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Narrative Review

Bacteriostatic Potential of Ginger, Garlic, and Fennel Seeds Against Helicobacter Pylori

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ABSTRACT

Background: H. pylori infection is a global health concern associated with various gastrointestinal disorders. Conventional antibiotic treatments face challenges and side effects like antibiotic resistance, leads toward the exploration of alternative therapeutic options with minimum or no side effects.

Objective: This review explores the bacteriostatic potential of natural remedies, specifically ginger (Zingiber officinale), garlic (Allium sativum), and fennel seeds (Foeniculum vulgare), against Helicobacter pylori (H. pylori).

Methods: A comprehensive search was conducted in order to identify relevant studies investigating the impact of ginger, garlic, and fennel seeds on Helicobacter pylori. Databases including PubMed, and Google Scholar were systematically queried to ensure the therapeutic potential of ginger, garlic and fennel seeds against Helicobacter pylori.

Results: Ginger, with its bioactive compounds such as gingerol and shogaol, exhibits inhibitory effects on H. pylori growth through anti-adhesive, antibacterial, and immunomodulatory mechanisms. Garlic, rich in allicin and other active components, demonstrates antibacterial properties against H. pylori, showing promising effect in both preclinical and clinical studies. Fennel seeds, traditionally recognized for culinary purposes, reveal antimicrobial potential against H. pylori.

Conclusion: This review highlights the bacteriostatic potential of ginger, garlic, and fennel seeds against H. pylori. Comparative analysis suggests potential therapeutic effects, while methodological considerations and challenges indicate avenues for future research. The integration of natural remedies with conventional approaches may present novel strategies for H. pylori management.

Keywords: H. Pylori, Ginger (Zingiber officinale), Garlic (Allium sativum), Fennel seeds (Foeniculum vulgare), Gastritis, Bacteriostatic

INTRODUCTION

Helicobacter pylori (H. pylori) is the Gram negative bacterium that makes the colonies in the stomach lining and has been recognized as a major factor in the etiology of various gastrointestinal disorders. It was discovered in 1982 by Barry Marshall and Robin Warren, and has since been implicated in the development of gastritis, peptic ulcers, and even gastric cancer (1). Its ability to survive and replicate in the acidic environment of the stomach and evade the body's immune responses makes it a persistent and challenging pathogen to eliminate from the body (2). The prevalence of H. pylori infection is widespread, affecting a significant portion of the global population. It has long-term consequences that extend to more severe conditions such as gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma (3). The prevalence of *H. pylori* infection ranged from 18.9% to 87.7% globally in 2015, with an estimated 4.4 billion infected people (4). *H. pylori* infects more than 50% of the population in the world, and it is represented as one of the most common infections in human's body, usually influenced by poorer living conditions during childhood (5). By keeping in mind the fact of increasing antibiotic resistance and the side effects associated with conventional therapeutic approaches, there is a growing interest in exploring alternative and complementary strategies to manage H. pylori infection. As an example, almost all of the World Health Organization (WHO) regions now experiencing resistance rates to metronidazole,

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clarithromycin, and levofloxacin of more than 15% (6). Therefore, natural remedies derived from plants, herbs, and other sources have gained much attention because of their wide variety of secondary metabolites, such as terpenoids, tannins, flavonoids, alkaloids and have potential antimicrobial properties and minimal adverse effects (7,8). The health implications of H. pylori infection extend beyond the immediate symptoms of gastritis and peptic ulcers. Chronic infection has been linked to a range of systemic conditions, including cardiovascular diseases, iron deficiency anemia, vitamin B12 deficiency (pernicious anemia), and autoimmune thyroid diseases (9,10). Moreover, *H. pylori* increases the development of gastric cancer due to reduced ability of the infected cells to repair damaged DNA, because of the presence of specific bacterial virulence factors and chronic inflammatory responses especially the vacuolating cytotoxin-A and cytotoxin-associated gene-A, that damages the DNA of host cell (11, 12). Therefore, it may increase the genetic instability that progressively leads to mutations, deactivation of tumor suppressor genes and activation of oncogenes ultimately, increasing the risk of developing gastric cancer over long time (13). Therefore, the present review focuses on the multidimensional approaches to address this persistent bacterial infection.

