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Review

The Power of Herbal Extracts and Essential Oils in the Fight Against *Helicobacter pylori*: A Current Review

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Abstract
Helicobacter pylori is a human pathogen bacterium that causes gastric and duodenal diseases. This bacterium, which infects approximately half of the global population, is classified as a Group I carcinogen. Diseases caused by this bacterium, which can lead to very serious conditions ranging from gastritis to stomach cancer, can develop due to iron deficiency anemia or B12 vitamin deficiency. The presence of this bacterium in the saliva, feces, and vomit of infected individuals indicates the possibility of transmission through these routes. Due to the emergence of antibiotic-resistant strains of *H. pylori*, there is a need for natural complementary treatments. The side effects of drugs have led researchers to turn to nature, and plant-based functional foods have gained importance. It is well recognized that active ingredients frequently present in plant extracts are crucial in the treatment of *H. pylori*. It is very valuable for literature to draw attention to these alternative treatments and make them available.

1. Introduction

The gram-negative *Helicobacter pylori* bacterium of the order Campylobacterales is 2-4 µm long and 0.5-1 µm wide. The organism under consideration possesses a bundle of 2-6 unipolar sheathed flagella, which enable it to move rapidly in viscous solutions, such as the mucus layer on gastric epithelial cells. As illustrated in Figure 1, the electron microscope image of *H. pylori* is presented [1]. The genome of *H. pylori*, measuring 1.6 Mbp, comprises a single circular chromosome that encodes approximately 1,600 proteins [2].

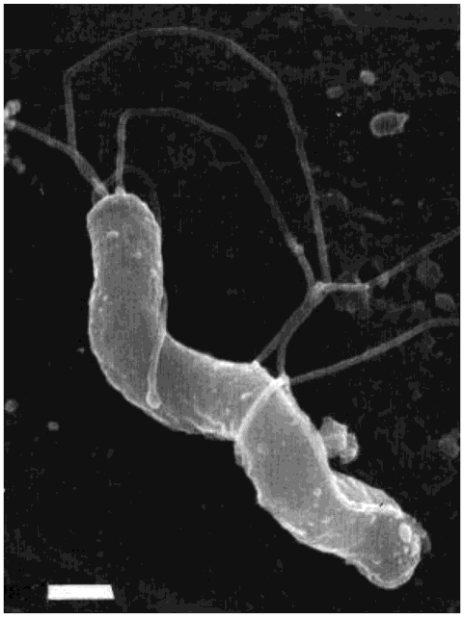

Figure 1. Electron microscopy image of *H. pylori* [1]

H. pylori can maintain its existence by various mechanisms including mobility in the gastric mucus layer, urease production, adhesion, etc. Figure 2 shows the connection of these mechanisms [3].

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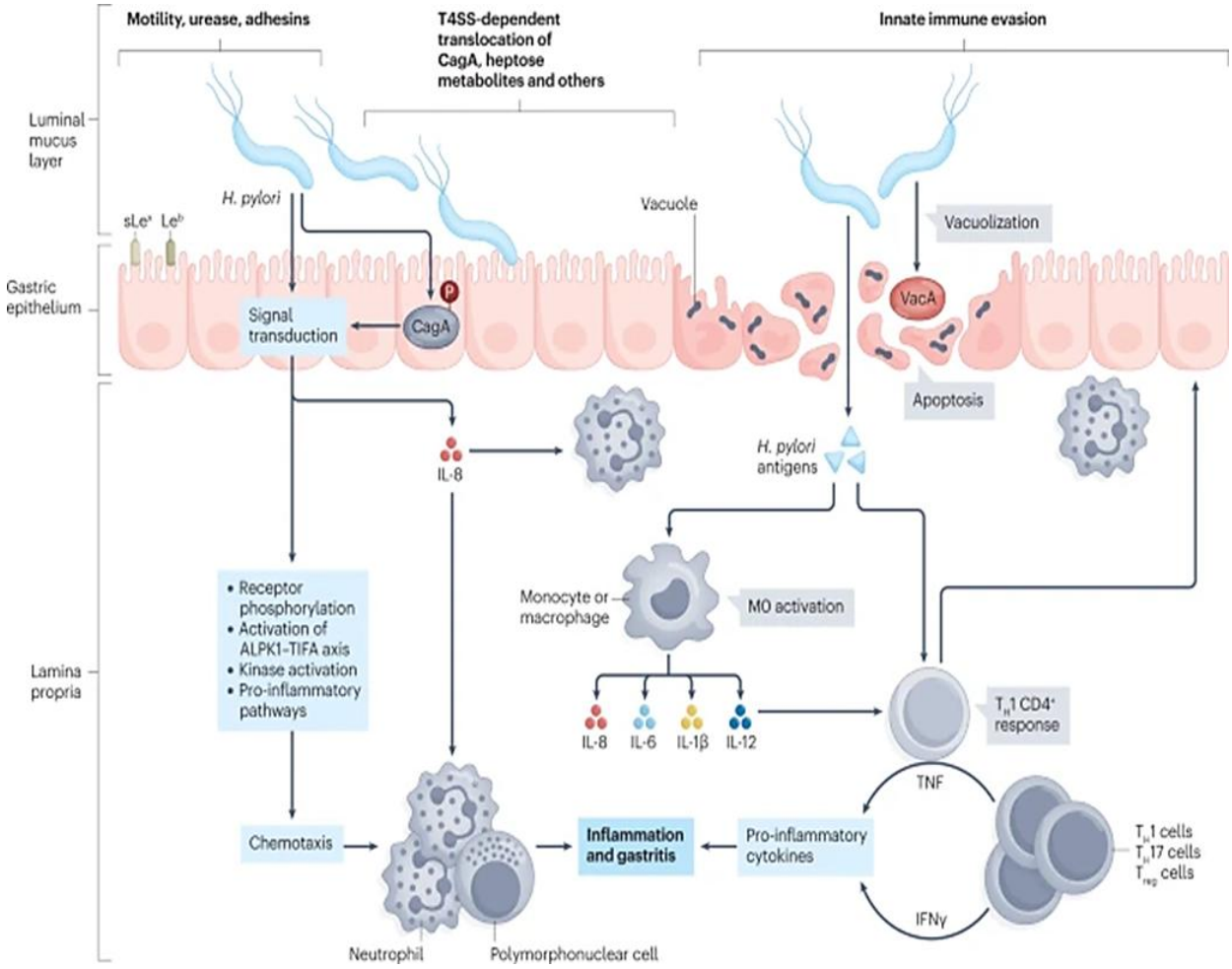

