergiou V, Karatapanis S. "Current options for the treatment of Helicobacter pylori". Expert Opin Pharmacother. 2013; 14(2): 211-223. Available from: https://doi.org/10.1517/14656566.2013.763926.
5. Ierardi E, Giorgio F, Iannone A, Losurdo G, Principi M, Barone M et. al. Noninvasive molecular analysis of Helicobacter pylori: Is it time for tailored first-line therapy?. World J Gastroenterol. 2017; 23(14): 2453-2458. Available from: DOI: 10.3748/wjg.v23.i14.2453.
6. Ierardi E, Giorgio F, Losurdo G, Di Leo A, Principi M. How antibiotic resistances could change Helicobacter pylori treatment: A matter of geography?. World J Gastroenterol. 2013; 19(45): 8168-8180. Available from: doi: 10.3748/wjg.v19.i45.8168.
7. Bin Z, Ya-Zheng X, Zhao-Hui D, Bo C, Li-Rong J, Yvan V. The Efficacy of Saccharomyces boulardii CNCM I-745 in Addition to Standard Helicobacter pylori Eradication Treatment in Children. Pediatr. Gastroenterol. Hepatol. Nutr. 2015; 18(1): 17-22. Available from: DOI: 10.5223/pghn.2015.18.1.17 .
8. Mehling H, Busjahn A. Non-viable Lactobacillus reuteri DSMZ 17648 (Pylopass) as a new approach to Helicobacter pylori control in humans. Nutrients. 2013; 5(8): 3062–3073. Available from: DOI: 10.3390/nu5083062.
9. Losurdo G, Leandro G, Principi M, Giorgio F, Montenegro L, Sorrentino C, et. al. Sequential vs. prolonged 14-day triple therapy for Helicobacter pylori eradication: the meta-analysis may be influenced by 'geographical

weighting. Int. J. Clin. Pract. 2015; 69 (10): 1112-1120. Available from: DOI: 10.1111/ijcp.12687.
10. Vitor JM, Vale FF. Alternative therapies for Helicobacter pylori: probiotics and phytomedicine. FEMS Immunol Med Microbiol. 2011; 63(2): 153–64. Available from: DOI: 10.1111/j.1574-695X.2011.00865.x .
11. Garcia CA, Henriquez AP, Retamal RC, Pineda CS, Delgado Sen C, Gonzalez CC. Probiotic properties of Saccharomyces boulardii isolated from gastric biopsies of Helicobacter pylori infected and non infected individuals. Rev. Med. Chil. 2009; 137(3): 369–76.
12. Ianiro G, Molina-Infante J, Gasbarrini A. Gastric Microbiota. Helicobacter. 2015; 20 (Suppl. 51): 68-71.
13. Mack DR, Michail S, Wei S, McDougall L, Hollingsworth MA. Probiotics inhibit enteropathogenic E. coli adherence in vitro by inducing intestinal mucin gene expression. Am. J. Physiol. 1999; 276(4): G941-G950. Available from: DOI: 10.1152/ajpgi.1999.276.4.G941.
14. Coconnier MH, Lievin V, Hemery E, Servin AL. Antagonistic activity against Helicobacter infection in vitro and in vivo by the human Saccharomyces boulardii strain LB. Appl Environ Microbiol.1998; 64(11): 4573-4580.
15. De Keersmaecker SC, Verhoeven TL, Desair J, Marchal K, Vanderleyden J, Nagy I. Strong antimicrobial activity of Lactobacillus rhamnosus GG against Salmonella typhimurium is due to accumulation of lactic acid. FEMS Microbiol Lett. 2006; 259(1): 89-96. Available from: https://doi.org/10.1111/j.1574-6968.2006.00250.x.
16. Matteo MJ, Armitano RI, Romeo M, Wonaga A, Olmos M, Catalano M. Helicobacter pylori bab genes during chronic colonization. Int J Mol Epidemiol Genet. 2011; 2(3): 286-291.
17. Shrestha S, Paudel P, Pradhan GB, Shrestha L, Bhattachan CL. Prevalence Study of H. pylori infection in Dyspeptic patients coming to Nepal Medical College Teaching Hospital, Jorpati, Kathmandu. Nepal. Med. Coll. J. 2012; 14 (3): 229-233.
18. Kable ME. Host Determinants of Expression of the Helicobacter pylori BabA Adhesion. Scientific Reports. Nature J. 2017; 10(2017): 1-12. Available from: https://doi.org/10.1038/srep46499.
19. Jing W, Wei-Hong W, Jiang L, Fang-Xun L. Celecoxib inhibits Helicobacter pylori colonization -related factors. World. J. Gastroenterol. 2010; 16(7): 846-853. Available from: doi: 10.3748/wjg.v16.i7.846.
20. Solnick L. Modification of Helicobacter pylori outer membrane protein expression during experimental infection of rhesus macaques. PNAS. J. 2004; 101(7): 2103-2111. Available from: DOI: 10.1073/pnas.0308573100.
21. Homayoun Z, Mehdi G, Hassan R, Elnaz A, Somayeh M, Jahani S. The efficacy and safety of adding the probiotic Saccharomyces boulardiito standard triple therapy for eradication of H.pylori: a randomized controlled trial. Gastroenterol Hepatol Bed Bench. 2013; 6(Suppl. 1): S99–S104.
22. Ansari S, Kabamba ET, Shrestha PK, et al. Helicobacter pylori bab characterization in clinical isolates from Bhutan, Myanmar, Nepal and Bangladesh. Journal pone. 2017; 10(11): 1-17. Available from: doi: 10.1371/journal.pone.0187225.