Pathogenesis of *Helicobacter pylori*

This bacterium is attached to the surface receptors and mucin layer of gastric epithelial cells due to its forward movement of flagella and spiral shape. Moreover, H. Pylori is resistant to stomach acid due to its urease activity and its releases some toxic factors including vacuolating cytotoxin-A (vacA), cytotoxin associated gene-A (cagA), and lipopolysaccharides (LPS) into the cytoplasm of host cells that ultimately causes inflammation and chronic infection (14). Due to this, epigenetic alterations occurs in the gastric epithelium. According to the study, MGMT is the gene that encodes the DNA repair protein O-6-methylguanine methyl transferase, was found to be hyper methylated in patients with positive H. pylori infection, and this effect was moderately reversible after the bacterial eradication. Disrupted DNA repair during H. pylori gastritis, increases the further risk of mutagenesis in the infected gastric mucosa (15).

Furthermore, this infection also causes an oxidative stress, that plays a crucial role in changing the proliferation of epithelial cells, thereby, increasing DNA damage (16) and apoptosis (17). Along with it, the decreased levels of vitamin C resulting from the infection is also associated with the increase in pro-oxidative status. H. pylori also activates the number of transcription factors such as NF-KB and inflammatory cells such as T-cells and macrophages because of its toxic factors. These activated transcription factors, induce the expression of inflammatory cytokines interleukin-6 and 8, inflammatory regulators such as cyclooxygenase-2, reactive oxygen species, and chemokines (18).

Bacteriostatic Properties of Ginger (*Zingiber officinale*) Against H. pylori

Historically the root of ginger (*Zingiber officinale*) had been used for a wide range of digestive disorders such as severe dyspepsia, peptic ulcer, vomiting, and inflammatory diseases (19). Ginger exerts a lot of benefits, including antiulcer, antioxidant, anti-tumor, anti-inflammatory, and anti-bloating properties (20). Moreover, ginger has the variety of phenolic compounds including 6-shogaol, 6 gingerol, 8 gingerol, 10 gingerol, phenolic acids and their derivatives having an anti H. pylorus activity (21). Ginger rhizome powder exhibits a noteworthy composition with diverse bioactive compounds and nutritional elements. High levels of saponins, measured at 4.01 g/100g, contribute to the potential antimicrobial and anti-inflammatory properties associated with these bioactive compounds. In addition to the bioactive compounds, it contains dry matter 93.68%, moisture content of 6.32%, crude protein (8.52%), crude fiber (10.36%), ash (1.07%), ether extract (5.21%), and nitrogen-free extract (64.82%) revealed by its proximate analysis as represented in the Figure 1.

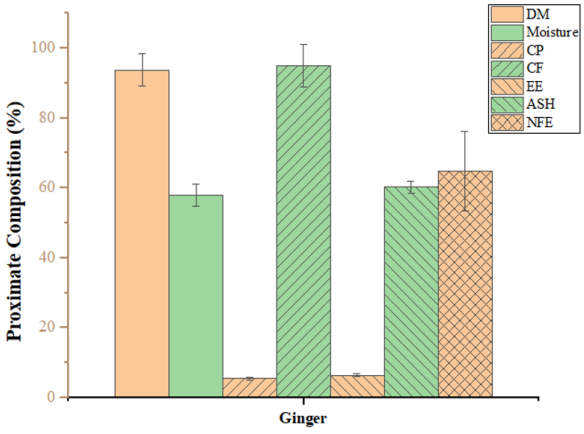

Figure 1. Proximate Composition of Ginger (*Zingiber officinale)*

According to a research study, ginger extract was orally administered by the rate of 100mg/kg body weight 3 weeks prior to the induction period of H. pylori infection in lab animals was proved to reduce the risk of infection by the bacteria. Along with it, the ginger extract could also significantly decrease the rate of ulcers, corrosion of stomach tissue, destruction of epithelial cells in the stomach, acute and chronic inflammation (22). Similarly, another pilot study was conducted by Attari *et al.,* (23), on 15 patients with positive H. pylori infection. They were fed with 3 grams per day ginger in the powder form for 4-weeks. Surprisingly, the results showed 53.3% eradication of H. pylori as (P = 0.019) and showed significant changes in the symptoms of dyspepsia after the

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administration of ginger supplementation. Another study conducted by Gaus *et al.,* (24), on rodent model (Mongolian gerbil) of H. pylori induced disease, to explore the effects of ginger extract on both the prevention and eradication of infection. The extract was administered at a daily dose of 100 mg per kg body weight in feed from three weeks before and 6 weeks after infection. At the end of the trial, results of the study proved that the ginger extract significantly inhibited the activity of COX-2, nuclear factor-κβ, tumor necrosis factor-α, interleukin (IL)-1β, IL-6, and IL-8 respectively. These results suggest that ginger extracts can be useful remedy for prevention and management of H. pylori-induced hyper-inflammation gastric cancer.