Figure 2. Contamination with *H. pylori.*

The damage to the gastric epithelium (through motility, urease activity, adhesion mechanisms and vacuolisation) is summarised as follows [3]. It is evident that the gastric lumen does not possess an acidic pH level conducive to the survival of *H. pylori*. Consequently, this bacterium must expeditiously traverse the mucus layer, a feat facilitated by its flagellum. The mucus layer, which is reached by *H. pylori* with great alacrity thanks to its rapid movement and urease enzyme, consists of sulphated polysaccharide and functions as a protective buffer against gastric acid [4]. Chemotaxis and energy taxis mediate the flagellum's direction of movement, enabling bacteria to traverse the pH and bicarbonate gradients in stomach mucus [5]. The urease enzyme breaks down urea released by gastric epithelial cells, converting it into ammonia and creating an environment in which the enzyme can survive [4]. Urea provides the organism with a continuous supply of nitrogen due to its urease action [3].

H. pylori has been observed to attach itself to gastric epithelial cells by binding surface molecules (adhesins) to its outer membrane and attaching them to host cell receptors. Notwithstanding the physical forces involved in the processes of gastric emptying, mucus layer exchange and epithelial cell shedding, which are instrumental in reducing colonisation, adherence enables *H. pylori* to achieve significant colonisation [6]. Members of the large hop superfamily producing outer membrane proteins encode the best studied adhesins. These adhesins are shown in Table 1 [2].

Table 1. *H. pylori* surface molecules (adhesins)

Adhesin	Host Binding Target / Function
BabA	Lewis b blood group antigens synthesized on gastric epithelial cells are bound by BabA.
SabA	Host sialyl-Lewis x antigens, which are mostly expressed on epithelial cell surfaces during inflammatory conditions, are bound by SabA adhesin.
HopQ	HopQ is crucial for Cag T4SS activity and binds to various carcinoembryonic antigen–related cell adhesion molecules.
AlpA and AlpB	Laminin, a glycoprotein found in the extracellular matrix, is bound by AlpA and AlpB.

Vacuole-forming cytotoxin A (VacA), an autotransporter protein toxin, is secreted by *H. pylori*. The induction of large intracellular vacuoles, apoptotic cell death or necrosis, autophagy and the inhibition of T and B cell proliferation are all

effects of VacA [7]. Protease, VacA, cytotoxin-associated gene (cag), lipopolysaccharide (LPS, which facilitates immune evasion and promotes mucosal adaptability), and pathogenicity island (cagPAI), of which cagPAI is the most significant virulence factor, are also connected with *H. pylori*'s pathogenicity [8].

