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REVIEW ARTICLE

Medicinal plants in the treatment of *Helicobacter pylori* infections

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Abstract

Context: *Helicobacter pylori* is a small, spiral, Gram-negative bacillus that plays a role in the pathogenesis of a number of diseases ranging from asymptomatic gastritis to gastric cancer. Schedule compliance, antibiotic drug resistance, and side-effects of triple or quadruple therapy have led to research for novel candidates from plants.

Objective: The purpose of this paper is to review the most potent medicinal plants of recently published literature with anti-*H. pylori* activity. For centuries, herbals have been used by traditional healers around the world to treat various gastrointestinal tract disorders such as dyspepsia, gastritis, and peptic ulcer disease. The mechanism of action by which these botanicals exert their therapeutic properties has not been completely and clearly elucidated. Anti-*H. pylori* properties may be one of the possible mechanisms by which gastroprotective herbs treat gastrointestinal tract disorders.

Materials and methods: Electronic databases such as PubMed, Google scholar, EBSCO, and local databases were explored for medicinal plants with anti-*H. pylori* properties between 1984 and 2013 using key words "medicinal plants" and "*Helicobacter pylori*" *or* "*anti-Helicobacter pylori*".

Results: A total of 43 medicinal plant species belonging to 27 families including Amaryllidaceae, Anacardiaceae, Apiaceae, Apocynaceae, Asclepiadoideae, Asteraceae, Bignoniaceae, Clusiaceae, Chancapiedra, Combretaceae, Cyperaceae, Euphorbiaceae, Fabaceae, Geraniaceae, Lamiaceae, Lauraceae, Lythraceae, Menispermaceae, Myristicaceae, Myrtaceae, Oleaceae, Papaveraceae, Plumbaginaceae, Poaceae, Ranunculaceae, Rosaceae, and Theaceae were studied as herbs with potent anti-*H. pylori* effects.

Conclusion: Traditional folk medicinal use of some of these plants to treat gastric infections is substantiated by the antibacterial activity of their extracts against *H. pylori*.

Keywords

Anti-*H. pylori*, gastric adenocarcinoma, gastroprotective herbs, peptic ulcer

History

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Introduction

Helicobacter pylori, a Gram-negative and microaerophilic bacterium, was identified in 1982 by Marshall and Warren (1984). It was shown that this organism is an important etiological agent of peptic ulcer disease and gastric neoplasia, including gastric adenocarcinoma and gastric mucosa-associated lymphoid tissue (MALT) lymphomas (Megraud & Lehours, 2007; Nakhaei Moghaddam, 2011).

Helicobacter pylori is a highly heterogeneous bacterial species, with a high degree of both genotypic and phenotypic heterogeneities, and is highly adapted for survival in the gastric niche. The genomic diversity of *H. pylori* parallels that of its host species, consistent with colonization of the earliest humans and co-migration out of East Africa at least 60 000 years ago (Dore et al., 1998; Linz et al., 2007). *Helicobacter pylori* causes a persistent infection and chronic inflammation in the majority of infected individuals. Following ingestion, the bacteria have to evade the bactericidal activity of the gastric luminal contents and enter the mucous layer. After infection, *H. pylori* cause acute gastritis characterized by neutrophil infiltration into the foveolar and surface epithelium and epithelial degenerative changes (Suerbaum & Michetti, 2002; Versalovic, 2003).

Despite advances in antimicrobial therapy, there is still no ideal treatment and indications for therapy continue to evolve (Suerbaum & Michetti, 2002). Increasing antimicrobial resistance, side effects, and falling eradication rates underline the importance of the updated guidelines on the management of *H. pylori*. Clinical practice evidence has revealed that eradication rates are in the range of 80–90%. For example, 14-d quinolone-containing triple therapies as a second-line therapy can provide a 90% *H. pylori* eradication rate (Tai et al., 2013). A randomized trial of standard triple therapy, 5-d concomitant, and 10-d sequential therapies for *H. pylori* in seven Latin American sites revealed that the eradication with standard therapy was 82.2% which was higher than the other therapies (Greenberg et al., 2011).

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Antimicrobial resistance has decreased eradication rates for *H. pylori* infection worldwide (Bytzer & O'Morain, 2005; Egan et al., 2008; Malfertheiner et al., 2007).

Plants have been used as medicines for thousands of years (Balunas & Kinghorn, 2005). Nature has been a source of medicinal agents since antiquity to date and an impressive number of modern drugs have been isolated from natural sources (Cragg & Newman, 2005). Isolation and biochemical characterization of pharmacologically active compounds from medicinal plants continue today (Soejarto et al., 2012).

Nowadays, for developing new potential anti-*H. pylori* candidates, scientists in the medicinal chemistry field are also equally concerned with the creation of new synthetic drug compounds (Foroumadi et al., 2008a,b, 2009a,b; Letafat et al., 2008; Mohammadhosseini et al., 2008, 2009; Moshafi et al., 2011; Tafti et al., 2011). Complementary and alternative modes of treatment, particularly non-toxic, natural, and inexpensive products are attractive. There are many studies on the antibacterial properties of vegetables and plant extracts. The focus of this review will be on those recent studied medicinal plants with potent anti-*H. pylori* activity.

Pathophysiology of *H. pylori*

The gastric mucosa is well protected against bacterial infections due to the acidic pH of the lumen, the production of mucus, and rapid epithelial cell turnover (Amieva et al., 2002). *Helicobacter pylori* is highly adapted to its unusual ecological niche in the human stomach, with a unique array of features that permit entry into the mucus, oriented swimming and multiplication in the mucus, attachment to epithelial cells, evasion of the immune response, and, as a result, persistent colonization and transmission (Suerbaum & Michetti, 2002).

Over 90% of the *H. pylori* bacteria are thought to remain in the deep portions of the mucus gel layer and in between the mucus gel layer and the apical surfaces of the gastric mucosal epithelial cells. The smaller proportion *H. pylori* adhere to the luminal surfaces of gastric epithelial cells (Chatterjee et al., 2012). *Helicobacter pylori* colonization itself is not a disease, but *H. pylori* infections are also strongly associated with the development of gastric ulcers and even stomach cancer. This infection depends on a variety of bacterial, host, and environmental factors that mostly relate to the pattern and severity of gastritis (Kusters et al., 2006).

Based on earlier documents, in response to *H. pylori* colonization of the antral mucosa, G endocrine cells in the distal antral region of the stomach are activated to release the hormone gastrin, which circulates and stimulates parietal cells in the corpus (body) region of the stomach to hypersecrete acid. This increased acid production is likely to play a key role in the pathophysiology of duodenal ulcer disease (el-Omar et al., 1995; McColl et al., 1998).

Recent studies have shown that *H. pylori* bacteria mainly release specific cytotoxins causing duodenal ulcer. Several infection-related factors of *H. pylori*, such as urease, catalase, lipase, adhesion molecules, cytotoxin-associated gene protein (CagA), a homologue of the *Bordetella pertussis* toxin secretion protein (picB) and vacuolating cytotoxin (VacA), associate to gastric mucosal surface, and the induction of disease (Chatterjee et al., 2012; Tummuru et al., 1995). All known gastric *H. pylori* species are urease positive (Solnick & Schauer, 2001). Urea is taken up by *H. pylori* through a proton-gated channel; its hydrolysis generates bicarbonate and ammonia, which help to neutralize gastric hydrochloric acid and protect the bacterium in the acidic environment of the stomach (Weeks et al., 2000). It appears that *H. pylori* infection damages the mucosal cells directly, and indirectly by enhancing the secretion of gastric HCl and reducing epithelial cell bicarbonate secretion, which ultimately leads to excessive diffusion of HCl into the mucosa, causing damage of the gastro-duodenal lining and leading to ulcer formation (Chatterjee et al., 2012; Konturek et al., 2001).

Treatment of *H. pylori*

Conventional treatment for *H. pylori* eradication therapy involves multiple drug short course therapy (Mahady et al., 2005). The most effective therapies of *H. pylori* infection require a minimum of two antibiotics in combination with a gastric acid inhibitor to ensure high eradication rates (Fukuda & Sakagami, 2004; Trust et al., 2001). With few exceptions, the most commonly recommended triple *H. pylori* regimen including a proton pump inhibitor (PPI), and a combination of amoxicillin and clarithromycin now provide unacceptably low treatment success (Graham & Fischbach, 2010; Selgrad et al., 2011). After the failure of standard triple therapy, a bismuth-containing quadruple therapy can be employed as a rescue treatment. The main reasons for eradication failure of *H. pylori* infection include factors such as the bacterial resistance to the commonly used antimicrobial agents, poor compliance, and rapid metabolism of PPI because of cytochrome P450 2C19 (CYP) 2C19 polymorphisms (Chuah et al., 2011).

In many European countries, second-line treatment with quadruple therapy combining bismuth, metronidazole, tetracycline, and a PPI is recommended (Egan et al., 2008). Unfortunately, bismuth salts are not available in all countries. The reason for this is the claim of side effects associated with the medication (Cavallaro et al., 2006; Malfertheiner et al., 2007). However, triple therapy and bismuth quadruple therapy are universal treatment used in the eradication of *H. pylori* and *H. pylori*-induced gastrointestinal disorders, but they often cause nausea, antibiotic resistance, recurrence, and other side effects (Chatterjee et al., 2012). Novel anti-*H. pylori* therapies include sequential therapy, concomitant quadruple therapy, hybrid (dualconcomitant) therapy in addition to bismuth-containing quadruple therapy (Chuah et al., 2011).

With the rising prevalence of resistance to antimicrobial agents, antibiotic resistance-based selection of therapy should be used in areas known to already have a prevalence of strains resistant to currently used antibiotics (Selgrad et al., 2011).

In addition, a permanent cure is not always possible and the treatment of *H. pylori* is not always effective, particularly in developing countries where re-infection from environmental sources is extremely common (Sullivan et al., 1990). Due to the high level of morbidity worldwide, and to the increasing prevalence of infection and antimicrobial resistance, much interest has been generated in the development of new non-toxic, antiulcer formulations from medicinal plants to treat *H. pylori*-induced infection (Mahady et al., 2005).

