

Scientific Rationale for Choosing an Alternative Herbal Composition for the Treatment of Helicobacter Pylori Infection

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ARTICLE INFO

Received:  September 01, 2024

Published:  September 19, 2024

Citation: Mahbuba Valiyeva, Sevil Mehraliyeva, Nurana Kapitanova, Natiq Aliyev, Nigar İsmayilova. Scientific Rationale for Choosing an Alternative Herbal Composition for the Treatment of Helicobacter Pylori Infection. Biomed J Sci & Tech Res 58(4)-2024. BJSTR. MS.ID.009198.

ABSTRACT

Obtaining phyto compositions with new ingredients against Helicobacter pylori, which is widespread among the world's population, is one of the priority areas of medicine and pharmaceutical science. According to a recent report by Market.us, the global Helicobacter Pylori diagnostics market size is expected to grow from US\$ 627.4 million in 2023 to approximately US\$ 1,245.8 million by 2033, growing at a CAGR of 7.1% during the forecast period from 2024 to 2033. The market size is expected to grow from US\$ 627.4 million in 2023 to US\$ 1,245.8 million by 2033. Helicobacter pylori diagnosis refers to the methods and techniques to detect the presence of Helicobacter pylori bacteria in the human gastric mucosa. This bacterium is associated with various gastrointestinal problems, including gastritis, peptic ulcers, and even gastric cancer; thus, accurate detection methods such as stool antigen tests, breath tests, blood tests, or tissue biopsy analysis using endoscopy for endoscopy are needed to accurately determine the presence of H. pylori infection and accordingly formulate effective treatment plans. "Global Helicobacter Pylori Diagnostics Market Demand and Growth Opportunities to 2024" offers a comprehensive analysis of the market by evaluating research and data from various sources. This report enables global decision makers to positively impact the global economy by providing a detailed overview of the market including statistics, market size, and competitive landscape (Figure 1) [1]. The aim of this research work is to select the composition of the phyto composition based on scientific research based on plant materials rich in essential oils and flavonoids - licorice, ginger, oregano, garlic.

Helicobacter pylori is a spiral-shaped bacterium 3.5 microns long and 0.5 microns wide. It has flagella, with the help of which it moves freely along the wall of the stomach or firmly attaches to it. The H. pylori bacterium is very variable, its strains (types) differ from each other in their ability to attach to the gastric mucosa, cause inflammation, and have different degrees of pathogenicity [2]. Diseases associated with H. pylori (Figure 2).

Abbreviations: MIC: Minimum Inhibitory Concentration; MALT: Mucosal Lymphoid Tissue; PUD: Peptic Ulcer Disease; NUD: Non-Ulcer Dyspepsia; GE: Garlic Extract