H. pylori is one of the pathogens specifically studied in research for causing various diseases such as peptic ulcer, gastritis, and stomach cancer. The standard treatment method is based on antibiotic-based eradication protocols. However, the increase in antibiotic resistance has heightened interest in alternative treatments. In this context, natural products such as essential oils are an important area of research. Essential oils are highly important due to their rich content with antimicrobial properties. Some studies in literature are quite important in terms of choosing these oils as alternatives. For example, cinnamon oil has been used against *H. pylori* and significant results have been obtained. It has been reported that cinnamon oil can be considered as an alternative because its active component, cinnamaldehyde, inhibits bacterial growth and can interfere with pathogenic mechanisms [9]. Another study reported that silver fir, pine needle, tea tree, lemon balm, and cedarwood oils are effective against *H. pylori*. It was emphasized that cedarwood and thyme oils may play an active role in H. pylori eradication. Furthermore, cedarwood oil has been selected as a candidate for alternative treatments because it inhibits urease activity [10]. Based on these data, essential oils are promising candidates for alternative therapies. However, numerous clinical studies are needed to clarify their significance and ensure their usability.

This review was prepared by searching databases such as Google Scholar, PubMed, and Web of Science to access the current literature. The review was researched in the literature covering the period 2000–2025. During the search, word combinations such as 'Helicobacter pylori', herbal extract', 'essential oil', and 'phytotherapy' were preferred. Articles containing herbal extracts or essential oils that have been studied for their effect on H. pylori, published in a peer-reviewed journal, and clearly presenting the methods and results were preferred. Conference abstracts, articles lacking methodological information, and studies unrelated to the topic were excluded from the evaluation. Duplicate publications were removed at the end of the screening, and suitable studies were reviewed and included in the study.

2. History of *H. pylori*

In 1980s, *H. pylori* was initially effectively isolated from gastric mucosa biopsies taken from individuals suffering from chronic antral gastritis. With this discovery, Warren and Barry, who realised that most patients with chronic gastritis, gastric ulcer or duodenal ulcer contain these bacteria, were awarded the Nobel Prize in 2005 [8]. Table 2 provides a comprehensive overview of the subjects of *H. pylori* research on an annual basis [3].

Table 2. Historical development of *H. pylori* [3]

Year	Advancement
1982	*H. pylori* was discovered by Marshall and Warren.
1989	*H. pylori* renamed from *Campylobacter pylori.*
1990	Additional Helicobacter species found in human diseases. The first trial demonstrating that removal of *H. pylori* cures duodenal ulcers
1991	First epidemiologic evidence that *H. pylori* is a risk factor for gastric cancer. Start of experimental *H. pylori* vaccine research.
1994	*H. pylori* is classified as a class I carcinogen by the WHO. US National Institutes of Health advise eradicating *H. pylori.*
1996	Updated gastritis classification system (Sydney–Houston system).
1999	PPI-triple therapy becomes world standard for *H. pylori* eradication; high efficacy shown in RCTs.
2000	Test-and-treat strategy recommended for dyspeptic patients under 45 with no alarm symptoms (Maastricht II).
2000 onwards	Increasing resistance to levofloxacin and clarithromycin; triple therapy increasingly replaced by quadruple therapy.
2001	First prospective clinical trial demonstrating *H. pylori*'s major role in gastric cancer development.
2004	First randomized controlled trial of *H. pylori* eradication for gastric cancer prevention.
2005	Nobel Prize awarded to Marshall and Warren.
2008	OLGA and OLGIM systems introduced for histologic staging and gastric cancer risk prediction.
2010	In areas with high clarithromycin resistance, bismuth triple therapy becomes first-line. First randomized vaccine trials for prevention of *H. pylori* infection.
2012	MAPS guidelines for surveillance of atrophic gastritis and early gastric cancer detection.
2013 onwards	Major trials evaluating *H. pylori* screen-and-treat strategies for gastric cancer prevention.
2015	Kyoto Global Consensus defines *H. pylori*-associated gastritis as an infectious disease.
2016	PPIs in dual and triple therapy increasingly replaced by potassium-competitive acid blockers (P-CABs).
2019	MAPS II guideline update.
2021	Florence Consensus + Maastricht VI: new insights on *H. pylori*, gut microbiota, gastric cancer prevention, and susceptibility-guided therapy.
2024	Development of a highly immunogenic multi-epitope H. pylori vaccine using AI-assisted immunoinformatics [11].

3. Clinical Implications of *H. pylori* Infection

One of the most common human infections, *H. pylori* is known to be the main cause of a number of gastroduodenal conditions, such as peptic ulcers, gastric adenocarcinoma, chronic gastritis, and mucosa-associated lymphoid tissue (MALT) lymphoma [12]. *H. pylori* infection has also been linked to a number of neurological conditions, including Parkinson's, multiple sclerosis, and Alzheimer's [13]. The various diseases associated with *H. pylori* infection are the result of a complex interplay between host genetics, bacterial virulence and environmental variables that produce various chronic gastritis phenotypes. The several illness characteristics linked to *H. pylori* infection are depicted in Table 3 [3].