Helicobacter pylori and medicinal plants

Plants have been utilized as herbal medicines for thousands of years (Balunas & Kinghorn, 2005). By using medicinal chemistry, and combinatorial chemical and biosynthetic technology, novel natural product lead, as promising bioactive molecules, will be optimized on the basis of their biological activities to yield effective bioactive agents (Cragg & Newman, 2005).

In recent years, a number of studies have suggested that *H. pylori* infection can be suppressed through the use of medicinal plants. Some potent medicinal plants and structures of the isolated compounds from herbs that recently evaluated in the literature for the treatment or eradication of *H. pylori* are discussed below. This review was carried out by searching bibliographic databases such as PubMed, Google scholar, EBSCO, and local databases for studies reported between 1984 and 2013. These studies were mainly *in vitro* and a small number of studies were *in vivo* which are summarized in detail in Tables 1 and 2, respectively.

Acacia nilotica

Different parts of *A. nilotica* L. (Fabaceae) are traditionally used in folk medicine due to known antihyperglycemic, antimicrobial, molluscicidal, anti-hypertensive, and anti-platelet aggregation activities (Amin et al., 2013; Eldeen et al., 2005; Mahesh & Satish, 2008). According to the results of a recent study, hydroethanol extract of young seedless pods of *A. nilotica* has antiulcer activity in pylorus ligation, swimming stress, and non-steroidal anti-inflammatory drugs induced rat ulcer models (Bansal & Goel, 2012). The results of a study clearly revealed that methanol and acetone extracts of *A. nilotica* (flowers) showed stronger anti-*H. pylori* activity than metronidazole, and almost the same activity as tetracycline. However, activity was less potent than amoxicillin and clarithromycin. Methanol and acetone extracts of *A. nilotica* showed significant urease inhibitory activity by a competitive mechanism (Amin et al., 2013).

Alchornea triplinervia

The leaves and aerial parts of *A. triplinervia* (Spreng.) Muell. Arg (Euphorbiaceae) are commonly used in folk medicine for the cure of gastric disorders (Lima et al., 2008). Recently, the antibacterial (Calvo et al., 2010), anti-inflammatory (Lopes et al., 2010), antioxidant (Bonacorsi et al., 2013), antisecretory, gastroprotective, and anti-*H. pylori* effects (Lima et al., 2008) of this species were reported. *Alchornea triplinervia* methanol extract was found to display antibacterial activity against the standard strain of *H. pylori*. Also, the plant exhibited effective gastroprotective action with antibiotic effects since the pretreatment with methanol extract of *A. triplinervia* in ethanol-induced ulcer rats decreased the gastric injuries (Lima et al., 2008). In the other study, oral administration of the ethyl acetate fraction from *A. triplinervia* leaves accelerated the healing process in rats with acetic acid-induced gastric ulcers by promoting epithelial cell proliferation, increasing neutrophil number, and increasing mucus production (Lima et al., 2011).

Allium sativum

Allium sativum L. (Amaryllidaceae), commonly known as garlic, has extensively been used worldwide for centuries, due to its preventive characteristics in regulating blood pressure, cardiovascular diseases, lowering blood sugar and cholesterol levels, effective against bacterial, fungal, viral, and parasitic infections, enhancing the immune system and having antitumor and antioxidant features (Ayaz & Alpsoy, 2007). Garlic materials including garlic oil, garlic powder, allicin (allyl 2-propene thiosulfinate and their diallyl constituents), all showed substantial but widely differing anti-*H. pylori* effects against all strains and isolates tested. The MICs of diallyl tetrasulfide and allicin were lower than those of garlic oil, powder, and diallyl disulfide (O'Gara et al., 2000). The results of a study revealed that selenium-enriched garlic administration inhibits the development and progression of chronic gastritis induced by *H. pylori* (Gu et al., 2007). According to another study, long-term administration of garlic supplements has not reduced the prevalence of *H. pylori* infection (Gail et al., 2007). *In vivo* investigation on 10 subjects receiving garlic showed that garlic had no *in vivo* effect on *H. pylori* (Graham et al., 1999). Allitridi (diallyl trisulfide), a proprietary garlic derivative, showed a dose-dependent inhibitory effect on *H. pylori* growth (Liu et al., 2010).

Arrabidaea chica

Arrabidaea chica (Humb. & Bonpl.) B. Verl (Bignoniaceae) leaf extract has been used as an infusion to treat diseases such as gastric ulcers, intestinal colic, diarrhea, inflammation, infections, and anemia (Siraichi et al., 2013). The antioxidant (Siraichi et al., 2013), liver protective (Lima de Medeiros et al., 2011), and antimicrobial activity (Hofling et al., 2010) of this plant has been reported recently. Antimicrobial activity of hydroethanol extract of *A. chica* leaves was tested by the broth microdilution method using a panel of bacteria and yeast of clinical interest. The results demonstrated a pronounced activity against *H. pylori* (MIC = 12.5 μg/mL) (Mafioleti et al., 2013).

Bridelia micrantha

The hepatoprotective, antioxidant (Nwaehujor & Udeh, 2011), antimicrobial (Abo & Ashidi, 1999), and anticonvulsant activities (Ngo et al., 2012) of *Bridelia micrantha* (Hochst) Baill (Euphorbiaceae) have been reported. Different solvent extracts of *B. micrantha* were tested against 31 clinical and one standard strain of *H. pylori*. The acetone extract with 100% susceptibility and ethyl acetate extract with 93.5% susceptibility of strains were observed to be the most active, compared with other solvent extracts used in this study (Okeleye et al., 2011). Adefuye and Ndip (2013) showed that the ethyl acetate extract of the stem bark of *B. micrantha* can provide lead compounds for the treatment of infections caused by Gram-positive and Gram-negative organisms.

Calophyllum brasiliesnse

Calophyllum brasiliesnse Camb. (Clusiaceae) is a popular remedy employed in folk medicine for the treatment of several

Table 1. Thea *in vitro* anti-*H. pylori* studies on some medicinal plants.

Scientific Names	Family	Part/Extract	Anti-*H. Pylori* Activity	References
Acacia nilotica	Fabaceae	Acetone and methanol extracts of leaves and flowers	The acetone and methanol extracts of leaves exhibited almost a similar activity against clinical isolates. The acetone extract of flowers was found to be more active against *H. pylori* local isolates while methanol extract exhibited slightly lower activity MIC[a] of extracts from leaves: 8–128 μg/mL MIC of acetone extracts from flowers: 4–64 μg/mL MIC of methanol extracts from flowers: 8–64 μg/mL	Amin et al. (2013)
Alchornea triplinervia	Euphorbiaceae	Methanol extract of leaves	Methanolic extract of *A. triplinervia* presented excellent antimicrobial action against the standard strain of *H. pylori*. The results suggested that methanolic extracts from the leaves of *A. triplinervia* exhibited an antisecretory property and a gastroprotective action. However, the ethyl acetate fraction showed a more efficient gastroprotective effect than methanolic extract at a lower dose and the gastroprotective action occurred by increasing the prostaglandin E2 level MIC: 0.25 mg/mL	Lima et al. (2008)
Allium sativum	Amaryllidaceae	Garlic oil, garlic powder, and diallyl constituents	The effects of garlic oil, garlic powder, and their major allyl sulfur constituents, upon *H. pylori* cells were determined MIC range of garlic oil: 8–32 μg/mL MIC range of garlic powder: 250–500 μg/mL MIC range of diallyl disulfide: 100–200 μg/mL MIC range of diallyl tetrasulfide: 3–6 μg/mL MIC of allicin: 6 μg/mL	O'Gara et al. (2000)
Arrabidaea chica	Bignoniaceae	Hydroethanolic extract of the leaves	Hydroethanolic extract A. chica leaves was active against *H. pylori* clinical isolates. According to phytochemical analysis, the predominant presence of flavones and flavonols, possibly involved in the antimicrobial action of this plant extract MIC of hydroethanolic extract: 12.5 μg/mL	Mafioleti et al. (2013)
Bridelia micrantha	Euphorbiaceae	Acetone and ethyl acetate extracts of stem bark	Among five extracts, acetone, and ethyl acetate extracts were the most potent extracts against 32 strains of *H. pylori*. About 100% and 93.5% susceptibility were noted for the acetone and ethyl acetate extracts, respectively MIC_{50} range of ethyl acetate extract: 0.0048–0.156 mg/mL MIC_{50} range of acetone extract: 0.0048–0.313 mg/mL	Okeleye et al. (2011)
		Ethyl acetate extract of stem bark and eluted fractions	The antimicrobial activity of ethyl acetate extract from the stem-bark of *B. micrantha* that performed on Gram-positive and Gram-negative organisms including *H. pylori* revealed that this plant possess potent bioactive phytocompounds that may be developed into new antimicrobials MIC_{50} range of eluted fractions: 1.25–5 mg/mL	Adefuye and Ndip (2013)
Calophyllum brasiliesnse	Clusiaceae	Hydroethanolic extract and dichloromethanic fraction of stem bark	Hydroethanolic extract and dichloromethanic fraction of the stem bark showed the greatest activity and potency against *H. pylori* among the tested extracts and fraction of *C. brasiliesnse* MIC of hydroethanolic extract: 31 μg/ mL MIC of dichloromethanic fraction: 31 μg/ mL	Souza et al. (2009)

(*continued*)