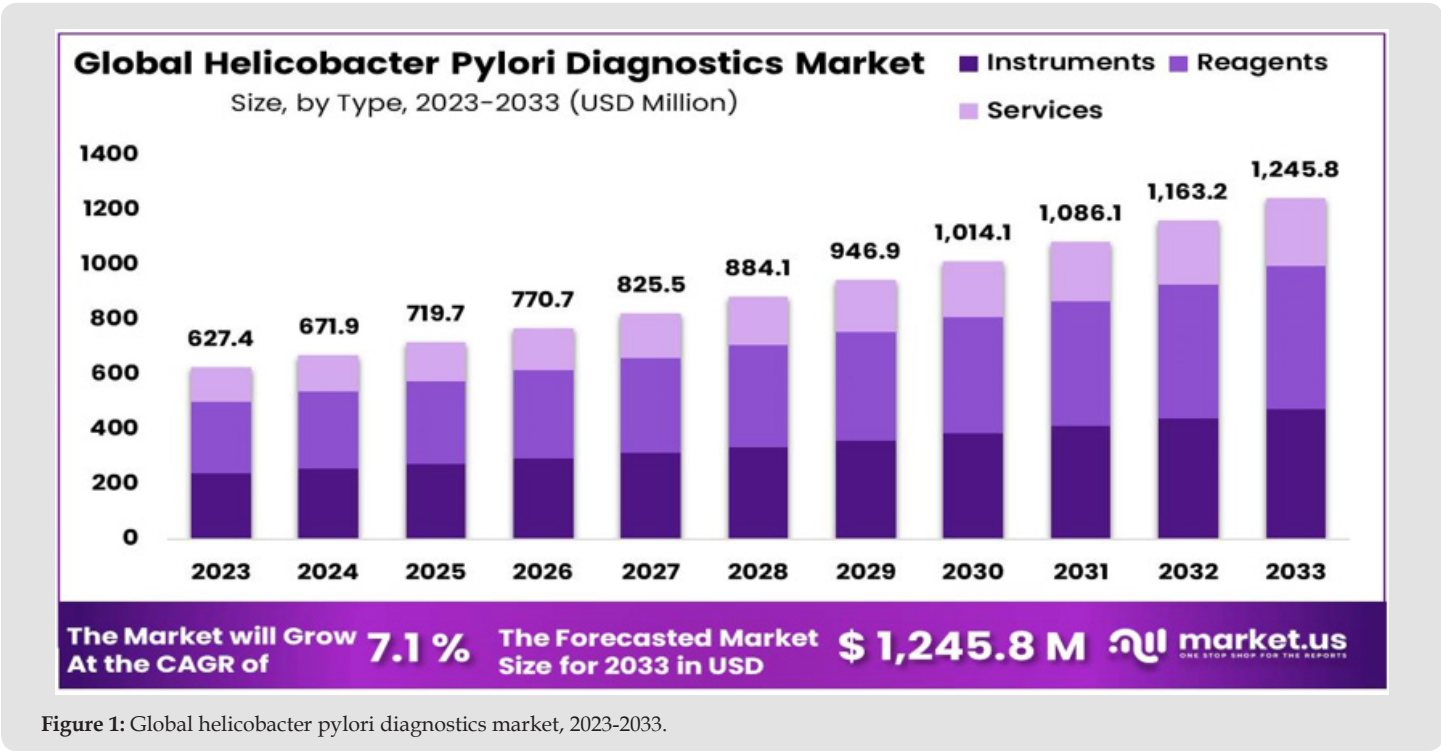


Figure 1: Global helicobacter pylori diagnostics market, 2023-2033.

