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Zingiber officinale Syrup Reduces Bacterial Load in Study Cases Infected with *Helicobacter pylori* in Northeast-Libya

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Authors' contributions

This work was carried out in collaboration between all authors. Author FAK designed the study and wrote the protocol. Author MSA performed the statistical analysis and wrote the first draft of the manuscript. Authors SRMQ and RF managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: *Helicobacter pylori* plays a profound role in the pathogenesis of chronic gastritis, peptic ulcer, including gastric mucosa-associated lymphoid tissue and carcinoma. All the different lines of therapy have not shown maximal efficacy in the eradication/cure of the infection in patients. Consequently, alternative therapies including traditional medicines have been introduced both in the quest for better eradication therapies and in addressing the problem of *H. pylori* relapse such as *Zingiberis rhizome*.
Methods: The objective of this study was to test the antimicrobial activity of *Z. officinale* syrup against *H. pylori* with fifty volunteers at Health center of Omar El-Mokhtar University, El –Beyda city

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in Libya. 2 gm of *Z. officinale* syrup were drunk daily for three months, samples of blood analyzed after 3 and 6 months of treatment.
Results: From total samples examined after 3 and 6 months of treatment; level of antibody against *H. pylori* were decreased to be nearly up normal values at serum in most volunteers.
Conclusion: The study revealed a component within natural remedies such as ginger could be further used for prevention and treatment of *H. pylori* -induced gastritis in humans.

Keywords: Helicobacter pylori (H. pylori); Zingiber officinale syrup; ELISA test.

1. INTRODUCTION

Helicobacter pylori, is a Gram-negative, microaerophilic bacterium, identified in 1982 by Australian scientists Barry Marshall and Robin Warren [1]. It was first described in scientific circles in 1984 [2]. In 1994, it been first bacterium classified as Group 1 carcinogen and a definite cause of gastric cancer in humans by the International Agency for Research on Cancer, these germs can enter body and live in digestive tract [3]. This bacteria can cause sores, called ulcers, in the lining of stomach or the upper part of small intestine. It is linked to the development of duodenal ulcers and stomach cancer. However, over 80% of individuals infected with the bacterium asymptomatic, and it may play an important role in the natural stomach ecology [1]. Moreover, up to 85% of people infected with *H. pylori* never experience symptoms or complications [4].

Taking into account that half of the population is infected with *H pylori*, if the infection is not treated, the bacteria can persist throughout life and lead to chronic disease [5]. Acute infection may appear as an acute gastritis with abdominal pain (stomach ache) or nausea [6]. Where this develops into chronic gastritis, the symptoms, if present, are often those of non-ulcer dyspepsia: stomach pains, nausea, bloating, belching, and sometimes vomiting or black stool [7]. Individuals infected with *H. pylori* have 10% to 20% lifetime risk of developing peptic ulcers and 1% to 2% risk of acquiring stomach cancer [8-9]. A meta-analysis conducted in 2009 concluded the eradication of *H. pylori* reduces gastric cancer risk in previously infected individuals, suggesting the continued presence of *H. pylori* constitutes a relative risk factor of 65% for gastric cancers [10]. It has been associated with colorectal polyps and colorectal cancer [11], on the other hand, many articles were published on the extra gastric diseases related to *H. pylori* infection [12].

An increasing number of infected individuals are found to harbor antibiotic-resistant bacteria. This results in initial treatment failure and requires additional rounds of antibiotic therapy or alternative strategies, like a quadruple therapy, which adds a bismuth colloid, such as bismuth subsalicylate [13], levofloxacin [14]. Ingesting lactic acid bacteria exerts and supplementing with Lactobacillus and Bifidobacterium-containing yogurt has been also used [15]. Symbiotic butyrate producing bacteria which are normally present in the intestine are sometimes used as probiotics to help suppress *H. pylori* infections as an adjunct to antibiotic therapy [16]. Butyrate itself is an antimicrobial which destroys the cell envelope of *H. pylori* by inducing regulatory T-cell expression (specifically, FOXP3) and synthesis of an antimicrobial peptide called LL-37 [17]. The substance sulforaphane, which occurs in broccoli and cauliflower, has been proposed as a treatment [18]. Periodontal therapy or scaling and root planting has also been suggested as an additional treatment [19].