Table 1. Bacteriostatic Potential of Ginger Against H. pylori Induced Infection and Inflammation

Food Item	Study Model	Study Dose	Results	Citation
Ginger extract	Lab animals (H. pylori infection induction)	100mg/kg body weight, orally administered for 3 weeks prior to infection induction	Reduced risk of H. pylori infection, decreased ulcers, stomach tissue corrosion, destruction of epithelial cells, acute and chronic inflammation	WHO, (22)
Ginger (powder form)	15 patients with positive H. pylori infection	3 grams per day for 4 weeks	53.3% eradication of H. pylori, significant improvement in dyspepsia symptoms	Attari *et al.,* (23)
Ginger extract	Rodent model (Mongolian gerbil) of H. pylori-induced disease	100 mg/kg body weight daily, administered 3 weeks before and 6 weeks after infection	Inhibited activity of COX-2, nuclear factor-κβ, tumor necrosis factor-α, interleukin (IL)-1β, IL-6, and IL-8	Gaus *et al.,* (24)

Bacteriostatic Properties of Garlic (*Allium sativum*) Against H. pylori

From centuries, garlic has been used as a dietary component especially in meat gravies due to its sharp odor and it has also an important role in medicinal remedies (25). The proximate and phytochemical analysis of garlic content on a dry matter basis revealed that it comprises of 4.55% moisture, 73.22% carbohydrates, and 15.33% crude protein. Additionally, the garlic samples contained 0.72% crude fat, 2.10% crude fiber, and 4.08% ash as represented in the figure 2. In terms of essential minerals, garlic exhibited concentrations of 10.19 mg/100g potassium, 26.30 mg/100g calcium, 5.29 mg per 100g iron, 10.19 mg per100g phosphorus, 0.34 mg per 100g zinc, 0.001 mg per 100g magnesium, and 0.001 mg per 100g manganese. Notably, lead and cobalt were undetectable in the analysis. The pH of garlic was measured at 3.91, indicating its acidic nature. Furthermore, garlic contained 4.21 mg/100g of alkaloids, 3.54 mg/100g of tannins, 0.64 mg/100g of carotenoids, 0.80 mg/100g of saponin, 5.56 mg/100g of flavonoids, 0.04 mg/100g of steroids, and 0.02 mg/100g of cardenolides (26).

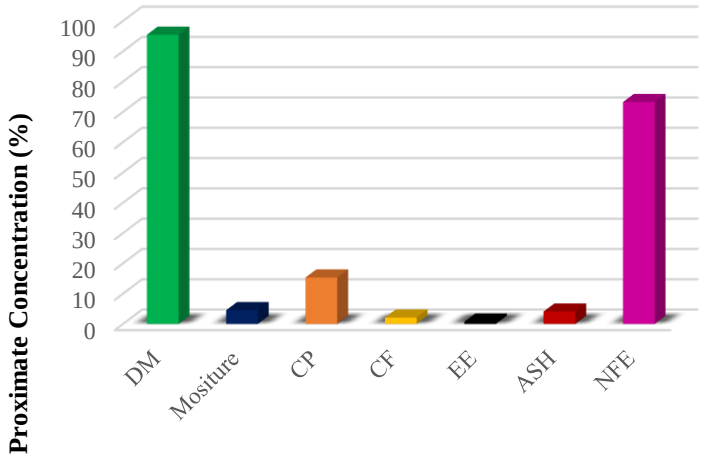

Figure 2. Proximate Composition of Garlic (*Allium sativum*)

Mainly its prophylactic and therapeutic effects are due to water soluble organo-sulfur compounds and specific oil, that are responsible for typical flavor and odor of garlic. During cutting or crushing of garlic cloves, an odorless amino acid known as alliin, is metabolized by an allinase enzyme to produce allicin & other thio-sulfinates, the major source of its sharp odor. Along with thiosulfinates, there are other secondary metabolites present in garlic, including scordinins, steroids, γ-glutamyl peptides, terpenoids, flavonoids, and other phenolic compounds, are responsible for wide range of therapeutic effects. Garlic is proved to be beneficial for the inhibition of *Aerobacter, Micrococcus, Mycobacterium, Aeromonas, Bacillus, Citrella, Citrobacter, Helicobacter pylori, Clostridium, enterobacter, Escherichia, Klebsiella, Lactobacillus, Leuconostoc, Providencia, Proteus, Pseudomonas, Salmonella, Serratia, Staphylococcus, Streptococcus, Shigella, and Vibrio* (27). Many studies showed that garlic (*Allium sativum*) has an anti-cancer, antibiotic, antioxidant properties and anti-inflammatory potential (28). Allicin increases the effectiveness of omeprazole and proton pump inhibitors used for the treatment of H. pylori infection in-vitro (29). The increased intake of garlic family vegetables has