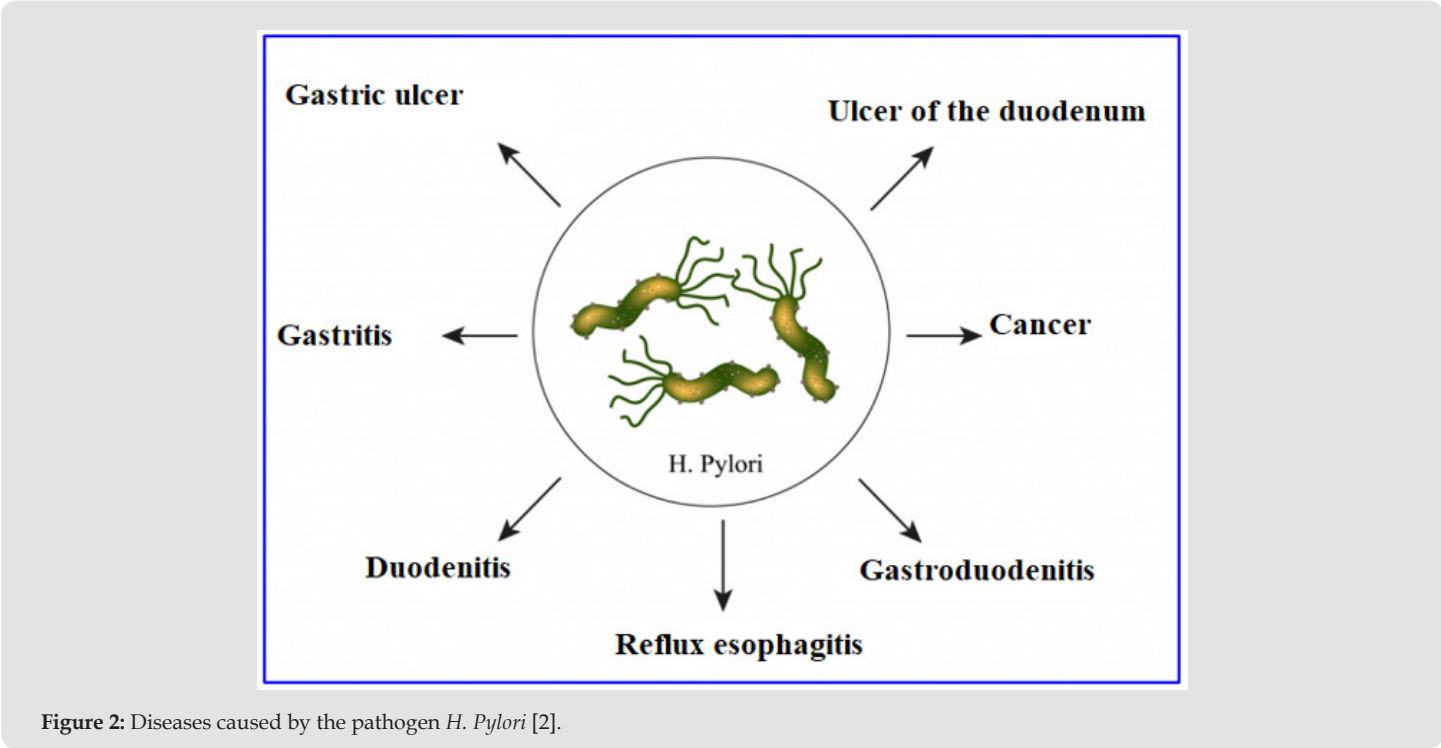


Figure 2: Diseases caused by the pathogen *H. Pylori* [2].

Introduction

Prevention of Heli Co Bacteriosis

Proper nutrition, hand and oral hygiene, and examination of persons who have been in contact with those already infected are important steps in preventing the disease caused by *Helicobacter pylori*. To prevent infection, it is necessary to wash your hands thoroughly, use only your own personal hygiene products (towels, toothbrushes, etc.), fully treat gastrointestinal diseases, and undergo regular preventive medical examinations.

The most effective measure for preventing complications of the disease is eradication therapy of *H. pylori* infection in chronic gas-

tritis, including asymptomatic cases. Eradication of *H. pylori* leads to recovery of gastritis, which is the basis for preventing long-term complications or relapses of the disease. To consolidate the results of treatment and strengthen the immune system, vitamin complexes and a number of microelements are prescribed [2]. Herbs and spices. Their list is quite extensive, and their abundance allows you to significantly enrich and diversify your diet with healthy products. Products such as cinnamon, ginger, cardamom, coriander, rosemary, marjoram, oregano, allspice, sage, mint, basil, oregano, turmeric, anise and cumin significantly reduce the growth of *Helicobacter pylori*. The high concentration of essential oils and a number of other biologically active substances in the plant allows it to have antibacterial and antifungal effects (Figure 3) [3].

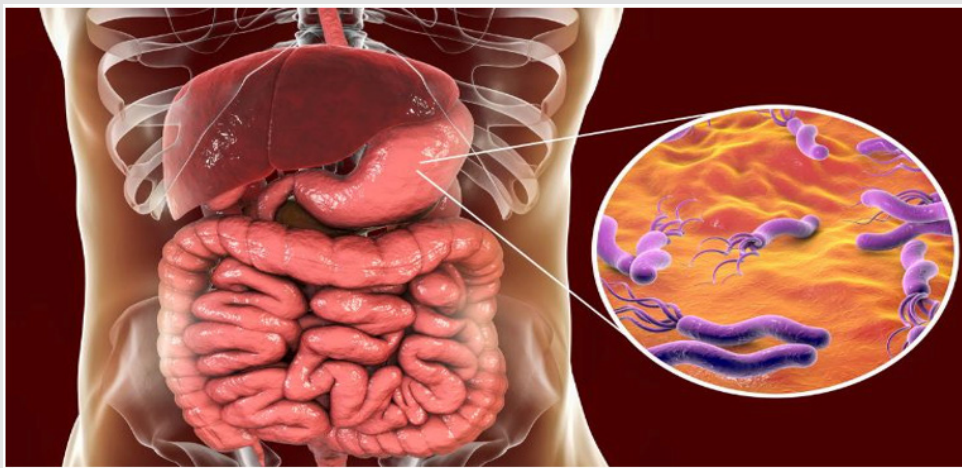


Figure 3.