Table 3. The symptoms related to an *H. pylori* infection [3]

Phenotype	Frequency	Impact on Secretory Function	Potential Results
Mild gastritis	Most patients	Normal acid secretion	Most individuals are asymptomatic, with no significant clinical consequences.
Duodenal ulcer	10–15% of patients	Acid secretion and gastrin levels are elevated, and inhibitory regulation of acid secretion is compromised.	Dyspeptic symptoms, duodenal ulcer
Gastric cancer	~1% of patients	Variable gastrin secretion; little or no acid secretion	Severe atrophic gastritis, intestinal metaplasia, gastric cancer

Numerous gastrointestinal conditions, such as gastritis, stomach cancer, duodenal ulcers, and gastric ulcers, have been linked to *H. pylori*. The pathophysiology of duodenal and stomach disorders linked to *H. pylori* is depicted in Figure 3 [2].

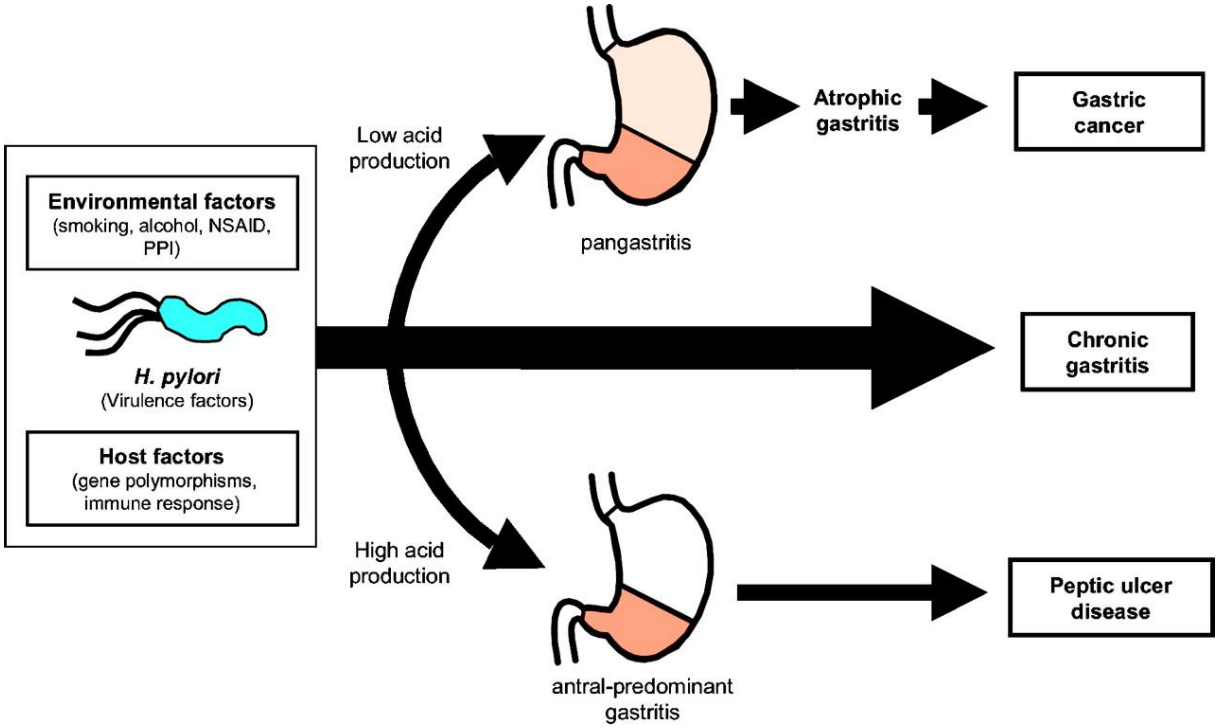

Figure 3. Pathophysiology of H. pylori associated gastric and duodenal diseases [2]

Chronic gastritis caused by *H. pylori* is characterised by the proliferation of immunocompetent lymphocytes and plasma cells secreting IgA, IgG and IgM in the gastric mucosa. In the literature, 'superficial gastritis' is a common term used to describe the early nonatrophic inflammatory phase of chronic gastritis. Chronic gastritis caused by *H. pylori* is a permanent disease that cannot be cured [14]. The paucity of information regarding acute gastritis is striking. The available data are derived primarily from the results of infected persons who have either knowingly or unknowingly ingested this bacterium or interacted with contaminated material. As posited by the extant literature, there is a possibility that acute gastritis may be associated with transient symptoms such as nausea and vomiting, as well as significant inflammation of both the proximal and distal gastric mucosa, otherwise known as pangastritis. The spontaneous resolution of acute gastritis remains uncertain, as does the frequency with which such occurrences are observed [1].