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a positive effect in reducing the development of stomach cancer against H. pylori infection (30). According to a study conducted by Sivam *et al.,* (31) in order explore the antimicrobial activity of garlic. For this purpose, an aqueous extract of garlic cloves was checked for its antimicrobial activity against H. pylori, grown in the chocolate agar plates due to its thiosulfinates concentration and the minimum inhibitory concentration was 40 mcg thiosulfinates/ml. Results of the study demonstrated that H. pylori was susceptible to garlic extract because of its known thiosulfinate concentration. Similarly, another study conducted by Iimuro *et al.,* (32) on 6-week-old, specific pathogen-free male Mongolian gerbils. They were fed with 1%, 2%, and 4% garlic extract in the diet of gerbils for 6 weeks. At the end of the trial, the results demonstrated that garlic extract has significant effect on reduction of hemorrhagic spots and edematous thickening in the gastric mucosa, especially in the pylorus region of the stomach after administration of 4% garlic extract in the diet. Similarly, another study performed by Zardast *et al.,* (33), to evaluate the bacteriostatic effect of garlic against H. pylori infection. Initially, the patients were restricted from consuming an antibiotics or acid-reducing drugs, garlic or any product from alliums family. At the end of 3-day the quantitative urease breath test (UBT) was performed and recorded as control. After that 2 medium raw garlic cloves of 3 grams were administered to every patient two times per day with meals. At the end of the 3-day treatment course, quantitative urease breath test (UBT) counting was performed again and results demonstrated the reduced UBT count as compared to the control.

Table 2. Bacteriostatic Potential of Garlic Against H. pylori

Food Item	Study Model	Study Dose	Results	Citation
Aqueous extract of garlic cloves	H. pylori grown on chocolate agar plates	40mcg, standardized for thiosulfinate concentration	H. pylori susceptible to garlic extract	Sivam *et al.,* (31)
Garlic extract	6 weeks old, pathogen-free male Mongolian gerbils	Garlic extract in the diet by the ratio of 1, 2, 3%	Reduction in hemorrhagic spots and edematous thickening in the gastric mucosal linings, especially in the pylorus region upon administration of 4% garlic extract	Iimuro *et al.,* (32)
Garlic Cloves	15 patients with positive *H. pylori* infection	Two medium garlic cloves almost 3g in weight with meals 2 times a day	The mean Urease Breath Test (UBT) was significantly reduced after the consumption of garlic as compared to control group.	Zardast *et al.,* (33)

Bacteriostatic Properties of Fennel seeds (*Foeniculum vulgare*) Against H. pylori

Fennel seeds, derived from the flowering plant *Foeniculum vulgare*, are a popular spice and culinary ingredient having a distinctive licorice like flavor (34). Beyond the culinary properties, fennel seeds have been recognized for their potential health benefits historically. They have antioxidant properties, because they are rich in polyphenols and flavonoids. These antioxidants help to combat oxidative stress within the body. Moreover, fennel seeds have been used traditionally in the herbal medicine to address issues like bloating and indigestion (35). Proximate analysis of fennel seeds revealed that they have moisture 7.83%, crude protein 11.86%, ether extract 10.31% crude fiber 19.14%, ash 11.39% and nitrogen free extract 39.47% respectively. Moreover, fennel seeds have the best mineral profile including calcium, fennel seeds have 588.93 milligrams per 100 grams, potassium 409.64 milligrams, sodium 57.34 milligrams, Iron 0.94 milligrams, phosphorus 47.84 milligrams, magnesium, 19.44 milligrams, zinc 0.41 milligrams, and manganese 20.30 milligrams (36).