Scientific Names	Family	Part/Extract	Anti-*H. Pylori* Activity	References
		Hexane extract and mixture of chromanone acids of stem bark	None of concentrations tested for the hydro-ethanolic extract and fraction containing a mixture of chromanone acids showed complete inhibition of bacterial growth. However, partial inhibitions of *H. pylori* growth were observed for a certain concentration range (25–400 μg/mL) IDZ[b] of hexane extract: 14 mm at 400 μg/mL IDZ of mixture of chromanone acids: 12 mm at 400 μg/mL	Lemos et al. (2012)
Calotropis procera	Asclepiadoideae	Acetone and methanol extracts of leaves and flowers	Both acetone and methanol extracts of leaves exhibited a similar activity against clinical isolates, while acetone extracts were active in the lower concentrations MIC range of extracts from leaves: 32–256 μg/mL MIC range of acetone extracts from flowers: 8–128 μg/mL	Amin et al. (2013)
Camellia sinensis	Theaceae	Methanol and water extracts of young shoots	Both non-fermented and semi-fermented extracts had inhibitory effects against *H. pylori* and urease production. A concentration of 4 mg/mL of non-fermented and 5.5 mg/mL semi-fermented extract were bacteriocidal for *H. pylori*. IDZ of non-fermented extracts: 22.5 mm at 4 mg/mL IDZ of semi-fermented extracts: 18 mm at 4 mg/mL	Shoae Hassani et al. (2009)
Chamomilla recutita	Asteraceae	Oil extract of flowers	The oil extract of *C. recutita* flowers exhibited anti-*H. pylori* activity. It was shown that the *C. recutita* oil extract influenced the morphological and fermentative properties of *H. pylori* and inhibited the production of urease by *H. pylori* MIC_{50} of oil extract: 62.5 mg/mL MIC_{90} of oil extract: 125.0 mg/mL	Shikov et al. (2008)
		70% aqueous methanol	According to data of other study 70% aqueous methanol extracts of C. recutita were active against one standard strain and 15 clinical isolates of *H. pylori* MIC range of aqueous methanol extracts: 0.625–>5 mg/mL	Stamatis et al. (2003)
Cinnamomum verum	Lauraceae	Essential oils of dry bark	*Cinnamomum* essential oil exhibited potent anti-*H. pylori* effect IDZ of essential oils: 24.8 mm at 0.5 μL/mL MIC of essential oils: 0.3 μL/mL	Hosseininejad et al. (2011)
		Commercial preparations of cinnamaldehyde	In the other study, cinnamaldehyde completely inhibited the growth of standard *H. pylori* strain in 12 h of incubation. Also, the growth of bacteria was completely inhibited in only 9 h when the MIC was doubled. At acidic pH, increased activity was observed for this compound MIC of cinnamaldehyde: 2 μg/ mL	Ali et al. (2005)
Cocculus hirsutus	Menispermaceae	Ethanol extract of leaves	The ethanol extract of C. hirsutus was found to be active against two *H. pylori* strains, but resistant against two other strains. The aqueous and acetone extracts of this plant showed no significant zone of inhibition against the tested *H. pylori* except one strain IDZ of ethanol extract: 2–24 mm at 1000 μg/mL	Poovendran et al. (2011)
Combretum molle	Combretaceae	Acetone extract of stem bark	Among five solvent extracts of C. molle that were screened against 32 clinical strains of *H. pylori* and a reference strain, the acetone extract was bactericidal with complete elimination of the test organisms in 24 h. The results demonstrated that *C. molle* may contain therapeutically	Njume et al. (2011)

(*continued*)

Table 1. Continued

Scientific Names	Family	Part/Extract	Anti-*H. Pylori* Activity	References
			useful compounds against *H. pylori*, which are mostly concentrated in the acetone extract MIC_{90} range: 1.25–5 mg/mL MIC range: 2.5–5 mg/mL	
Cuminum cyminum	Apiaceae	Ethanolic extracts of seeds	The ethanolic extracts of C. cyminum, among ethanolic or aqueous extracts from 17 plant materials, showed a significant *in vitro* effect against 11 *H. pylori* clinical isolates and 1 reference strain MIC_{90} range: 0.075–0.6 mg/mL	Nostro et al. (2005)
Cyrtocarpa procera	Anacardiaceae	Hexanic extract from stem bark	Among the five different polarity extracts (hexanic, CH_2Cl_2, CH_2Cl_2–MeOH, methanolic, and aqueous), the hexanic extract showed the highest inhibitory effect against *H. pylori* and the aqueous extract had the lowest activity. Anti-*H. pylori* activity of the five extracts was more effective than that of metronidazole MIC of hexanic extract: 7.81 μg/mL MIC of metronidazole: 300 μg/mL	Escobedo-Hinojosa et al. (2012)
Daucus carota	Apiaceae	Commercial preparation essential oil of carrot seed	The inhibitory effects of the carrot seed essential oil were determined after 1 h and 24 h of contact. A decrease in the pH from 7.4 to 4.0 (acidic conditions) resulted in a marked reduction in the minimal concentration required to completely inhibit *H. pylori* cell viability MBC[c] after 1 h: 0.5 mg/mL MBC after 24 h: 0.02 mg/mL MBC at pH 7.4: 0.75 mg/mL MBC at pH 4: 0.13 mg/mL	Bergonzelli et al. (2003)
Derris trifoliate	Fabaceae	Petroleum ether and chloroform extracts of stem	Different extracts (petroleum ether, chloroform, and methanol extracts) of D. trifoliate stem were tested against *H. pylori* isolate and selectively inhibited *H. pylori*. Petroleum ether and chloroform extracts exhibited strong activity against *H. pylori* MIC_{50} of petroleum ether: 1 μg/mL MIC_{90} of petroleum ether: 2 μg/mL MIC_{50} of chloroform extracts: 2 μg/mL MIC_{90} of chloroform extracts: 4 μg/mL	Uyub et al. (2010)
Desmostachya bipinnata	Poaceae	Methanolic extracts and ethyl acetate fraction of whole plant	Screening for anti-*H. pylori* activity of 18 wild Egyptian medicinal plant extracts revealed that the wild plant, D. bipinnata extract proved to be the most active one. After fractionation of this plant extract, ethyl acetate fraction which includes most of the flavonoids of the plant exhibited excellent anti-*H. pylori* activity MIC of methanol extract: 0.04 mg/mL MIC of ethyl acetate fraction:0.79 mg/mL MIC of 4-methoxy quercetin-7-O-glucoside: 0.062 mg/mL	Ramadan and Safwat (2009)
Dittrichia viscosa	Asteraceae	70% aqueous methanol	The extract of D. viscose has been proved active against one standard strain and 15 clinical isolates of *H. pylori* MIC range: 0.625 to > 5 mg/mL	Stamatis et al. (2003)
		Essential oil of aerial parts	The crude essential oil of D. viscose at a concentration of 0.33 μL/mL reduced the initial population of *H. pylori* of 8.52 ± 0.30 log 10 cfu/mL to 7.67 ± 0.22 log 10 cfu/mL The oxygenated fractions of the oil, mainly constituted by 3-methoxy cuminyl isobutyrate, revealed a higher activity against the six *H. pylori* strains	Miguel et al. (2008)

(*continued*)

Scientific Names	Family	Part/Extract	Anti-*H. Pylori* Activity	References
Eucalyptus torelliana	Myrtaceae	Hexane extract of leaves	Among *n*-hexane, chloroform, and methanol extracts of E. torelliana against six clinical isolates of *H. pylori*, the hexane extract of leaves demonstrated potent activity. Also the other extracts showed good activity MIC range: < 12.5–50 μg/mL	Adeniyi et al. (2009)
Eugenia caryophillus	Myrtaceae	Ethanol extracts of flowers	Among 30 herbal medicines, ethanol extracts from the flowers of *E. caryophyllata* exhibited strongest growth inhibitions against all the six test strains of *H. pylori* MIC of ethanol extracts : 40 μg/mL	Li et al. (2005)
		Commercial preparations of eugenol	According to results of the other study eugenol inhibited standard *H. pylori* strain totally in 9 h at 2 μg/mL and in 6 h at double the MIC. Eugenol revealed increased activity at acidic pH (pH 4.0) and a dose-dependant bactericidal activity was also observed. Eugenol was found to completely inhibit the bacteria at a concentration of double the MIC (4 μg/mL) in about 1 h of incubation at acidic pH MIC of eugenol: 2 μg/ mL	Ali et al. (2005)
Geranium wilfordii	Geraniaceae	Ethanol extracts and ethylacetate fraction	The ethanol and ethyl acetate fraction, corilagin, and 1,2,3,6-tetra-O-galloyl-b-D-glucose were found to be strongly inhibitory to a standard strain and five clinical isolates of *H. pylori* MIC of ethanol extracts: 40 μg/mL MIC of ethyl acetate fraction: 30 μg/mL MIC of corilagin: 4 μg/mL MIC of 1,2,3,6-tetra-*O*-galloyl-b-D-glucose: 8 μg/mL	Zhang et al. (2013)
Geum iranicum	Rosaceae	Aqueous fraction of the roots	The aqueous fraction was the most effective fraction of the extract against all clinical isolates of *H. pylori*. The subfraction which contained tannins was the effective subfraction. It appeared that tannins were probably the active compounds responsible for the anti-*H. pylori* activity of G. iranicum IZD of aqueous fraction: 24–35 mm at 100 μg/mL	Shahani et al. (2012)
Glycyrrhiza uralensis	Fabaceae	Methanol extract of roots and isolated licoricidin and licoisoflavone B	Methanol extract of *G. uralensis* has anti-*H. pylori* activity. Licoricidin and licoisoflavone B, chemical constituents of *G. uralensis*, exhibited inhibitory activity against the growth of *H. pylori* IDZ of methanol extract: 19 mm at 10 mg/mL MIC range of licoricidin: 6.25–12.5 μg/mL MIC of licoisoflavone B : 6.25 μg/mL	Fukai et al. (2002)
Hancornia speciosa	Apocynaceae	Hydroalcoholic extract of bark	Hydroalcoholic extract of *H. speciosa* displayed anti-*H. pylori* effect MIC: 125 μg/mL	Moraes et al. (2008)
Hydrastis canadensis	Ranunculaceae	Methanol extract of rhizome	The crude methanol extract of *H. canadensis* rhizomes was active against 15 strains of *H. pylori in vitro*. Two isoquinoline alkaloids, berberine and hydrastine, isolated from H. canadensis, inhibited the growth of *H. pylori* MIC_{50} of methanol extracts: 12.5 μg/mL MIC_{50} of berberine: 12.5 μg/mL MIC_{50} of hydrastine: 100 μg/mL	Mahady et al. (2003)
Mallotus phillipinesis	Euphorbiaceae	70% aqueous-ethanol extract of powder covering fruit	The 70% aqueous-ethanol extracts of *M. phillipinesis* demonstrated strong anti-*H. pylori* activity against seven clinical isolates and one reference bacteria MBC range: 15.6–31.2 μg/mL	Zaidi et al. (2009)
Myristica fragrans	Myristicaceae	Methanol extracts of seeds	Methanol extracts of *M. fragrans* (seed) inhibited the growth of 15 *H. pylori* strains. The results of this work	Mahady et al. (2005)