Peptic ulcers, also known as gastric or duodenal ulcers, are characterised by mucosal defects that perforate the mucosa and are at least 0.5 cm in diameter. The most common location for the development of gastric ulcers is along the slight curvature of the stomach, particularly at the junction of the corpus and antrum mucosa. The duodenal bulb, the area most

exposed to stomach acid, is where duodenal ulcers typically develop. The prevalence of stomach ulcers is highest among individuals over the age of 40, while duodenal ulcers predominantly affect individuals between the ages of 20 and 50 [1].

Approximately 90 per cent of stomach cancer cases are caused by *H. pylori* infections [15]. With 812,000 gastric malignancies (including non-Hodgkin's lymphoma of the stomach) recorded in 2018, *H. pylori* is the most prevalent carcinogenic pathogen and about 37% of all cancers brought on by a chronic infection [16]. *H. pylori* infection increases the risk of stomach cancer in several cultures. This could be brought on by genetics, home conditions, or eating habits. East Asian communities, for instance, typically eat more pickled or salty dishes [17]. Although dietary, lifestyle and socioeconomic factors, including smoking and salt intake, all play a role in the development of gastric cancer, they are all dependent on the presence of *H. pylori* infection [1].

Vitamin B12 deficiency, unexplained iron deficiency anemia, and certain types of idiopathic thrombocytopenic purpura have all been linked to *H. pylori* infection. Furthermore, an increasing body of research has identified a multitude of links between *H. pylori* infection and a wide range of non-gastric conditions, including but not limited to metabolic syndrome, heart disease, hepatobiliary diseases, diabetes mellitus, non-alcoholic fatty liver disease, neurodegenerative diseases and cardiovascular diseases associated with persistent and low-grade systemic inflammation. Despite the absence of definitive evidence, a number of symptoms have been reported to exhibit a substantial improvement following *H. pylori* eradication [3].

4. Epidemiology of *H. pylori*

H. pylori infects approximately 44.3% of the global population according to recent meta-analysed systematic reviews [18,19]. According to studies, the disease agent is more common in developing nations than in developed ones, although reported infection rates differ by region. In fact, the prevalence of *H. pylori* infection in developing nations is 85–95%, which is much greater than in wealthy nations (30–50%) [20]. Similarly, compared to economically developed locations, *H. pylori* infection rates are higher in economically poor regions. Numerous factors, including financial class, population density, race, poor sanitation methods, and health conditions, might be blamed for this disparity [21]. The most likely routes of transmission of *H. pylori* are oral-oral and faecal-oral [22]. In underdeveloped countries, contaminated water can serve as a vector for the spread of infection. The presence of the bacterium in the saliva, faeces and vomit of infected individuals indicates the potential for transmission via these means [3]. Chronic smoking, insufficient vitamin supplementation, excessive daily salt consumption, and host variables can all change the stomach's acidic environment and make this population more vulnerable to *H. pylori* infection [20]. According to data on incidence worldwide, the highest rates of *H. pylori* are found in Libya, Egypt, Nigeria, and Bangladesh (over 90%), followed by Brazil, Bolivia, Saudi Arabia, Turkey, Russia, and India (80–90%), and China, Pakistan, Sri Lanka, and Liberia (70–80%) [23].

5. Diagnosis and Treatment of *H. pylori*

The bacterium has been living with humans for more than 100,000 years, and its symbiotic relationship with humans and its ability to be transmitted from person to person increases the risk of this bacterium [24,25]. Atrophic gastritis and intestinal metaplasia are two precancerous disorders that can be avoided by promptly diagnosing and then eliminating *H. pylori* in adults. This also eliminates inflammatory alterations in the gastric mucosa. However, the International Agency for Research on Cancer has classified *H. pylori* as a group I carcinogen since 1994 [26]. According to some reports, *H. pylori* colonization is not a disease in and of itself; rather, it is intimately linked to the emergence of stomach ulcers and gastric cancer [27]. The manifestation of this infection is contingent upon the bacterial strain, the host, and environmental factors. *H. pylori* has been demonstrated to stimulate infiltrated mononuclear and polymorphonuclear cells, thereby prompting the production of free oxygen radicals. These radicals have been shown to cause DNA damage in gastric epithelial cells, which can ultimately lead to the development of cancer [8].