The Role of Medicinal Plants in the Treatment of Helicobacter Pylori

Medicinal plants have been widely used for centuries in the treatment and prevention of various diseases. By using medicinal chemistry and combinatorial chemical and biosynthetic technologies, new natural products will be optimized based on their biological activity to produce effective bioactive substances as promising bioactive molecules [4]. In recent years, several studies have shown that *H. pylori* infection can be suppressed by medicinal plants. The structures of some potent medicinal plants and compounds isolated from plants recently evaluated in the literature for the treatment or eradication of *H. pylori* are discussed below. This review was performed by searching bibliographic databases such as PubMed, Google Scholar, EBSCO, and local databases for studies published between 1984 and 2013. These studies were mostly conducted in vitro, and only a few studies were conducted in vivo. *Helicobacter pylori* is a highly heterogeneous bacterial species, possessing both genotypic and phenotypic heterogeneity and highly adapted to survive in the gastric niche. The genomic diversity of *H. pylori* coincides with the diversity of its host species,

dating back at least 60,000 years, corresponding to the first colonization and co-migration of humans from East Africa. *Helicobacter pylori* causes a persistent infection and chronic inflammation in most infected individuals. Once in the body, the bacteria must evade the bactericidal activity of the gastric lumen contents and penetrate the mucosa. Once infected, *H. pylori* causes acute gastritis characterized by neutrophilic infiltration of the foveal and superficial epithelium and degenerative changes in the epithelium.

Medicinal Plants in the Treatment of Helicobacter Pylori Infection

Flavonoids: The chemical structure of plant metabolic products determines their pharmacological action. At this time, a number of biosynthesis mechanisms produce substances with a complex chemical structure. Such structures can also be responsible for other functions in the biological environment. One of the groups whose secondary metabolites have pharmacological significance are flavonoids. Flavonoids are phenolic compounds that act as adaptive agents in plants. They act in response to bacterial penetration under stress

conditions. Due to these properties, flavonoids are of great interest for the preparation of new medicinal forms with antibacterial action. (Behari, et al. 2020). Of the flavonoids, E. coli rutin and In S. aureus can prevent the formation of a biological layer. The main mechanism of this effect is due to a decrease in the production of exopolysaccharides. Such molecules are responsible for the high durability of the antibacterial action of the biofilm, creating several layers on its surface and causing adhesion.

Use of flavonoid-containing extracts against *h. Pylori* in medicine*: *H. pylori* Since 1994, the International Agency for Research on Cancer has classified it as a Group I carcinogen. *H. pylori* accounts for approximately 5% of all tuberculosis patients worldwide. *H. pylori* is also associated with diseases such as chronic gastritis, peptic ulcer disease, and gastric mucosal lymphoid tissue lymphoma. *H. pylori* secretes a special enzyme, urease, which can convert urea in gastric acid into ammonia. At this time, the pH of the stomach increases, and thus bacterial colonization becomes possible. The bacterium lives incognito and causes chronic inflammation, gastritis, and peptic ulcer disease, which can ultimately lead to gastric perforation. In the next stage, the epithelial tissue of the stomach undergoes metaplasia, metaplastic cells begin to divide uncontrollably, which leads to gene mutation and the formation of malignant tumor tissue. (Figure 4) The use of preparations containing physiologically active substances in folk medicine allows the use of flavonoid compounds for medicinal

purposes. Thus, they have antimicrobial, antitumor, anti-inflammatory and antioxidant effects, and this effect makes flavonoids act on different microorganisms with different mechanisms of action. Flavonoids cause membrane disintegration, disruption of membrane integrity, synthesis of the cell wall and nucleic acids, electron transport chains during ATP synthesis, formation of flavonoid compounds with the participation of metals, inhibition of toxins secreted by bacteria. Catechin, epicatechin, epigallocatechin and quercetin flavonoids in black, white and green tea weaken the electron membrane responsible for the transport chain by oxidizing. They disrupt the phosphorylation process and block the flow of protons associated with dehydrogenase, thereby blocking the flow of electrons at the cytochrome level.

However, in this case, phenolic compounds with poor solubility and low hydrophobicity cannot have an effect. The outer lipopolysaccharide layer of *H. pylori* prevents oxidative phosphorylation, as a result of which the membrane creates a hydrophobic microenvironment along the surface of the bacteria. Soluble phenols also inhibit H⁺-adenosine triphosphatase, which is necessary for the synthesis of adenosine triphosphate, causing hyperacidity due to the donation of protons to the plasma membrane or the intracellular cytosolic pathway, in other words, they cause adhesion of the hydrophobic part of the polyphenols to the cell wall. This, in turn, leads to destabilization of the membrane, disruption and delay of transmembrane transport.