(*continued*)

Table 1. Continued

Scientific Names	Family	Part/Extract	Anti-*H. Pylori* Activity	References
			demonstrated *M. fragrans* which was used traditionally for the treatment of gastro-intestinal disorders that had a better MIC than metronidazole MIC: 12.5 μg/mL MIC range of metronidazole: 64–128 μg/mL	
		Methanol extracts of aril	Methanol extracts of *M. fragrans* (aril) inhibited the growth of all *H. pylori* strains MIC: 12.5 μg/mL	Bhamarapravati et al. (2003)
Myrtus communis	Myrtaceae	Essential oil	The essential oil of *M. communis* displayed clear activity against 10 clinical isolates of *H. pylori* that the majority were resistant to two or more antibiotics (metronidazole, clarithromycin, and levofloxacin) MIC: 0.075–2.5 (%, v/v)	Deriu et al. (2007)
Olea europaea	Oleaceae	Commercial preparations of olive leaf extract	The commercial extract derived from the leaves of *O. europaea* showed high activity against *H. pylori* strains. Also, olive leaf extract was found to be most active against *Campylobacter jejuni*. Given specific activity, olive leaf extract may have a potential role in beneficially altering the composition of the gastric flora by selectively reducing levels of *H. pylori* and C. jejuni MIC: 0.62% (% v/v).	Sudjana et al. (2009)
Persea americana	Lauraceae	Methanol extracts of leaf	Methanolic extracts of *P. americana* showed the high inhibitory effect on *H. pylori* standard strain. The extracts of this plant were noted to be more effective inhibitors as compared with reference antibiotic metronidazole MIC $<$ 7.5 μg/mL	Castillo-Juárez et al. (2009)
Phyllanthus niruri	Chancapiedra	Aqueous extracts of leaves	Water extracts of *P. niruri* showed anti-*H. pylori* activities and a dose-dependent trend was observed when four different concentrations of sample were tested IZD: 13 mm at 25 mg/mL IZD: 25 mm at 100 mg/mL	Ranilla et al. (2012)
Pistacia lentiscus	Anacardiaceae	Isolated pure triterpenic acids fraction	The acid fraction containing triterpenic acids were found to be the most active fraction against a panel of 11 *H. pylori* clinical strains MBC of acid fraction: 0.139 mg/mL	Paraschos et al. (2007)
		Mastic gum	The results of an evaluation of the antibacterial activity of *P. lentiscus* against a panel of clinical isolates of *H. pylori* revealed that it can kill 50% of the strains tested at a concentration of 125 μg/mL and 90% at a concentration of 500 μg/mL MIC_{50} of mastic gum: 125 μg/mL MIC_{90} of mastic gum: 500 μg/mL	Marone et al. (2001)
Plumbago zeylanica	Plumbaginaceae	Water, ethanol, acetone, and ethyl acetate of rhizome and radix	Excluding the water extract, higher anti-*H. pylori* activity was demonstrated for all the extracts of *P. zeylanica*. The ethyl acetate extract exhibited high anti-*H. pylori* activities followed, in ascending order, by the acetone, ethanol, and water analogs MIC of ethyl acetate extract: 0.32–1.28 mg /mL	Wang and Huang (2005a)
		Ethanol extract of stem	The ethanol extracts of P. zeylanica inhibited *H. pylori* growth. Among 50 Taiwanese folk medicinal plants, five plants had strong anti-*H. pylori* activity and 26 herbs were classified as moderate anti-*H. pylori* activity herbs MIC of ethanol extract: 0.64–10.24 mg/mL	Wang and Huang (2005c)

(*continued*)

Scientific Names	Family	Part/Extract	Anti-*H. Pylori* Activity	References
Potentilla fruticosa	Rosaceae	Aqueous extracts of herbs	Aqueous extracts from aerial part of nine *Potentilla* species have been evaluated against some bacterial and one fungal pathogen. The aqueous extracts of *P. fruticosa* and two other species showed the strongest antimicrobial activity against *H. pylori* MIC: 0.1 mg/mL	Tomczyk et al. (2008)
Prunus dulcis	Rosaceae	Polyphenol-rich extracts from natural almond skin	Almond skin extracts rich in flavonoids and three pure flavonoid compounds were evaluated on 34 strains of *H. pylori*, including two reference strains. Natural almond skin was the most effective compound against *H. pylori* followed by natural skin post gastric digestion, and natural almond skin post gastric plus duodenal digestion. Among the pure flavonoid compounds, protocatechuic acid showed the greatest activity against *H. pylori* strains MIC range of almond skin: 64–128 μg/mL MIC range of almond skin gastric digestion: 128–512 μg/mL MIC range of almond skin post-gastric plus duodenal digestion: 256–512 μg/mL MIC range of protocatechuic acid: 128–512 μg/mL	Bisignano et al. (2013)
Punica granatum	Lythraceae	Ethanolic extract of fruit rind	The ethanolic extracts of *P. granatum* significantly increased the hydrophobicity of *H. pylori* isolates. The ethanolic extract and semi-purified fractions of P. granatum demonstrated significant anti-*H. pylori* effects. MIC range of ethanolic extract: 0.78–6.25 mg/mL MBC range of ethanolic extract: 3.12–6.25 mg/mL	Voravuthikunchai et al. (2006)
		Methanol extract from peel of fruit	Among 23 Iranian plants, the extracts of *P. granatum* and *Juglans regia* had remarkable anti-*H. pylori* activity. In view of the results obtained with *P. granatum*, the peel extracts of nine cultivars of pomegranate were further assayed against the clinical isolates of *H. pylori*. Iranian pomegranate cultivars, except one of them, all showed significant *in vitro* anti-*H. pylori* activity against the clinical isolates of *H. pylori* IZD P. granatum: 39 ± 3.4 mm at 100 mg/disc IZD of cultivars of pomegranate: 16–40 mm at 50 mg/disc	Hajimahmoodi et al. (2011)
		Methanol extract and aqueous and butanol fractions from peel of fruit	Methanol extracts of pomegranate rind showed the highest inhibition against *H. pylori* clinical isolates. Aqueous and butanol fractions of pomegranate peel showed good activity on *H. pylori* clinical isolates. Chloroform fraction had no activity against tested *H. pylori* isolates IDZ of methanol extract: 27.96 ± 0.97 mm at 2 mg/disc MIC of aqueous fractions: 156 μg/mL MIC of butanol fractions: 195.12 μg/mL	Nakhaei Moghaddam (2011)
Salvia mirzayanii	Lamiaceae	Methanol extract of leaves	Among the 12 Iranian medicinal plants used in folk medicine for the treatment of gastric ailments including peptic ulcers disease *S. mirzayanii* was the most active plant, with strong antibacterial activity against 12 clinical isolates of *H. pylori* MIC: 32–64 μg/mL	Atapour et al. (2009)

(*continued*)

Table 1. Continued

Scientific Names	Family	Part/Extract	Anti-*H. Pylori* Activity	References
Sanguinaria canadensis	Papaveraceae	Methanol extracts of rhizome	The methanol extracts of *S. canadensis* rhizome inhibited the growth of 15 strains of *H. pylori in vitro*. Also, sanguinarine and chelerythrine, two benzophenanthridine alkaloids isolated from the rhizome extract of *S. canadensis*, inhibited the growth of the bacterium MIC_{50} of methanol extracts: 12.5 μg/mL MIC_{50} of Sanguinarine: 50 μg/mL MIC_{50} of Chelerythrine: 100 μg/mL	Mahady et al. (2003)
Scleria striatinux	Cyperaceae	Methanol extract of roots	Among the 10 plants extracts, the methanol extract of *S. striatinux* along with two other plants showed potent antibacterial activity on clinical isolates of *H. pylori* circulating in Cameroon MIC range: 0.032–1 mg/mL MBC range: 0.098–15 mg/mL	Ndip et al. (2007)
Stachys setifera	Lamiaceae	Methanol extracts of aerial parts	Stachys setifera among 10 species of *Stachys* and *Melia* showed the most potent anti-*H. pylori* activity on the 12 isolates. IZD: 38.3 at 8 mg/disc	Khanavi et al. (2008)
Terminalia chebula	Combretaceae	Aqueous extracts of fruit	Aqueous extracts of plant were significantly more active than ether and alcoholic extracts of fruit. The aqueous extract of *T. chebula* showed uniform antibacterial activity against 10 clinical strains of *H. pylori* MIC: 125 mg/L MBC: 150 mg/L	Malekzadeh et al. (2001)
Trachyspermum copticum	Apiaceae	Equal mixture of methanol/petroleum. Benzene/diethyl ether extract of aerial parts	Extracts of T. copticum showed anti-*H. pylori* activity against 70 clinical isolates from children. Over 93% of *H. pylori* isolates were sensitive to the extracts of *T. copticum* MIC range: 31.25–250 μg/mL	Nariman et al. (2004)
		Equal mixture of methanol/diethyl ether/petroleum benzene extract of fruit	Of the 20 plant extracts, analyzed for antibacterial effects, *T. copticum* and some other plants exhibited good anti-*H. pylori* activity MIC range: 31.25–125 μg/mL	Nariman et al. (2009)
Zataria multiflora	Lamiaceae	Essential oils of aerial parts	The essential oils of *Z. multiflora* demonstrated potent anti-*H. pylori* effect against clinical isolate of bacteria IDZ: 23.6 mm at 0.5 μL/mL MIC: 0.3 μL/mL	Hosseininejad et al. (2011)

[a]MIC represented minimum inhibitory concentration.
[b]IDZ represented inhibition diameter zones.
[c]MBC represented minimum bactericide concentration.

ailments including rheumatism, varicose, hemorrhoids, and chronic ulcers (Sartori et al., 1999). The activity against protozoans and human pathogenic yeasts (Albernaz et al., 2010), cancer chemopreventive properties, antifungal (Ruiz-Marcial et al., 2007; Suffredini et al., 2007), antisecretory, antiulcer (Sartori et al., 1999), gastroprotective (Reyes-Chilpa et al., 2006), and analgesic activities (da Silva et al., 2001) have been reported in different studies. Souza et al. (2009) evaluated the effects of various extracts of *C. brasiliense* stem bark, against *H. pylori in vivo* and *in vitro*. Among the tested products, the hydroethanol extract and dichloromethan fraction showed the greatest activity and potency against the *H. pylori* strains. In the *in vivo* assays, treatment with hydroethanol extract and dichloromethanic fraction reduced the ulcerated area in ulcerated rats inoculated with *H. pylori* in a dose-dependent manner (Souza et al., 2009). Lemos et al. (2012) showed a fraction containing a mixture of chromanone acids from *C. brasiliense* stem bark prevented the gastric ulceration caused by ethanol and indomethacin treatments due to reduction of malondialdehyde and catalase levels in the gastric tissue. However, partial inhibition of *H. pylori* growth was observed by a hexane extract and a mixture of chromanone acids, indicating that both fractions possess some anti-*H pylori* activity (Lemos et al., 2012).