Diagnostic methods used to detect *H. pylori* infections are generally classified as invasive and non-invasive. While non-invasive testing include immunological methods (serology, stool antigen test), the 13 C-urea breath test (UBT), and molecular approaches (PCR of stool with detection of *H. pylori* DNA in stool), invasive procedures necessitate investigation of gastric biopsies and upper endoscopic techniques [11,28].

In the treatment of *H. pylori*, triple therapy, comprising amoxicillin, clarithromycin and metronidazole antibiotics, in addition to a proton inhibitor, is utilised. In light of the escalating failure rate observed in clarithromycin treatments, there has been a notable shift towards the utilisation of levofloxacin-based triple therapies and bismuth-based quadruple therapies. Tetracycline and rifampicin are also among the antibiotics commonly used in the treatment of *H. pylori*. Nevertheless, the mounting resistance to antibiotics jeopardises the efficacy of eradication treatments [29]. For example, the resistance rate to clarithromycin increased from 15.6% in the early 2000s to 40.0% in the 2020s. Similarly, the metronidazole resistance rate has also shown an increasing trend, rising from 57.8% in the early 21st century to 77.5% in the 2020s [30]. Consequently, the quadruple therapy using bismuth salts, which has recently been employed for the treatment of the disease, is not appropriate for individuals with antibiotic resistance because it still contains antibiotics. Furthermore, the administration of antibiotics has been demonstrated to induce a range of deleterious effects on the human gastrointestinal tract, including, but not limited to, diarrhoea, anorexia, vomiting, abdominal distension and pain [31]. Antibiotic resistance has been identified as one of the most significant and growing challenges in the treatment of *H. pylori* infection in recent studies and current treatment guidelines. Significant reductions in susceptibility to commonly used antibiotics such as clarithromycin and metronidazole have been observed, and it has been reported that triple therapy

is no longer preferred in many regions [32]. Increases in resistance rates have been observed in many regions. Research conducted in Taiwan emphasised the need to consider geographical resistance. This study, carried out in Taiwan between 2019 and 2024, reported a marked increase in clarithromycin and levofloxacin resistance rates over the years [33]. Similar results to those obtained in the Taiwanese study have been reported in another study conducted in China. This Chinese study reported high levels of resistance to clarithromycin and metronidazole [34]. The emergence of resistance to key agents such as clarithromycin and metronidazole over the years and the resulting decline in eradication success rates necessitate different treatment approaches. Due to their anti-urease, anti-adhesion and virulence-reducing effects, the use of plant extracts as alternative treatments has become quite interesting in recent years. In this context, various studies have supported that phenolic compounds, flavonoids and certain volatile oil fractions can exhibit synergistic effects when used in combination with antibiotics. [20,35]. Since these results are laboratory-based, large-scale studies using accurate and standardized methods are needed to proceed to the clinical application stage. For example, probiotics and combination therapies have been reported in some studies to reduce side effects and be effective for treatment. However, these alone are not sufficient to replace standard treatments. For safety reasons, antimicrobial therapy is not advised for children, pregnant women, nursing mothers, or the elderly. As a result, the need for alternative treatments that can successfully treat *H. pylori* infection is growing. Probiotic and phytotherapy therapies may lessen the adverse effects of antibiotics and result in fewer resistant strains than antibiotic treatment. Additionally, probiotics and phytotherapy are beneficial dietary remedies [20]. Plant extracts rich in phenolic compounds, thanks to their natural antibacterial properties, provide an alternative treatment for patients in need of treatment.

6. Phytotherapy in *H. pylori* Treatment

From ancient times to the present, therapeutic compounds have been found in nature, and a remarkable number of contemporary medications have been derived from natural sources. Complementary and alternative treatment modalities based on plants, especially non-toxic, natural and inexpensive products, are becoming increasingly attractive [27]. The following factors make the use of phytotherapy—which includes active chemicals derived from plants—a significant substitute for conventional antibiotics in recent years: (i) plant extracts and the majority of plant-derived compounds work on several targets, producing a positive therapeutic effect; (ii) plant-derived compounds, which have a different mechanism of action from traditional antibiotics, show activity against bacteria that are resistant to drugs; and (iii) plant-based medications are considered safe as long as they are taken at the recommended dosage levels. Numerous plants with anti-*H. pylori* activity have been reported in the literature [8]. Sources from these plants have been found to have synergistic activity against bacteria in combination with many antibiotics, as well as when used individually. The word ‘synergy’ implies that the resulting effect of a combination of antimicrobial agents produces significantly greater therapeutic efficacy than the sum of the individual antimicrobial agents. For example, *Zingiber officinale* (ginger) extract and clarithromycin have been shown to have synergistic antimicrobial effects against *H. pylori* when administered together [36].