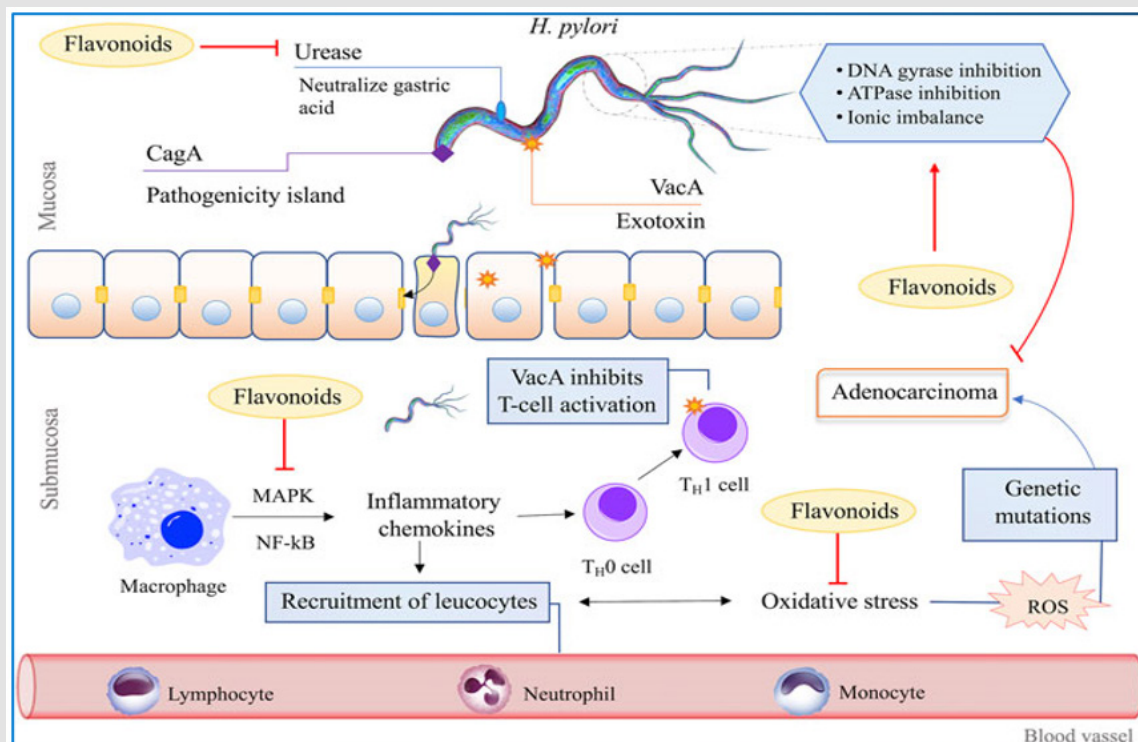


Figure 4: Mechanisms of action of flavonoids against *H. pylori*.

These mechanisms may act synergistically: the disturbing and destabilizing action of polyphenols may contribute to an increase in the acidity of simple soluble phenols. *H. pylori* There is no general treatment for complete elimination. Instead, a course of treatment consisting of antiulcer drugs and a combination of two types of antibiotics is used. Our research results have shown that the study of natural products, especially plant extracts rich in flavonoids, is very relevant in this direction. Such combinations will allow us to obtain positive results in the treatment of diseases caused by *H. pylori* and in the fight against it [5]. In this direction, scientists prepared aqueous and alcoholic extracts from 17 plant materials. *H. pylori* in one standard strain and 11 wedges isolate conducted studies using the disk diffusion method and assessment of the minimum inhibitory concentration (MIC) in solid media Inhibitory activity against *H. pylori* strains was observed in a significant part of the tested plants.

The MIC values of ethanol extracts were two to four times lower than those of aqueous extracts. In particular, ethanol extracts of *Cuminum cyminum* L. and propolis showed MIC₉₀ values of 0.075 mg[sol] ml. The results demonstrate a significant in vitro effect of plant extracts against *H. pylori*, which can be considered as a valuable support in the treatment of infection and may help in the development of new and safe anti-H agents [6] *Helicobacter pylori* infection causes lifelong chronic gastritis that can lead to peptic ulcers, mucosal lymphoid tissue (MALT) lymphoma and gastric cancer. The problem of increasing host resistance to antibiotics requires the search for new candidates from plant sources. In this study, we evaluated the in vitro activity of some selected medicinal plants against *H. pylori* in clinical isolates of *H. pylori*. Gastric biopsy samples were collected from patients with gastroduodenal complications. *Helicobacter pylori* was isolated from the samples using standard microbiological techniques. The sensitivity of three *H. pylori* isolates to methanol extracts of 23 Iranian plants was determined using the disk diffusion method.