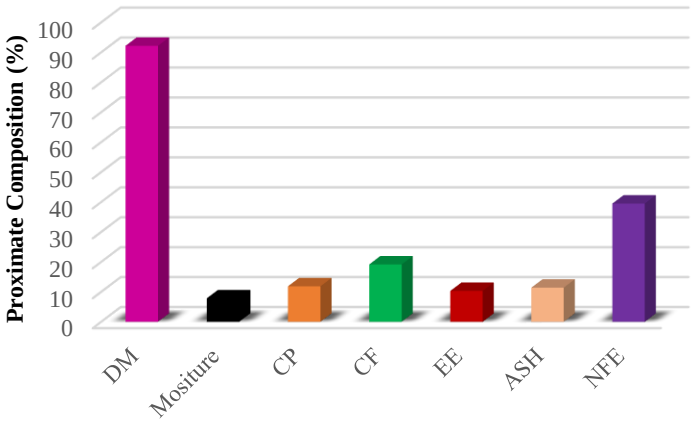

Figure 3. Proximate Composition of Fennel seeds (*Foeniculum vulgare*)

Essential oil present in the fennel has been widely recognized for its potent antimicrobial effects, exhibiting both antibacterial and antifungal activities. This is supported by various studies and scientific literature (37). Specifically, fennel seeds extract has been proved to have bacteriostatic effects against H. pylori (38). Jazani *et al.*, (39) reported that fennel essential oil exhibits antibacterial

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effects against Acinetobacter baumannii, a gram-negative bacterium. This finding suggests the broad-spectrum nature of fennel oil's antibacterial activity.

In a study conducted by Diao *et al.*, (40), the antibacterial efficacy of fennel seed essential oil was assessed using kill time assay techniques against various foodborne pathogens. The findings of this study demonstrated that fennel seed essential oil exhibited significant antibacterial activity against a range of pathogens commonly associated with foodborne illnesses. The pathogens inhibited by fennel seed essential oil included *Bacillus subtilis, Shigella dysenteriae, Staphylococcus albus, Escherichia coli* and *Pseudomonas aeruginosa, Salmonella typhimurium* with minimum inhibitory concentration of fennel seed essential oil with the lowest recorded concentration being 0.125 mg/mL. This indicates that even at relatively low concentrations, fennel seed essential oil demonstrated potent inhibitory effects against the tested bacteria. Another study conducted by Benabdallah *et al.,* (41) to investigate the gastro protective effects of the aqueous extract of *Foeniculum vulgare* and the results revealed its capacity to safeguard the stomach from lesions induced by 70% ethanol. Administering the doses of 200 mg per kg and 400 mg per kg resulted in notable gastro protection, with percentages of protection recorded at 55.54% ± 6.99% and 71% ± 3.09%, respectively. These findings underscore the potential of the aqueous extract of *F. vulgare* as a potent gastro protector, indicating its efficacy in mitigating ethanol-induced stomach lesions.

Table 3. Bacteriostatic Properties of Fennel seeds (*Foeniculum vulgare*)

Food Item	Study Model	Study Dose	Results	Citation
Fennel Seed Essential Oil	In vitro	0.125 mg/mL	Inhibition of Staphylococcus albus, Bacillus subtilis, Shigella dysenteriae, Pseudomonas aeruginosa, Escherichia coli, and Salmonella typhimurium	Diao *et al.*, (40)
Aqueous Extract of Foeniculum vulgare	In vivo (Animal Model)	200 mg/kg	Gastro protection: 55.54% ± 6.99% against lesions induced by 70% ethanol	Benabdallah *et al.,* (41)
Aqueous Extract of Foeniculum vulgare	In vivo (Animal Model)	400 mg/kg	Gastro protection: 71% ± 3.09% against lesions induced by 70% ethanol	Benabdallah *et al.,* (41)

CONCLUSION

In conclusion, the comprehensive exploration of ginger and garlic extracts, and antimicrobial properties of fennel seed's essential oil and the gastro protective effects of the aqueous extract of Foeniculum vulgare, presents a promising array of natural remedies in the context of Helicobacter pylori (H. pylori) infection and related gastric conditions. The studies collectively demonstrate the potential of ginger extract in significantly decreasing the risk of H. pylori infection and alleviating associated symptoms, as well as the effectiveness of garlic in inhibiting H. pylori growth and reducing inflammation in animal models. Fennel seed essential oil exhibits robust antibacterial properties against various pathogens, including H. pylori, and gastro protective effects. These findings collectively suggest that these natural extracts could serve as valuable resources for developing complementary and alternative approaches in the prevention and management of H. pylori-induced gastrointestinal issues. However, further research, clinical trials, and mechanistic studies are needed.

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