Active compounds commonly found in plant extracts are known to play an important role in the treatment of *H. pylori*. These include phenolic compounds such as simple phenols, polyphenols, flavonoids, quinones, coumarins, terpenoids, alkaloids [37]. Various mechanisms play a role in the use of plant extracts and active compounds obtained from plants against *H. pylori* treatment. For example;, *Calotropis procera*, *Camellia sinensis*, *Fagonia arabica*, *Acacia nilotica* and *Casuarina equisetifolia* extracts inhibit the growth of *H. pylori* by inhibiting urease enzyme activity. Extracts from the roots of *Glycyrrhiza glabra* have been shown to inhibit the activities of bacterial DNA gyrase and dihydrofolate reductase. The inhibition of DNA synthesis by blocking the activity of DNA gyrase and dihydrofolate reductase results in the death of bacterial cells. The compounds resveratrol and zerumbone, which are derived from Zingiberaceous plants and strawberries, grapes, and red wine, respectively, have been shown to decrease the urease enzyme activity and virulence factors of *H. pylori*. In addition to dihydrofolate reductase enzyme, some plants are also effective on myeloperoxidase N-acetyltransferase enzyme [8,38]. The potential effects of natural compounds such as plant extracts and essential oils against *H. pylori* have been investigated, and the findings of these studies are summarized in Table 4.

Table 4. Evaluation of herbal extracts used against *H. pylori*

Plant / natural product	Extract type	Study method	Reported effect on *H. pylori*	References
Juglans regia, Punica granatum	Methanolic extracts	Disc diffusion, MIC	Strong inhibition zones; dose-dependent antibacterial effect	[39]
Cuminum cyminum, propolis	Ethanolic extract	MIC determination	Significant antibacterial activity; potential adjunct agent	[40]
Bixa orellana, Ilex paraguariensis, Chamomilla recutita	Aqueous & alcoholic extracts	Disc diffusion	Several extracts showed inhibitory activity	[41]
Glycyrrhiza aspera, Ligustrum vulgare, Juglans regia	Crude extracts	Disc susceptibility	Broad-spectrum inhibition of H. pylori	[42]
Acanthus montanus, Ageratum conyzoides	Methanol extracts	MIC / MBC	Strong bactericidal effect in vitro	[43]
Canarium album extract	Fruit extract	Growth inhibition assay	Effective against resistant & sensitive strains	[44]

In addition, the antibacterial activity of 23 different Iranian medicinal plants against clinical isolates of *H. pylori* was investigated in vitro. The researchers proved that and Juglans regia and Punica granatum have remarkable anti-*H. pylori* activity with a mean inhibition zone diameter of 39 and 16 mm at 100 µg disc-1, respectively [39]. The antibacterial activity of different plant extracts was studied in one standard and 11 clinical isolates of *H. pylori* samples by means of disc diffusion test in solid media and determination of minimum inhibitory concentration (MIC) value. In this study, it was reported that herbal extracts, especially *Cuminum cyminum* L. and propolis, are new and reliable tools in the supportive treatment of *H. pylori* [40]. The antibacterial activity of plant extracts obtained from *Bixa orellana* L., *Ilex paraguariensis* A. St.-Hil., *Chamomilla recutita* L., *Plantago major* L., *Malva sylvestris* L., and *Rheum rhaponticum* L. was evaluated against two reference strains and eleven clinical isolates of *H. pylori* by disc diffusion test in agar and MIC value. The study revealed that *C. recutita* L., *B. orellana* L., *M. sylvestris* L. and *I. paraguariensis* A. St.-Hil. were able to inhibit the growth of *H. pylori* in vitro [41]. *Glycyrrhiza aspera*, *Ligustrum vulgare*, *Juglans regia*, *Trachyspermum copticum*, *Thymus kotschyanus* and *Xanthium brasilicum* plants had anti-*H. pylori* effect in disc susceptibility test [42]. Similarly, MIC and minimum bactericidal concentration (MBC) values of plant extracts of *Acanthus montanus*, *Ageratum conyzoides*, *Scleria verrucosa*, *Scleria striatinux*, *Lycopodium cernua*, *Emilia coccinea*, *Eryngium foetidium*, *Tapeinachilus ananassae*, *Aulutandria kamerunensis* and *Euphorbia hirta* were analysed against bacterial isolates by agar dilution method. According to the aforementioned study, *S. striatinux*, *A. conyzoides* and *L. cernua* showed very strong antibacterial activity on the isolates [43]. According to the study of Yan et al. [44], *Canarium album* Raeusch. fruit extracts have antibacterial potential on both antibiotic resistant and sensitive *H. pylori* strains.