This time, all tests were repeated three times. Among them, *Punica granatum* and *Juglans regia* extracts showed excellent activity against *H. pylori* with mean inhibition zone diameters of 39 and 16 mm at a dose of 100 µg disc-1, respectively. Based on the results obtained with *P. granatum* (pomegranate), peel extracts of nine pomegranate cultivars were further analyzed for comparison with clinical isolates of *H. pylori*. The results showed that all Iranian pomegranate varieties except Alak-e-Shirin *H. pylori* and gave results against its clinical isolates. (mean inhibition zone ranged from 16 to 40 mm at a dose of 50 µg disk-1) [7-12]. Research has shown that various plants have important benefits in preventing *Helicobacter pylori* infection. The mechanism of action of plants in this direction is explained. Given all of the above, our studies also included phyto cosms of licorice, ginger, oregano and garlic plants. For this, let us consider the scientific basis of these stories on the elimination of the *Helicobacter pylori* pathogen or the prevention of complications in the gastrointestinal system due to its influence.

Glycyrrhiza Glabra

Since ancient times, herbal treatment has found its place in the treatment of gastric ulcers. Among such plants, it was found that the roots and rhizomes of licorice have an anti-*Helicobacter* effect, and in modern medicine, licorice extract is used for gastric ulcers and as an alternative to bismuth. This, in turn, plays a protective role against the secretion of gastric acid and pepsin, covers the injured area and causes mucus secretion. In the Gas troentero hepatology Center of Shiraz University of Medical Sciences, 40 patients with peptic ulcer disease were divided into two equal groups and double-blind studies were conducted. At the first stage, all patients underwent endoscopic examination for histological confirmation of peptic ulcer disease, and a urea breath test was performed to confirm the presence of bacteria. The first group of patients received antibiotics amoxicillin (500 mg 3 times a day for 15 days after the diet) and metronidazole (250 mg 4 times a day for 15 days after the diet), as well as omeprazole (20 mg 2 times a day half an hour before the diet, 30 days after the diet) and bismuth subnitrate preparations (500 mg 3 times a day half an hour before the diet for 30 days). In the 2nd group, the prescription was the same, only licorice was replaced by bismuth subnitrate (250 mg 3 times a day half an hour before the diet for 30 days). After 1 month of treatment, all patients underwent endoscopy again, during which time histological examination, biopsy to determine the rate of healing of the gastric ulcer and urea breath test to determine the degree of eradication of *H. pylori* were performed, and the degree of pain reduction was determined at the same time. The studies were approved by the university ethics committee, and informed consent was obtained from each participant [13].

The effect of licorice root on the eradication of *H. pylori* was studied in patients with peptic ulcer disease (PUD) or non-ulcer dyspepsia (NUD) compared with a standard clarithromycin-based triple therapy. This randomized controlled clinical trial included 120 patients with a positive rapid urease test who were assigned to two treatment groups: a control group receiving a clarithromycin-based triple therapy and, six weeks later, an evaluation of two-week *H. pylori* treatment. The inclusion of licorice root in a clarithromycin-based triple therapy regimen has been shown to predominantly increase *H. pylori* eradication in peptic ulcer disease [14,15].

H. pylori One hundred and eighty clinical isolates of the bacterium were isolated in the susceptibility testing to licorice extract. *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* were also included in this study for comparison and control. Agar dilution assay was used to test the susceptibility of clinical isolates of *H. pylori* to different concentrations of licorice extract. on test boards Licorice extract at doses of 25, 50, 100, 150, 200, 300, and 400 mg/ml inhibited *H. pylori* strains [16-19].