Z. officinale Roscoe, (Zingiberaceae) have enjoyed worldwide popularity both as spices and as traditional medicines [20]. Both anti-oxidative [21], and androgenic activities of *Z. officinale* were reported in animal models [22]. Previous study reported that the main components of ginger are 6-gingerol, 6-shogaol, 8-gingerol and 10- gingerol and these constituents had exhibited strong anti-oxidative activity [23]. The components in ginger include: extractable oleoresins, many fats, carbohydrates, vitamins, minerals and a potent proteolytic enzyme called zingibain. Oleoresins contribute to the sensory perception of ginger. There are 5-8% of oleoresins in crude *Z. officinale*, which consist of two distinct groups of chemicals: volatile oils and non-volatile pungent compounds [24]. However, the precise mechanism by which ginger and its chemical constituents exert their chemo-preventative effects has not been fully elucidated. As well as antibiotic resistance of *H. pylori* is not known in Middle East, it is reported to be increasing world over. The need therefore arises to find an alternative with anti-microbial properties. Studies conducted mainly in

the developed countries have demonstrated inhibition of *H. pylori* by extracts of ginger, black tea, garlic, thyme, and mint [25]. As well as, considering the well-established use of ginger for the treatment of gastrointestinal ailments, and the strong association between *H. pylori* and gastric and colon cancer [26]. We hypothesized that ginger may exert its chemo preventative effects by directly inhibiting the growth of *H. pylori*. This study therefore were designed to find out effect of *Z. officinale* as syrup, by dissolved 2 gram of powder in water and taken as tea every day for three month by fifty volunteers. This would be given alternative way of treatment to consider.

2. MATERIALS AND METHODS

The study was carried out during the period between November 2015 and July 2016. Fifty volunteers (24 males and 26 females) were enrolled in this study with rang of *H. pylori* antibody from 0.1 to 5.1 U/ml in their serum. Ginger was obtained from Superior Nutrition and Formulation by Jarrow Formulas, Los Angeles, USA. Syrup of *Z. officinale* were used. The ingestion of 2 gram of ginger in syrup was drunk as tea daily for three months [27]. Follow up of up to three and six months, samples from blood were used to analysis by ELISA to detect *H. pylori* antibody in serum. Serology: The ELISA kit, Cobas core anti-*H. pylori* enzyme immunoassay (Roche SA, Basel, Switzerland) was used for qualitative and quantitative determination of IgG anti- *H. pylori* as specified by the instruction manual. Significant values were calculated (T-test *p< 0.05, **p<0.01, ***p<0.001).

3. RESULTS AND DISCUSSION

Serum samples for determining the presence of IgG antibodies were obtained at months 0, 3 and 6 months after the study was started. The samples were stored at −70°C until analysis. Follow-up serum samples from each patient, together with the baseline serum sample, underwent simultaneous assays for IgG antibody to *H. pylori* by means of quantitative ELISA (EUROIMMUN Medizinisch Labordiagnostika AG, United Kingdom). Titers ≥ 1.1-1.5 U/mL were considered positive [28]. Serum titers of IgG antibody for 50 subjects who completed a 6-month follow-up comparing with control subjects were presented in (Tables 1 and 2). The results in Table 1 showed that volunteers who had level of antibody against *H. pylori* less than 1.5 U/ml for subjects without treatment and subjects were get *Z. officinale* syrup. Same classification in Table 2 but with subjects who had levels of antibody against *H. pylori* more than 1.5 U/ml. Similarity of results were noted in couple of tables. Significantly decreasing in average levels of antibody against *H .pylori* in each subject at end of three and six months compared with first day of treatment. Results had been similar pattern for males and females.