Numerous plant extracts that are used to treat *H. pylori* have multiple uses. These plant extracts contain cytoprotective and anti-inflammatory qualities in addition to their anti-*H. pylori* activity. In order to minimize damage to gastric tissue, these extracts primarily work through three different mechanisms: (i) blocking NFkB nuclear translocation and the inflammatory cytokine production that follows; (ii) blocking *H. pylori*'s attachment to the gastric mucosa; and (iii) blocking the synthesis of proteases [8].

Table 5 summarizes in vitro studies showing how various plant extracts and natural products affect anti-*H. pylori* activity. It has been reported that these extracts alter anti-*H. pylori* activity through mechanisms such as urea suppression, growth inhibition, and membrane disruption. However, these findings are considered preliminary evidence and require sufficient and controlled human studies to proceed to clinical trials.

Table 5. In vitro studies with herbal extracts against *H. pylori*

Plant / natural product	Study design	*H. pylori* strains	Main anti-*H. pylori* findings	Reference
Juglans regia, Punica granatum	Disc diffusion, MIC	Clinical isolates	Strong inhibition: *Juglans regia* (39 mm), *Punica granatum* (16 mm)	[39]
Cuminum cyminum, Propolis	Disc diffusion, MIC	1 reference strain + 11 isolates	Significant antibacterial activity; potential adjunctive use	[40]
Bixa orellana, Ilex paraguariensis, Chamomilla recutita, etc	Disc diffusion, MIC	2 reference strains + 11 isolates	Several species inhibited *H. pylori* growth	[41]
Glycyrrhiza aspera, Ligustrum vulgare, Juglans regia, etc.	Disc susceptibility	*H. pylori* isolate	All listed plants showed anti-*H. pylori* effects	[42]
Acanthus montanus, Ageratum conyzoides, etc.	Agar dilution (MIC/MBC)	*H. pylori* isolate	Strongest activity: *S. striatinux, A. conyzoides, L. cernua*	[43]
Canarium album fruit extract	In vitro antibacterial test	Resistant & sensitive strains	Effective against both strain types	[44]

Table 6 shows clinical studies that include adjunctive approaches such as probiotics and cranberry polyphenols, which are natural and plant-derived products. Although it can be predicted that combining these supportive treatments with standard treatments may provide benefits, the lack of clinical evidence is noteworthy. Therefore, for alternative treatments to be applied for *H. pylori* eradication, it is important to prioritize clarifying the therapeutic value, optimal dosages, and long-term results of these treatments.

Table 6. Clinical studies on the effects of herbal and natural extracts against *H. pylori* infection

Population	Intervention	Comparator	Outcome	Reference
H. pylori–positive adults (double-blind RCT)	PPI + bismuth quadruple + probiotic	Quadruple therapy + placebo	Higher eradication rate and improved tolerability	[31]
H. pylori–positive adults (double-blind RCT)	Cranberry juice (polyphenol-rich)	Placebo drink	Reduced H. pylori positivity in a subgroup; eradication limited	[45]
Treatment-naïve *H. pylori* patients (RCT)	Berberine + amoxicillin + rabeprazole	Standard bismuth quadruple therapy	Non-inferior eradication with fewer adverse events	[46]

Note that only a limited number of clinical trials on herbal or natural adjunctive therapies exist. The studies listed represent the available human data. Considering the studies conducted, these herbal and natural extracts appear promising in the treatment of *H. pylori.* However, their clinical applicability remains limited due to pharmacological and formulation difficulties. Standardization of herbal products can be difficult due to their extraction methods, the compounds they contain, and the varying effects of different doses. In addition, many bioactive compounds have limited absorption. They may also exhibit poor bioavailability due to instability in the gastrointestinal system [47,48]. In addition, plant-drug interactions have not been sufficiently studied in the long term. Given these limitations, the need for better formulated standardized methods and doses for *H. pylori* and comprehensive clinical studies should be emphasized.

The potential use of many plant extracts and oils as alternatives against *H. pylori* can be attributed to several mechanisms. One of the most well-known mechanisms is said to be the neutralization of stomach acid by bacteria. The inhibition of urease activity, which helps prevent bacteria from surviving in the stomach environment, is also one of the first steps. Additionally, many components in plant extracts can limit tissue damage by preventing bacteria from adhering to stomach epithelial cells. A third mechanism could be that these components can disrupt the integrity of the bacterial membrane. When these data are evaluated, it can be said that these compounds have therapeutic value for *H. pylori* eradication.

7. Conclusion

Despite the extensive body of literature supporting the antibacterial properties of numerous plant extracts against *H. pylori*, further investigation into the potential of diverse herbal sources is imperative for several reasons. These include the emergence of antibiotic-resistant strains, the ineffectiveness and cost of antibiotic treatment alone, and the exploration of natural remedies for individuals with allergic sensitivities.

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