Calotropis procera

Calotropis procera W.T. Aiton (Asclepiadoideae), with multifarious medicinal and biological properties (Yesmin et al., 2008), has traditionally been used for the treatment of leprosy, wound infections, tumors, inflammation, fever, and diseases of the spleen and abdomen (Amin et al., 2013; Lima-Filho et al., 2010; Mossa et al., 1991;

Table 2. The *in vivo* anti-*H. pylori* studies on some medicinal plants.

Study	Plant	Part	Results
Gu et al. (2007)	*Allium sativum*	Selenium-enriched garlic suspension	Selenium-enriched garlic suspension was administrated daily at different dosages in chronic gastritis induced Mongolian gerbils. Pathological examination 4 weeks after selenium-enriched garlic treatment showed that administration of this suspension inhibits the development and progression of chronic gastritis induced by *H. pylori* remarkably
Souza et al. (2009)	*Calophyllum brasiliesnse*	Hydroethanolic extract and dichloromethanic fraction of stem bark	Treatment with hydroethanol (50, 100, and 200 mg/kg) and dichloromethanic fraction (100 and 200 mg/kg), in the inoculated of *H. pylori* rats which are ulcerated with acetic acid, reduced the ulcerated area in a dose-dependent manner. Histopathological analysis revealed that none of the animals showed atrophy or metaplasia and groups treated with 100 and 200 mg/kg of hydroethanolic extract presented a decreased pathogen presence (71.5%, $p < 0.01$ and 88.9%, $p < 0.001$, respectively
Matsubara et al. (2003)	*Camellia sinensis*	Green tea extract	The gastritis and the prevalence of *H. pylori*-infected animals were suppressed in a dose-dependent manner in *H. pylori*-inoculated Mongolian gerbils which were given green tea extract in drinking water. Proportions of animals with bacterial infection were 32%, 36%, and 16% for the 500, 1000, and 2000 ppm of green tea extract. The reduction of infection edema and hemorrhage was statistically significant at 2000 ppm
Takabayashi et al. (2004)	*Camellia sinensis*	Green tea catechins	Solutions of green tea catechins adsorbed to sucralfate were administered daily, for 10 d to Mongolian gerbils infected with *H. pylori*. Green tea catechins in combination with sucralfate decreased the number of *H. pylori* in the stomachs of Mongolian gerbils
Ruggiero et al. (2007)	*Camellia sinensis*	Green tea concentrates	In *H. pylori* -infected mice, green tea mixture significantly prevented gastritis and limited the localization of bacteria and VacA to the surface of the gastric epithelium
Paraschos et al. (2007)	*Pistacia lentiscus*	Total mastic extract without polymer	Administration of total mastic extract without polymer to mice infected with the *H. pylori* SS1 strain over the period of 3 months with an average dose of 0.75 mg/d led to an approximately 30-fold reduction in the *H. pylori* colonization
Dabos et al. (2010)	*Pistacia lentiscus*	Pure mastic gum	A randomized controlled trial study revealed that 4/13 patients in group received 350 mg of pure mastic gum and 5/13 patients received 1.05 g three times a day achieved eradication, whereas no patient in group received pantoprazole 20 mg twice a day plus pure mastic gum 350 mg three times a day for 14 d achieved eradication

Perumal & Chow, 2012). The findings of the Amin et al. (2013) revealed that methanol and acetone extracts of *C. procera* showed stronger anti-*H. pylori* activity than metronidazole, almost comparable activity with tetracycline, but were found to be less potent than amoxicillin and clarithromycin. Lineweaver–Burk plots indicated a mixed type of urease inhibition for extracts of *C. procera* (Amin et al., 2013).

Camellia sinensis

Camellia sinensis L. (Theaceae) is a plant species whose leaves and leaf buds are the source of tea, the most common beverage in the world. There are several reports of *in vivo* and *in vitro* antibacterial effects of *C. sinensis* extracts (Hamilton-Miller, 1995; Toda et al., 1991). In 1994, Diker et al. showed extracts of black and green tea inhibited *in vitro* growth of six clinical isolates of *H. pylori* in an agar diffusion assay (Diker & Hascelik, 1994). The results of a study revealed the protective effect of green tea against stomach cancer (Setiawan et al., 2001). Recently, it has been shown that non-fermented and semi-fermented methanol:water mixture extracts of young shoots of *C. sinensis* can inhibit the growth of *H. pylori* and, in lower concentrations, inhibit the function and the production of enzyme urease that is a major colonization factor for this bacterium. The lower concentration of non-fermented extract was bactericidal for *H. pylori*. The superior activity of this extract is due to its rich polyphenolic compounds and catechin content. Decrease in *H. pylori* numbers and low urease production affect *H. pylori* colonization and, therefore, decrease the risk of chronic gastritis, peptic ulceration, MALT lymphoma, and gastric adenocarcinoma (Shoae Hassani et al., 2009). Green tea extract clearly suppresses *H. pylori*-induced gastric lesions in Mongolian gerbils (Matsubara et al., 2003). Oral administration of green tea catechins in combination with sucralfate in Mongolian gerbils infected with *H. pylori* revealed that the colony-forming units (CFU) of *H. pylori* was significantly decreased (Takabayashi et al., 2004). In line with these findings, another study revealed that green tea concentrates could influence gastric colonization or gastric pathology in *H. pylori*-infected or VacA-treated mice (Ruggiero et al., 2007).

Chamomilla recutita

Chamomilla recutita L. Rausch. (Asteraceae) is one of the most popular single ingredient herbal teas, or tisanes, used traditionally for several medicinal purposes as gastrointestinal tract ailments such as flatulence, nervous diarrhea, spasms, colitis, gastritis, and hemorrhoids (Rodriguez-Fragoso et al., 2008). Oil extract of *C. recutita* flowers was prepared by olive oil extraction using rotary pulsation. The oil extract demonstrates anti-*H. pylori* activity by inhibiting the reference strain. Moreover, that study found that urease production of *H. pylori* was inhibited by the *C. recutita* oil extract (Shikov et al., 2008). In another study, 70% aqueous methanol extracts of *C. recutita* have been proved active against one standard strain and 15 clinical isolates of *H. pylori* (Stamatis et al., 2003).

Cinnamomum verum (C. zeylanicum)

Cinnamomum verum Presl. (Lauraceae) is an efficacious remedy for the treatment of gastritis in traditional Iranian folk medicine (Arzani, 2005). *Cinnamomum verum* contains mainly cinnamaldehyde (61.57%) which is an aromatic aldehyde with an antimicrobial (Langeveld et al., 2014; Visvalingam et al., 2013) and antiviral activity (Ding et al., 2010). Cinnamaldehyde inhibited the growth of all the 30 *H. pylori* strains tested, at a concentration of 2 μg/mL, in the 12th h of incubation. The organism did not acquire resistance to this bioactive compound at subinhibitory concentrations (0.25 and 0.5 μg/mL) even after 10 passages (Ali et al., 2005). According to other studies, *H. pylori* strains acquired resistance to amoxycillin and clarithromycin after 10 sequential passages (DeLoney & Schiller, 2000). It should also be mentioned that *C. verum* can inhibit urease activity and prevent gastric upset (Nabati et al., 2012). Tabak et al. (1999) demonstrated that the methylene chloride extract of cinnamon is able to inhibit growth of *H. pylori*, while the ethanol extract counteracted its urease activity. According to results of a study, the essential oils of *C. verum* demonstrated potent anti-*H. pylori* effect against clinical isolates (Hosseininejad et al., 2011).

Cocculus hirsutus

Cocculus hirsutus L. (Menispermaceae) is a reputed medicine for the treatment of various common diseases in traditional and folk medicines (Jain et al., 2004). The nephroprotective properties (Gadapuram et al., 2013) and mosquito adulticidal activity against the malarial vector, *Anopheles subpictus* (Elango et al., 2011) have been reported. Ethanol extract and crude alkaloidal fraction have significant antimicrobial activity against Gram-positive and Gram-negative bacteria and the activity is found to be concentration dependent (Nayak & Singhai, 2003). The ethanol and acetone extracts have significant dose-dependent antimicrobial activity against *H. pylori* (Poovendran et al., 2011).

Combretum molle

The *Combretum molle* R. Br. Ex G. Don (Combretaceae) is popularly used in most African countries for the treatment of stomach pain, dysentery, gastric ulcers, abdominal disorders, and other illnesses (Eloff et al., 2008; Njume et al., 2011). The anthelmintic (Simon et al., 2012), antibacterial, and antifungal effects (Asres et al., 2006) of this plant have been proved. The susceptibility of 32 clinical isolates of *H. pylori* and a reference strain were evaluated against five solvent extracts of *C. molle*. Of these extracts, the acetone extract demonstrated remarkable activity against the test strains (Njume et al., 2011).