23. Skoog EC, Sjöling Å., Navabi N., Holgersson J., Lundin S.B. and Lindén S.K. "Human Gastric Mucins Differently Regulate Helicobacter pylori Proliferation, Gene Expression and Interactions with Host Cells". PloS one. 2012; 7(5): 36378. https://doi.org/10.1371/journal.pone.0036378.
24. Federico A, Gravina AG, Miranda A, Loguercio C, Romano M. Erad¬ication of Helicobacter pylori infection: which regimen first?. World J. Gastroenterol. 2014; 20(3): 665–672. Available from: doi: 10.3748/wjg.v20.i3.665.
25. Sheu BS, Sheu SM, Yang HB, Huang AH, Wu JJ. Host gastric Lewis expression determines the bacterial density of Helicobacter pylori in BabA2 genopositive infection. Gastroenterol. J. 2003; 52(7): 927–932. Available from: doi: 10.1136/gut.52.7.927.
26. Kable ME, Lori MH, Cathy MS, Samuel LD, Olena R, Anna S. Host Determinants of Expression of the Helicobacter pylori BabA Adhesin. Nature J. 2017; 10(2017): 1-12. Available from: https://doi.org/10.1038/srep46499.
27. Jiang X, Doyle MP. Growth supplements for Helicobacter pylori. J. Clin. Microbiol. 2000; 38 (5): 1984–1987.
28. De Francesco V, Giorgio F, Hassan C, Manes G, Vannella L, Panella C. Worldwide H. pylori antibiotic resistance: a systematic review. J. Gastrointestin Liver Dis. 2010; 19 (4): 409-414.
29. Bäckström A, Lundberg C, Kersulyte D, Douglas EB, Borén T, Arnqvist A. Metastability of Helicobacter pylori Bab adhesion genes and dynamics in Lewis b antigen binding. Proceedings of the National Academy of Sciences of the United States of Americ. 2004; 101(48): 16923–16928. Available from: DOI: 10.1073/pnas.0404817101.
30. Cadamuro AC, Rossi AF, Maniezzo NM, Silva AE. Helicobacter pylori infection: host immune response, implications on gene expression and micro RNAs. World J. Gastroenterol. 2014; 20(6): 1424-1437. Available from: doi: 10.3748/wjg.v20.i6.1424.
31. Kaparakis M, Anna KW, Jason DP, John SP, Nico VR, Martin JP. Macrophages Are Mediators of Gastritis in Acute Helicobacter pylori Infection in C57BL/6 Mice A. Infection and immune. J. 2008; 76(5): 2235–2239. Available from: DOI:10.1128/IAI.01481-07
32. Lenglinger J, See SF, Beller L, Cosentini E, Asari R, Wrba F. The cardia: esophageal or gastric? Critical reviewing the anatomy and histopathology of the esophagogastric junction. Acta Chir. Iugosl. 2012; 59 (3): 15–26. Available from: DOI: 10.2298/aci1203015l .
33. Brandt S, Kwok T, Hartig R, Konig W, Backer TS. NFkappaB activation and potentiation of pro inflammatory responses by the Helicobacter pylori CagA protein. Proc. Natl. Acad. Sci. J. USA. 2005; 102(26): 9300-9305. Available from: DOI: 10.1073/pnas.0409873102.
34. Atherton J. The Pathogenesis of H. pylori Induced Gastro-Duodenal Diseases. Annual Review of Pathology: Mechanisms of Disease. Annu Rev Pathol. 2006; 1: 63-96. Available from: DOI: 10.1146/annurev.pathol.1.110304.100125 .
35. Graham DY. Helicobacter pylori infection in the pathogenesis of duodenal ulcer and gastric cancer: a model. Gastroenterol. J. 1997; 113(6): 1983-1991. Available from: DOI: 10.1016/s0016-5085(97)70019-2 .
36. Dixon M. Pathology of Gastritis and Peptic Ulceration. In Helicobacter pylori: Physiology and Genetics. edited by Mobley HLT, Mendz GL, hazell SL. Wiley Online Library]. 2001; 43(x): 459-469. Available from: https://doi.org/10.1128/9781555818005.ch38.
37. Fischbach LA, Goodman KJ, Feldman M, Aragaki C. Sources of variation of Helicobacter pylori treatment success in adults worldwide: a meta-analysis. Int. J. Epidemiol. 2002; 31 (1): 128-39. Available from: https://doi.org/10.1093/ije/31.1.128.
38. Gotteland M, Brunser O, Cruchet S. Systematic review: are probiotics useful in controlling gastric colonization by Helicobacter pylori?. Aliment Pharmacol. Ther. 2006; 23(8): 1077-1086. Available from: DOI: 10.1111/j.1365-2036.2006.02868.x .
39. Pena JA, Versalovic J, Boulardii S. Lactobacillus rhamnosus GG decreases TNF-α production in lipopolysaccharide-activated murine macrophages by a contact-independent mechanism. Cell Microbiol. 2003; 5(4): 277-285. Available from: DOI: 10.1046/j.1462-5822.2003.t01-1-00275.x.
40. Schubert ML, Morus T, Stevan V, Adeams I, Bean H, Frenando Q. Regulation of gastric acid secretion. Curr. Opin Gastroenterol. 2009; 15: 457.
41. Mottet C, Michetti P. Probiotics: wanted dead or alive. Dig. Liver Dis. 2005; 37(1): 3-6. Available from: DOI: 10.1016/j.dld.2004.09.010.