Origanum Vulgare

The plant contains nine chemically studied essential oils, three of which are monoterpene alcohol-dominated components. This group includes essential oils obtained by hydrodistillation from the species *Thymus vulgaris*, *Origanum vulgare* and *Melaleuca alternifolia*. Accordingly, the main predominant compounds of these essential oils are thymol (36), carvacrol (37) and terpinen-4-ol (25). In addition to alcohols, the mentioned essential oils are characterized by the presence of monoterpene hydrocarbons. P-cymene is the main component of the essential oils of the plant's thyme and oregano. Among other essential oils, terpinenes such as α -, γ - and δ -terpinene (= terpinolene) and α -terpineol have been identified in the essential oil of tea tree. Among the world's population *H. pylori* One of the important nuances is the use of essential oils of cedar wood, oregano, lemon grass and lemon balm, which are widely used in the fight against. Phenolic metabolites of oregano, considered a source of natural antioxidants, have beneficial effects on human health, including the prevention of mutagenesis and carcinogenesis. Some of the phenolic phytochemicals of the plant are also known for their antimicrobial and antifungal activities. *Origanum vulgare* L. from a plant rich in phenolic compounds with antioxidant and antimicrobial activity. Anti-microbial activity against ulcer-associated *Helicobacter pylori* was evaluated. Antimicrobial activity against *H. pylori* was tested using the standard agar diffusion method. Phenolic profiles in oregano extracts were analyzed using HPLC. It was suggested that differences in the physicochemical properties of phenolic acids with C6-C1-COOH and C6-C3-COOH structures play a role in inhibiting the growth of *H. pylori* [14,15].

Allium Sativum

Allium sativum L. (Amaryllidaceae), Garlic is a plant that reduces cardiovascular disease, blood pressure, type 1 diabetes and cholesterol levels, has antibacterial, antifungal and viral properties, and is also effective against various parasites, has an immunosuppressive effect, anti-inflammatory and antioxidant properties. Garlic materials including garlic oil, garlic powder, allicin (allyl-2-propenethiosulfinate and their diallyl moieties) showed significant but highly variable activity against *H. pylori* against all strains and isolates tested. The minimum inhibitory concentrations of diallyl tetra sulfide and allicin were lower than those of garlic oil, powder and diallyl disulfide. The results of the study showed that selenium-enriched garlic intake suppressed the development and progression of chronic gastritis caused by *H. pylori*. According to another study, long-term use of garlic supplements did not reduce the prevalence of *H. pylori* infection. An *in vivo* study involving 10 subjects receiving garlic showed that garlic had no effect on *H. pylori* *in vivo*. Allitridum (diallyl trisulfide), a specific garlic derivative, exerted a dose-dependent inhibitory effect on the growth of *H. pylori* [16]. Garlic Extract (GE)/GM is derived from the *Allium sativum* plant species, which is traditionally used for its medicinal properties. GM contains several bioactive compounds, including allicin, alliin, and diallyl sulfide, which have various health

benefits, including antimicrobial and anti-inflammatory properties. Garlic extract contains several bioactive components, including allicin, ajoene, and diallyl sulfide.

Allicin has potent activity against *H. pylori*. The dosage of garlic extract varies depending on the specific product and the condition being treated. However, most studies have used between 400 and 1200 mg of garlic extract per day. Although garlic extracts are safe, high doses may cause gastrointestinal upset and bleeding in humans. Therefore, the permissible dose of garlic extract should not exceed the recommended daily dose. The chemical structure of allicin, one of the main biologically active components of garlic extract, is C₆H₁₀OS₂. Garlic extract can be obtained using various extraction methods, including water extraction, ethanol extraction, and supercritical fluid extraction. The choice of extraction method can affect the composition and biological activity of the extract [17].

Zingiber Officinale

Ginger is a popular spice and medicinal plant used in traditional medicine for centuries. Ginger extract contains several bioactive components such as gingerol, shogaol, and paradol. The main bioactive component of ginger extract is gingerol, which has strong activity against *H. pylori*. The dosage of ginger extract varies depending on the specific product and the condition being treated. However, most studies have used between 500 and 2000 mg of ginger extract per day. It is important to note that ginger extract is generally considered safe, but high doses may cause gastrointestinal upset and bleeding in some people. Therefore, the recommended daily dose of ginger extract should not exceed the recommended daily dose. The chemical structure of gingerol, one of the main bioactive components of ginger extract, is C₁₇H₂₆O₄. Ginger extract can be obtained using a variety of extraction methods, including solvent extraction, steam distillation, and supercritical fluid extraction. The choice of extraction method can affect the composition and biological activity of the extract [18-22]. Thus, in the course of studying the data of scientific literature it was established that for the treatment and prevention of *Helicobacter pylori* it is advisable to prepare and use a new phyto composition consisting of licorice, ginger, oregano and garlic plants, rich in flavonoids and essential oils, microelements and vitamins. In the future, it is also necessary to develop a technology for the production of floating tablets that are convenient for patients to take and have a selective effect based on the phytoextract obtained from this composition [23].

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2024.58.009198

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