Cuminum cyminum

Cuminum cyminum L. (Apiaceae) has been used since antiquity for the treatment of various indications in traditional healing systems in wide geographical areas (Johri, 2011). Numerous investigations have revealed a potential antioxidant, antimicrobial, antifungal (Allahghadri et al., 2010; Hajlaoui et al., 2010; Iacobellis et al., 2005), and fumigant activity (Sousa et al., 2013; Yeom et al., 2012). In a study done on a *H. pylori* standard strain and 11 clinical isolates, *C. cyminum* extract displayed a significant *in vitro* effect. In particular, *H. pylori* multi-drug-resistant strains were inhibited at a concentration of 0.075 mg/mL of alcoholic extracts of *C. cyminum*. The resistant strains, when tested against this plant extract, expressed a similar profile to the other sensitive ones (Nostro et al., 2005).

Cyrtocarpa procera

Cyrtocarpa procera Kunth (Anacardiaceae) is used in Mexican folk medicine to treat digestive disorders such diarrhea and dysentery (Rosas-Acevedo et al., 2008). Animal experiments revealed the anti-ulcerogenic activity of *C. procera* bark extracts in an ethanol induced gastric ulcer model in rats (Rosas-Acevedo et al., 2011). Antibacterial activity of methanol extract against a range of Gram-positive (*Staphylococcus aureus, Staphylococcus epidermidis, and Bacillus subtilis*) and Gram-negative bacteria (*Vibriocholerae* and *Shigellaboydii*) have been reported (Canales et al., 2005). Anti-*H. pylori* activity of aqueous and methanol extracts of *C. procera* has been detected previously (Castillo-Juarez et al., 2009). In another study, the effects of five different polarity extracts of *C. procera* bark were evaluated against *H. pylori* standard strain. The results showed that a hexane extract exerts the highest inhibitory effect against *H. pylori* followed by dichloromethane extract (Escobedo-Hinojosa et al., 2012).

Daucus carota

Daucus carota L. (Apiacea) is traditionally used in different regions throughout the world for the treatment of gastric ulcer, diabetes, nephritic colic, cutaneous infections, and muscle pain (Jabrane et al., 2009; Shebaby et al., 2013). The *in vitro* anti-*H. pylori* properties of 60 different commercial essential oils were examined in a study. A marked inhibition of *H. pylori* viability was observed in bacteria treated with carrot seed oil. Carvacrol, isoeugenol, nerol, citral and sabinene as pure constituents of different tested essential oils exhibited the strong anti-*H. pylori* activities. Administration of carrot seed oil to *H. pylori* infected mice did not result in significant decreases in the bacterial loads in

the group of treated animals compared with those in the control group (Bergonzelli et al., 2003).

Derris trifoliate

Cytotoxicity of the roots and stems from *Derris trifoliate* Lour. (Fabaceae) against brine shrimp has been evaluated recently (Jiang et al., 2012). The results of a study which evaluated the antimicrobial activity of ethnobotanical Malaysian plants used for the treatment of gastrointestinal disorders and wounds revealed that organic solvent extracts of *D. trifoliata* inhibited *H. pylori*. Petroleum ether and chloroform extracts showed strong activity against metronidazole-resistant clinical isolates of *H. pylori* so that MIC values for the extracts ranged from 1 to 4 μg/mL. Anti-*H. pylori* tests showed that the extracts were effective at low concentrations. Toxicity at the concentrations inhibitory to most *H. pylori* may undermine its usefulness (Uyub et al., 2010).

Desmostachya bipinnata

Desmostachya bipinnata (L.) Stapf. (Poaceae) has been used by traditional healers to treat various disorders such as asthma, dysentery, diarrhea, and wound healing (Parveen et al., 2007; Singh et al., 2014). Antimicrobial screening of wild Egyptian medicinal plant extracts revealed that *D. bipinnata* have good anti-*H. pylori* activity. The result of antimicrobial testing of *D. bipinnata* fractions showed that the ethyl acetate fraction was the most active against *H. pylori*. A flavonoid compound, spectroscopically identified as 4′-methoxy quercetin-7-*O*-glucoside, was isolated from *D. bipinnata* extract and shown to possess good *in vitro* anti-*H. pylori* activity (Ramadan & Safwat, 2009).

Dittrichia viscose

In traditional pharmacopeia, several species of *Dittrichia viscose* (L.) Greuter (Asteraceae) have been used for different medical purposes (Mamoci et al., 2011). It has been reported that the extracts of *D. viscose* made with organic solvents possess antifungal and antibacterial activities (Cohen, 1996; Maoz et al., 1999). This species has been used for years in folk medicine for treating gastroduodenal disease (Alarcon et al., 1993; Miguel et al., 2008). In screening natural resources which are used traditionally in folk medicine against gastric ailments and peptic ulcer, the extracts of *D. viscose* and some other plants showed anti-*H. pylori* activity (Stamatis et al., 2003). Moreover, the essential oil and oxygenated fractions of the *D. viscosa* oil that is generally responsible for biological activities have been shown to inhibit the growth of *H. pylori in vitro* (Miguel et al., 2008).

Eucalyptus torelliana

Plants of the genus *Eucalyptus* (Myrtaceae), including *Eucalyptus torelliana* F. Muell, are used in Nigerian traditional medicine to treat respiratory infections (Lawal et al., 2012) and gastrointestinal disorders (Adeniyi et al., 2006). The extracts of the leaves of *E. torelliana* are reported to decrease gastric acid output and increase the pH of gastric juice, thus appear useful for the treatment of gastric ulcers (Adeniyi et al., 2006). As a follow-up to the gastroprotective activity of this plant, the *in vitro* susceptibility of six *H. pylori* strains to extracts of *E. torelliana* leaves were measured. The data of this work indicate that the hexane extract of the leaves showed the most potent activity against *H. pylori.* Anti-*H. pylori* properties of *E. torelliana* may be attributed to their chemical constituents such as tannins and saponins, which are known to possess antimicrobial potential and offer protection against ulcers (Adeniyi et al., 2009).

Eugenia caryophyllus

Eugenia caryophyllus Spreng. (Myrtaceae) oil has different biological activities (Merchan et al., 2011; Nunez et al., 2001) and has been used traditionally as a savoring agent and antimicrobial material in food (Nunez & Aquino, 2012). Among the 30 tested Chinese herbal medicines which are used traditionally for treating gastritis-like disorders, the ethanol extracts of *E. caryophyllus* were strongly inhibitory to all the six *H. pylori* strains (Li et al., 2005). Eugenol, the main component of *E. caryophillis* oil, is a phenolic compound and is proven to be active against many pathogenic bacteria (Laekeman et al., 2006; Xu et al., 2013), fungi (Laekeman et al., 2006), and viruses (Tragoolpua & Jatisatienr, 2007). In one study, eugenol completely inhibited all the strains (both sensitive and resistant) at a concentration of 2 μg/mL. Furthermore, the organism did not develop any resistance towards this compound even after 10 successive passages grown in sub-inhibitory concentrations (Ali et al., 2005).

Geranium wilfordii

Some *Geranium* species with antidiabetic, hemostatic, antihemorrhoidal, antidiarrheic, antioxidant, hepatoprotective, and antimicrobial activities are used for the treatment of pain, fevers, and gastrointestinal ailments (Boukhris et al., 2013; Radulovic et al., 2012; Sohretoolu et al., 2008). *Geranium wilfordii* Maxim (Geraniaceae) possessed antioxidant capacity and could be a rich source of natural antioxidants associated with the treatment of rheumatic disease (Gan et al., 2010). The plant has been widely used in Chinese herbal medicine for the treatment of gastrointestinal disease, diarrhea, and dysentery. The anti-*H. pylori* activity of the extracts of *G. wilfordii* and its main active compounds, corilagin and 1,2,3,6-tetra-*O*-galloyl-β-D-glucose, have been investigated. The ethanol and the ethyl acetate extract of *G. wilfordii* were found to be strongly inhibitory to *H. pylori*. The main anti-*H. pylori* active constituents of the active extracts include orilagin and 1,2,3,6-tetra-*O*-galloyl-β-D-glucose (Zhang et al., 2013).

Geum iranicum

The genus *Geum* (Rosaceae) is a perennial rhizomatous herb with five species in Iran of which *G. iranicum* Khatamsaz is an endemic one (Shahani et al., 2012). Some *Geum* species are used as medicinal plants in folk medicine. In Iranian folk remedy, the infusion of the root of *G. iranicum* is employed to treat gastrointestinal disorders like diarrhea, and a decoction of the whole plant is mixed with wheat flour and used as a

poultice for frostbite (Abutorabi, 2001). In one study, the activity of various extracts, sub-fractions, and main components of *G. iranicum* against clinical isolates of *H. pylori* (resistant to metronidazole) were evaluated (Shahani et al., 2012).

Glycyrrhiza uralensis

Licorice is the name applied to the roots and stolons of some *Glycyrrhiza* species such as *Glycyrrhiza uralensis* Fisch. (Fabaceae) and has been used for medicinal purposes since at least 500 BC (Nassiri Asl & Hosseinzadeh, 2008). It is felt that an extract of *G. uralensis* may be effective in the treatment of peptic ulcer disease (Aly et al., 2005; Nassiri Asl & Hosseinzadeh, 2008). Recently, antiinflammatory, antioxidative (Wu et al., 2011), immunomodulatory, and other biological activities of this plant were reported (Cheng et al., 2008; Li et al., 2010). Anti-*H. pylori* activities of chemical constituents of the different *Glycyrrhiza* species, and methanol extract and flavonoids of *G. uralensis*, were studied. Semi-purified fractions of *G. uralensis* exhibited different anti-*H. pylori* activities. Most flavonoids isolated from *G. uralensis* were active against *H. pylori* stains (Fukai et al., 2002).