Table 1. Ratio of antibody against *H. pylori* in study group (≥1.5 U/ml)

Ratio of antibody against *H. pylori* ≥1.5 U/ml					
Sex	**Without treatment**	**Sex**	**0 day of treatment**	**After 3 months of treatment**	**After 6 months of treatment**
F	1.5	F	1.5	1.3	0.9
F	0.6	F	1.5	1.3	1.2
F	0.6	F	1.2	1.1	0.7
M	1.5	F	1.1	1	0.8
M	1.2	F	1	1	0.6
M	0.7	F	0.4	0.3	0.3
M	0.3	F	0.3	0.2	0.2
		M	1.4	0.9	0.6
		M	1.2	1	1
		M	0.8	0.7	0.6
		M	0.8	0.8	0.7
		M	0.3	0.1	0.1
Average	0.914286		0.958333	0.808333	0.641667
T-test				0.0022584**	0.0004245***

Table 2. Ratio of antibody against *H. pylori* in study group (≤ 1.5 U/ml)

Ratio of antibody against *H. pylori* ≤1.5 U/ml					
Sex	**Without treatment**	**Sex**	**0 day of treatment**	**After 3 months of treatment**	**After 6 months of treatment**
F	4.7	F	5	2.7	2.6
F	4.1	F	4.9	3.5	2
F	3.9	F	4.7	3.3	2.7
F	2.8	F	3.8	2.8	1.8
F	2.8	F	3.3	2.2	1.6
M	4.3	F	3.1	2.1	1.9
M	2.9	F	2.7	1.6	1.1
M	2.8	F	2.3	2.2	1.9
M	2.5	F	2.3	1.9	1.7
M	1.9	F	1.8	1.7	1
M	1.7	F	1.6	1.5	1.3
		M	5.1	3.5	1.9
		M	5	3.9	3
		M	4.1	3	2
		M	3	2.9	1.9
		M	2.7	1.9	1.3
		M	2.2	1.8	1.2
		M	2.1	1.7	1.4
		M	1.8	1.7	1
		M	1.6	1.1	0.9
Average	3.16		3.155	2.35	1.71
T-test				1.11E-05****	2.36542E-07*****

H. pylori infection is difficult to eradicate and therefore, it is necessary to combine several antibiotics. Many food and plant extracts have shown in *vitro* anti- *H. pylori* activity, but are less effective in *vivo*. The anti- *H. pylori* effects of these extracts are mainly permeabilitization of the membrane, anti-adhesion, inhibition of bacterial enzymes and bacterial grown [29]. For thousands of years ginger root has been used in traditional medicine to treat gastrointestinal disorders, including dyspepsia, peptic ulcer, motion sickness and inflammatory disorders [20]. The proximate chemical composition of ginger contains volatile oils (1%-4%), medically active elements of ginger [30], ginger extracts and the gingerols have been shown to have potential chemo-preventative activities. Dietary administration of gingerol to rodents ameliorated azoxvmethane-induced intestinal tumorigenesis [31]. However, very little is known about the mechanisms by which ginger or its chemical constituents exert these effects. From our result, levels of anti- *H. pylori* antibody were decreased significantly in all subjects who had low and high levels of bacteria compared with first results before treatment with *Z. officinale* syrup over a period of experiment. This agree with previous study of Siddaraju and Dharmesh 2007, who found that an aqueous extract of ginger can protect the gastric mucosa from stress induced mucosal lesions and inhibit gastric acid secretion, which can be done by blocking H+, K+- ATPase action, thus restricting *H. pylori* growth [32]. Ginger produces anti-oxidant protection against oxidative stress-induced gastric damage, thus, exhibiting anti-oxidative properties *H vitro.* Another study showed that gingerols and ginger extracts inhibit the development of *H. pylori* in *vitro* of 19 clinical strains. In addition, the fraction comprising the gingerols and 6-shogoal was very successful in inhibiting the growth of *H. pylori* CagA+ strains [33], these agents also active against *H. pylori* are very effective in the treatment of hyperemesis [33]. Moreover, the aqueous extract of *Z. officinale*, also showed an ameliorative effect against cadmium bromide or metalaxyl induced hepatotoxicity and nephrotoxicity [34] and [35].

4. CONCLUSION

The data presented in this simple study shows that ginger syrup inhibit level of anti-boy against *H. pylori in vivo*, it confirms the medicinal properties of ginger in medicines. Further studies are needed to clarify the mechanisms underlying this association, and advocate that ginger be

considered a new therapeutic approach in the treatment of gastric disorders.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The study protocol was reviewed and approved by Bio-ethics Committee at Biotechnology Research Center (BEC-BTRC).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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