Hancornia speciosa

Hancornia speciosa Gomez (Apocynaceae) traditionally have been used in folk medicine to treat skin diseases and inflammatory processes (Costa et al., 2008). This plant is frequently cited in ethnopharmacological inventories of the central region of Brazil against gastrointestinal disorders such as diarrhea, ulcer, gastritis, and stomachache (Moraes et al., 2008). The antifungal, antibacterial (Costa et al., 2008; Silva et al., 2011b), anti-inflammatory (Marinho et al., 2011), hypotensive (Silva et al., 2011a), and cancer chemoprevention effects (Endringer et al., 2010) have been reported recently. The hydroalcoholic extract exhibited anti-*H. pylori* effect and had the ability to prevent and heal rodent gastric ulcer. Hydroalcoholic extract decreased the severity of gastric damage induced by HCl/ethanol (52%), indomethacin/bethanechol (51%), stress (52%), or pylorus ligature experiments (54%) (Moraes et al., 2008).

Hydrastis canadensis

There is some justification in the scientific literature for the effectiveness of *Hydrastis canadensis* L. (Ranunculaceae) and its constituents as antidiarrheal and antimicrobial agents (Cybulska et al., 2011; Ettefagh et al., 2011; Junio et al., 2011). Traditionally, *H. canadensis* was used by the Iroquois for gastrointestinal issues (Junio et al., 2011). The crude methanol extract of the rhizomes of *H. canadensis* inhibited the growth of 14 clinical isolates and one ATCC strain of *H. pylori*. Berberine and β-hydrastine were the most active isoquinoline alkaloids in *H. canadensis* extract. Also, the results of the mentioned study revealed that these active isoquinoline alkaloids have antimicrobial activities (Mahady et al., 2003).

Mallotus phillipinesis

The fruit of *Mallotus phillipinesis* (Lam) Muell. (Euphorbiaceae) has long been used in the Chinese, Ayurvedic (Indian), Arabic, and Unani traditional medicine systems as an anthelminthic in man and animals (Jost et al., 1996). Other medicinal properties ascribed to this plant include cathartic, aphrodisiac, antifungal; antibacterial, anti-parasitic, antioxidant (Akhtar & Ahmad, 1992; Arfan et al., 2007; Kumar et al., 2006; Hussain et al., 2008). Zaidi et al. (2009) evaluated the anti-*H. pylori* activity of 50 commonly used traditional Pakistan medicines extensively utilized for the treatment of gastrointestinal disorders. Among the herbs evaluated, the most potent bactericidal activity was exhibited by *M. phillipinesis* which is comparable with amoxicillin minimum bactericide concentration (MBC) value (Zaidi et al., 2009).

Myristica fragrans

Myristica fragrans Houtt. (Myristicaceae) has played an important role in traditional medicine of some countries for the cure of stomach disorders (Mahady et al., 2005). The essential oil of *M. fragrans* is used for rheumatism, and as a carminative and postpartum medication (Olajide et al., 1999). The results of the *in vitro* screening of methanol extracts of 24 plant species, which have a history of traditional use in the treatment of gastrointestinal disorders, against 15 strains of *H. pylori*, revealed that the most active extracts were those of *M. fragrans* with an MIC of 12.5 μg/mL (Mahady et al., 2005). Previously, similar results were obtained in another study regarding the effects of Thai traditional medicine, which were used for the treatment of gastrointestinal ailments against 15 strains of *H. pylori* (Bhamarapravati et al., 2003).

Myrtus communis

Myrtus communis L. (Myrtaceae) has a long history of popular and traditional medicine in the world (Alem et al., 2008). The essential oils and extracts are gaining remarkable interest for their potential multipurpose use as an antioxidant (Amira et al., 2012; Serce et al., 2010), antibacterial (Appendino et al., 2006), antifungal (Cannas et al., 2013), and antiseptic (Cakir, 2004) agents. The effects of the essential oil of *M. communis* on the growth and survival of *H. pylori* were assessed and the results showed that the essential oil of this plant represented clear activity against clinical isolates of *H. pylori* (Deriu et al., 2007). In another study, *M. communis* extracts inhibited urease enzyme in concentrations less than 500 μg/mL (Nabati et al., 2012).

Olea europaea

Olive leaf extract is derived from the leaves of the olive tree (*Olea europaea* L. Cv. Cobrançosa Oleaceae) and marketed as a natural medicine with wide ranging health benefits (Sudjana et al., 2009). Olive leaf has been widely used in folk medicine for the cure of malaria and associated fever (Lee & Lee, 2010). The antiulcer activity (Sumbul, 2011), antioxidative, and antimicrobial properties (Lee & Lee, 2010; Pereira et al., 2007) of the *O. europaea* were experimentally confirmed in several studies. The commercial extract derived from the leaves of *O. europaea* against a wide range of microorganisms

was investigated. Olive leaf extract was found to be most active against *H. pylori* and some other microorganisms (Sudjana et al., 2009).

Persea americana

The leaves and fruits of *Persea americana* Mill. (Lauraceae) have been reported to possess anti-inflammatory, antimicrobial, cytotoxic, and insecticidal activities (Gomez-Flores et al., 2008; Oberlies et al., 1998). Methanol and aqueous extracts of 53 different plant species used in Mexican traditional medicine for gastrointestinal disorders were evaluated for their anti-*H. pylori* activity. Among them, the most active plant was methanol extract of *P. americana*, with MIC values of $<7.5\,\mu g/mL$. The aqueous extracts of plant exhibited no activity against *H. pylori* strain used in the study (Castillo-Juarez et al., 2009).

Phyllanthus niruri

Recently, hepatoprotective (Ho et al., 2012), antipyretic, anti-inflammatory, antinociceptive (Obidike et al., 2010), antiplasmodial (Mustofa et al., 2007), and antitumor activities by enhancing antioxidant defense (Sharma et al., 2011) have been reported for *Phyllanthus niruri* L. (Chancapiedra). In a screening test for the detection of plants with anti-*H. pylori* activity, *P. niruri* showed anti-*H. pylori* effects against metronidazole-resistant *H. pylori* strains (Uyub et al., 2010). The potential of aqueous extracts of the Amazon medicinal plant from Ecuador and Peru for antimicrobial activity against *H. pylori* was investigated. *Helicobacter pylori* was inhibited by both water extracts of *P. niruri* from Ecuador and Peru and a dose-dependent trend was observed when four different concentrations of sample were tested (25, 50, 75, and 100 mg of dried sample/mL) (Ranilla et al., 2012).

Pistacia lentiscus

Pistacia lentiscus L. (Anacardiaceae) has been referred to over the centuries as having medicinal properties to treat a variety of diseases such as gastralgia and peptic ulcers (Paraschos et al., 2012). *Pistacia lentiscus* resin known as ''Mastaki'' has traditionally been used in the treatment of gastritis in Iran (Akhawayni, 1965). *Pistacia lentiscus* at an oral dose of 500 mg/kg produced a significant reduction in the intensity of gastric mucosal damage on experimentally induced gastric and duodenal ulcers in rats. These observations support the effectiveness of mastic in the therapy of duodenal ulcer (Al-Said et al., 1986). The results of an evaluation of the antibacterial activity of *P. lentiscus* showed mastic gum can be effective against a panel of clinical isolates of *H. pylori* (Marone et al., 2001). There is the possibility that the ulcer-healing effect of mastic is due, at least in part, to the eradication of *H. pylori* (Gaby, 2001). Paraschos et al. (2007) showed that administration of total plant extract without polymer may be effective in reducing *H. pylori* colonization and that the major triterpenic acids in the acid extract may be responsible for such an activity. Also mastic extracts and isolated pure triterpenic acids were tested for *in vitro* activity against a panel of 11 *H. pylori* clinical strains. The acid fraction was found to be the most active extract (Paraschos et al., 2007). The results of a randomized controlled trial study showed mastic gum monotherapy could be effective as an alternative regime in patients unwilling to undergo eradication with the triple therapy regime (Dabos et al., 2010).

Plumbago zeylanica

Plumbago zeylanica L. (Plumbaginaceae) have been used as folk medicine in the treatment of rheumatic pain, dysmenorrhea, carbuncles, ulcers, and inflammation (Nguyen et al., 2004; Wang & Huang, 2005c). Antimicrobial (Jetty et al., 2010) and anti-cancer activities (Qiu et al., 2013) of this plant are presented recently. In a study that extracts from 50 Taiwanese folk medicinal plants were screened for anti-*H. pylori* activity, *P. zeylanica* ethanol extract demonstrated strong anti-*H. pylori* effects (Wang & Huang, 2005c). The authors used different extracts including water and the organic extracts, ethanol, ethyl acetate, and acetone to evaluate the anti-*H. pylori* activities of *P. zeylanica*. Among the four extracts, ethanol, acetone, and ethyl acetate extracts, which have a greater content of compounds with moderate polarity, exhibited relatively high anti-*H. pylori* activities. High stability was demonstrated for the ethyl acetate *P. zeylanica* extract in a wide range of pH (1–7), exhibiting all pH treatments bactericidal activity (Wang & Huang, 2005a). Plumbagin a naphthoquinone compound derived from *P. zeylanica* had anti-*H. pylori* activity, with MIC values in the range of from 0.02 to 0.16 mg/mL (Wang & Huang, 2005b).

Potentilla fruticosa

Potentilla species have been used for a long time in traditional medicine in Asia, Europe, and Northern America (Tomczyk et al., 2013). The aerial part of *Potentilla fruticosa* L. (Rosaceae) has been used to treat viral infections and impairment of the immune system in different regions of the world (Tomczyk & Latte, 2009). The protective effect on the liver (Kolpakov et al., 2001), as well as its antioxidant activity (Miliauskas et al., 2004) has been reported. In a study, the antibacterial and antifungal activities of aqueous extracts obtained from aerial parts of the selected *Potentilla* species were evaluated. Aqueous extracts of *P. fruticosa* and some other species such as *Potentilla grandiflora* L. and *Potentilla nepalensis* Hook. showed the strongest antimicrobial activity against *H. pylori* (Tomczyk et al., 2008).

Prunus dulcis (syn. *P. amygdalus*)

Prunus dulcis (Mill) D.A. Webb (Rosaceae), a rich source of nutrients and phytochemicals, are well documented for their biological effects, including anticancer, antiviral, anti-inflammatory, antioxidant, and antimicrobial activities (Amico et al., 2006; Mandalari et al., 2010, 2011; Takeoka & Dao, 2003). Bisignano et al. (2013) prepared polyphenol-rich extracts from natural almond skins and investigated the antimicrobial properties along with pure flavonoid compounds epicatechin, naringenin, and protocatechuic acid against *H. pylori* strains. Natural almond skin was found to be more effective against *H. pylori* followed by natural skin

post gastric digestion and protocatechuic acid, as a pure flavonoid compound.

Punica granatum

Punica granatum L. (Lythraceae) in traditional Iranian medicine has been used for the treatment of gastritis (Jorjani, 1998). The antibacterial, antiparasitic, antiviral, antioxidant, and anti-inflammatory effects have been reported for pomegranate peel (Bekir, 2013; Duman et al., 2009; Tayel & El-Tras, 2010). Also, the plant can minimize the problem of antibiotic resistance of *H. pylori* by increasing the cell surface hydrophobicity of *H. pylori* strains and inhibiting the attachment of the bacterium to the gastric mucosa (Voravuthikunchai et al., 2006). The evidence strongly suggests that *P. granatum* has a potential preventative effect on *H. pylori*-induced gastric disease by eradicating *H. pylori* as well as showing anti-inflammatory and anticancer effects (Rahimi et al., 2011). Repeated oral administration of 400 mg/kg of *P. granatum* significantly lowered the severity of ethanol-induced gastric damage (Alkofahi & Atta, 1999). Hajimahmoodi et al. (2011) showed a significant *in vitro* susceptibility of clinical strains of *H. pylori* to the extracts of several native Iranian pomegranate cultivars. The other study revealed that methanol extracts, butanol, and aqueous fractions of *P. granatum* were capable of inhibiting the *in vitro* growth of 27 clinical isolates of *H. pylori*. It is possible that some of anti-*H. pylori* activity of pomegranate peel is related to the presence tannin and phenolic compounds (Nakhaei Moghaddam, 2011).

Salvia mirzayanii

Decoctions of *Salvia mirzayanii* Rech. & Esfand. (Lamiaceae) have many supposed medicinal properties and are used in folk medicine for the treatment of digestive disorders such as stomachache (Soltanipoor et al., 2007). Several studies have shown the various biological activities of this plant including its antibacterial properties (Moshafi et al., 2004), immunoinhibitory effect (Ziaei et al., 2011), free radical scavenging, and antioxidant activity (Moein et al., 2008). In the screening of 12 Iranian medicinal plants, *S. mirzayanii* had the strongest activity against *H. pylori*, with a MIC of 32 μg/mL (Atapour et al., 2009).

Sanguinaria canadensis

Traditionally, extracts of *Sanguinaria canadensi* L. (Papaveraceae) was employed as homeopathic agents (Jaggi et al., 2004). It is known that sanguinarine, a benzophenanthridine alkaloid derived from the root of *S. canadensis*, performs a wide spectrum of biological activities such as antimicrobial (Obiang-Obounou et al., 2011) and anti-inflammatory effects (Bojjireddy et al., 2013). Native American Indians used hot water extracts of *S. canadensi* for the treatment of a variety of disorders including indigestion, dyspepsia, and gastritis. Experimental evidence has shown that methanol extracts of *S. canadensis* inhibited the growth of 15 strains of *H. pylori in vitro*. The constituent isoquinoline alkaloids, namely, sanguinarine, chelerythrine, and protopine, inhibited the growth of the bacterium with an MIC_{50} values of 50–100 μg/mL (Mahady et al., 2003).

Scleria striatinux

The antibacterial (Mbah et al., 2012) and antiplasmodial activity (Efange et al., 2009) of *Scleria striatinux* De Wild (Cyperaceae) have been reported recently. Ndip et al. evaluated the anti-*H. pylori* activity of 10 selected medicinal plant extracts from North West Cameroon on 15 isolates. Of these plants, *S. striatinux* showed potent antibacterial activity on the strains of *H. pylori*. The lowest MIC was 0.032 mg/mL recorded for this plant extract. The MIC values were found to be lower than the MBC (ranged from 0.098 to 15.0 mg/mL), suggesting that the *S. striatinux* extract was bacteriostatic at lower concentrations and bactericidal at higher concentrations (Ndip et al., 2007).

Stachys setifera

The genus *Stachys* is as a source of biologically active substances of various classes which are responsible for the broad spectrum of pharmaceutical–therapeutic action of plants of this genus and drugs prepared from them (Kartsev et al., 1994). Some species of this genus exhibited significant antibacterial activity (Skaltsa et al., 1999). Khanavi et al. (2008) showed that *Stachys satifera* C. A. MEYER. (Lamiaceae) exhibited potent anti-*H. pylori* activity on the strains isolated from patients.

Terminalia chebula

Terminalia chebula Retz. (Combretaceae) has been used in traditional Iranian medicine in southern and central parts of Iran as a remedy for human gastritis and peptic ulcers (Gharashi, 2008). The antioxidant (Cheng et al., 2003) antibacterial, antifungal (Jebashree et al., 2011), and antilithiatic activity (Tayal et al., 2012) of *T. chebula* has been reported recently. *Terminalia chebula* has a strong laxative effect and increases gastric emptying time. It seems that this action is balanced with a protective effect on the gastrointestinal mucosa, with the improvement in the secretory status of Brunner's gland involved in the protection against duodenal ulcer (Bag et al., 2013). Chebulinic acid isolated from *T. chebula* fruit has gastroprotective effect (Mishra et al., 2013). Water extracts of *T. chebula* showed significant antibacterial activity against *H. pylori*. Also, water extracts of the plant at a concentration of 1–2.5 mg/mL inhibited urease activity of *H. pylori* (Malekzadeh et al., 2001).

Trachyspermum copticum

The fruits of *Trachyspermum copticum* Link (Apiaceae) were used traditionally as carminative, diuretic, and antihelmentic (Mahboubi & Kazempour, 2011). The antibacterial activities of this plant (Mahboubi & Kazempour, 2011) have been shown. The results of six native Iranian plants screening introduced *T. copticum* as a strong *H. pylori* inhibitor (Nariman et al., 2004). Also, the crude organic (equal mixture of methanol, diethyl ether, and petroleum benzene) extracts of *T. copticum* fruit showed high activity against

H. pylori among the 20 Iranian plant extracts (Nariman et al., 2009). However, the results of other study showed that the methanol extract of the fruits of this plant had only very weak anti-*H. pylori* activity (Atapour et al., 2009).

Zataria multiflora

Zataria multiflora Boiss. (Lamiaceae) has been used for relief of gastric pains and irritable bowel syndrome in traditional medicine. The essential oil of the plant has shown high antioxidant and free radical scavenging effect *in vitro* and *in vivo* (Sharififar et al., 2007). The inhibitory effects of essential oil of *Z. multiflora* against wide range of Gram-positive and Gram-negative bacteria, fungi, and parasites have been reported (Azadbakht et al., 2003; Fazeli et al., 2007; Khosravi et al., 2008; Ravanshad & Dastgheib, 2007). The analysis of the plant essential oil showed the presence of thymol and carvacrol as major compounds of the oil (Sharififar et al., 2007). The antimicrobial activity of carvacrol and thymol, and its monoterpenic phenol isomer, has been reported (Didry et al., 1994). According to the Karimi-Zarchi and Babaei's study (2006), thyme-extracted juice with thymol showed anti-*H. pylori* activity.

In a study, among the plants from the Mint family which were tested and evaluated for inhibitory activity against some clinical isolates of *H. pylori*, total extracts of *Z. multiflora* were more effective (Ghannadi et al., 2004). The essential oil of *Z. multiflora* exhibited the most inhibition against *H. pylori* isolates in different tested concentrations (Hosseininejad et al., 2011).

Conclusion

There is a growing interest and need to find non-toxic, safe, and inexpensive anti-*H. pylori* formulations from medicinal plants. Ethnobotanicals that have been used traditionally for the treatment of gastrointestinal ailments could be useful lead to find selective and potent anti-*H. pylori* drugs. Some medicinal plants such as *C. verum, P. lentiscus, P. granatum*, and *T. chebula* have traditionally been used in the treatment of gastritis in Iran. It is concluded that the traditional folk medicinal use of these plants to treat gastric infections may be substantiated by the antibacterial activity of their extracts against *H. pylori*. Therefore, some medicinal plants evaluated for anti-*H. pylori* effects could have a more effective and less toxic therapeutic potential for the treatment of gastrointestinal diseases with *H. pylori* origin.

Isolation and characterization of the bioactive compounds could be a major focus in the anti-*H. pylori* drug discovery. Diallyl tetrasulfide and allicin from *Allium sativum*; polyphenolic catechins from *Camellia sinensis*; cinnamaldehyde from *Cinnamomum verum;* quercetin from *Desmostachya bipinnata;* 3-methoxy cuminyl isobutyrate of the oxygenated fractions from *Dittrichia viscose* essential oil; eugenol from *Eugenia caryophillis;* corilagin and 1,2,3,6-tetra-*O*-galloyl-β-D-glucose from *Geranium wilfordii;* tannins from *Geum iranicum;* licoricidin and licoisoflavone B from *Glycyrrhiza uralensis;* berberine and β-hydrastine from *Hydrastis Canadensis;* mastic and triterpenic acids from *Pistacia lentiscus;* plumbagin from *Plumbago zeylanica;* protocatechuic acid from *Prunus dulcis;* sanguinarine, chelerythrine and protopine from *Sanguinaria Canadensis;* and carvacrol, isoeugenol, nerol, citral, and sabinene from different essential oils are attributed to be responsible for anti-*H. pylori* properties of these plants. Further studies are needed to determine if the extracts are able to eradicate the bacteria in an *in vivo* infection model, and evaluation of the mechanism of action is a necessary issue.

Declaration of interest

The authors state that they have no conflict of interest and have received no payment in preparation of this manuscript.

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