***Helicobacter pylori* Outline**

**Introduction-Problem Statement**

*Helicobacter pylori* is a bacterium that has affected over half of the population in the world, primarily in developing countries. The bacterium *H. pylori* can infect an individual at any time and dependent on age and can be a determining factor of the type of infection. For example at a younger age, *H. pylori* will cause more intense inflammation followed by atrophic gastritis; it also gives a higher risk for gastric ulcer or cancer, or both. It has been seen to affect African-American and Hispanic populations greatly, which can possibly be attributed due to socioeconomic factors and limited resources. *H. pylori* can also lead to peptic ulcer and duodenal diseases dependent on the pH of the stomach. It is 2-7 times more likely that gastric cancer will develop if one is infected with this bacteria, contrary to someone who is not. (Wang 2015).

The problem with *H. pylori* is that it is able to adapt to antibiotics quit quickly due to cagA, a gene encoded on the cag pathogenicity island (cagPAI). CagA is a key virulence factor which initiates host cells NF-κB, MAPK, and SHP-2/ERK pathways to transcribe and translate inflammatory factors (COX-2, ICAM-1, iNOS, ROS) and pro-inflammatory cytokines (IL-6, IL-8, INF-γ, TNF-α). The genome plasticity is due to the transformation of conjugative transfer of genomic islands, which results in extensive polymorphic genes and differences in gene content among strains. (Vale 2015). VacA leads to osmotic force driving water influx and vesicle swelling, ultimately leading to vaculation (Wang 2015).



 If *H. pylori* is not eradicated completely with the antibiotics, then there is potential for the bacterial strain to become resistant to these antibiotics. Drug-resistant *H. pylori* and the adverse effects of antibiotics have weakened eradication therapy greatly. Antibiotics act to disturb gastrointestinal microflora; triple therapies have been performed, but sever complications such as liver and or kidney dysfunction have occurred. (Wang 2015). Due to side effects of drugs and antibiotic resistance, phytocomounds developed from plants are being investigated as a positive alternative. Since the phytocompounds use natural nutrients from plants, there has been no significant side effects.

Despite the fact that there is limited side effects to these methods, not many plants have been thoroughly studied with their antimicrobial effects on *H. pylori.* (Afr 2007).

**Active Plant Compounds Affecting *H. pylori***

The active compounds that have been reported for their anti-*H. pylori* activity include polyphenols, flavonoids, quinones, coumarins, terpenoids, alkaloids, and tannins. (Wang 2015). The following is a collaboration of compounds found from plants:

Anti-*Helicobacter pylori* activity of compounds from plants

| **Compound** | **Original plant** | **MIC/MBC** | **Ref.** |
| --- | --- | --- | --- |
| Phenolics/Simple phenols/Polyphenols |
| Boropinic acid | *Boronia pinnata* | MIC: 1.62 μg/mL | Epifano et al[[82](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B82)] |
| Sm. |
| Corilagin, 1,2,3,6-tetra-O-galloyl-b-D-glucose | *Geranium wilfordii* | MIC: 2-8 μg/mL | Zhang et al[[83](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B83)] |
| Egallic acid | *Rubus ulmifolius* leaves | MIC: 2-10 μg/mL | Martinia et al[[66](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B66)] |
| 3-Farnesyl-2-hydroxybenzoic acid | *Piper multiplinervium* | MIC: 3.75-12.5 μg/mL | Rüegg et al[[84](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B84)] |
| Epigallocatechin gallate, epicatechin gallate, epigallocatechin, |  | MIC: 8-256 μg/mL | Mabe et al[[85](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B85)] |
| epicatechin |  |  |  |
| Magnolol | *Magnoliae officinalis* | MIC: 10-20 μg/mL | Bae et al[[86](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B86)] |
| Psoracorylifols | *Psoralea corylifolia* | MIC: 12.5-25 μg/mL | Yin et al[[87](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B87)] |
| Resveratrol | Red wine | MIC: 25-100 μg/mL | Paulo et al[[88](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B88)] |
| Cinnamic acid |  | MIC: 80-200 μg/mL | Bae et al[[86](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B86)] |
| Allixin | *Allium sativum* | MIC90: 50 μg/mL | Mahady et al[[89](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B89)] |
| Paeonol, benzoic acid, methyl gallate, | *Paeonia lactiflora* Roots | MIC: 80-320 μg/mL | Ngan et al[[90](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B90)] |
| 1,2,3,4,6-Penta-O-galloyl-β-D-glucopyranose | MBC: 320-1280 μg/mL |
| Including 3-hydroxy-2,2-dimethyl-8-prenylchromane-6-propenoic | Brazilian propolis | MIC: 130-1000 μg/mL | Banskota et al[[91](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B91)] |
| acid 10 phenolic acids |  |  |  |
| Chlorogenic acid | *Anthemis altissima* | MIC: 312.5-1250 μg/mL | Konstantinopoulou et al[[92](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B92)] |
| Flavonoids |
| Quercetin 3-methyl ether, | *Cistus laurifolius* leaves | MIC: 3.9-62.5 μg/mL | Ustün et al[[93](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B93)] |
| quercetin 3,7-dimethyl ether, kaempferol 3,7-dimethyl ether |
| Kaempferol | *Rubus ulmifolius* leaves | MBC: 6 μg/mL | Martinia et al[[66](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B66)] |
| Kaempferol 4’-methyl ether, quercetin, rhamnetin, isoquercetrin, | *Anthemis altissima* | MIC: 6.25-50 μg/mL | Konstantinopoulou et al[[92](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B92)] |
| taxifolin, eriodictyol |  |  |  |
| Including licoisoflavone B and licoricidin 16 flavonoids | Licorice | MIC: 6.25-50 μg/mL | Fukai et al[[94](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B94)] |
| Cabreuvin | *Myroxylon peruiferum* | MIC: 7.8 μg/mL | Ohsaki et al[[57](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B57)] |
| 3,5,7-Trihydroxy-4’-methoxyflavanol, keampferol-3,4’-dimethyl ether | Brazilian propolis | MIC: 500-1000 μg/mL | Banskota et al[[91](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B91)] |
| Quinones |
| 2-Methoxy-1,4-naphthoquinone | *Impatiens balsamina* L. | MIC: 0.156-0.625 μg/mL | Wang et al[[95](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B95)] |
| MBC: 0.313-0.625 μg/mL |
| 2-(Hydroxymethyl)anthraquinone, anthraquinone-2-carboxylic acid, | *Tabebuia impetiginosa* | MIC: 2-8 μg/mL | Park et al[[96](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B96)] |
| Lapachol, plumbagin | Martius ex DC |  |  |
| Idebenone, duroquinone, menadione, juglone, benzoquinone, |  | MIC90: 0.8-25 μg/mL | Inatsu et al[[97](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B97)] |
| coenzyme Q1, coenzyme Q10, decylubiquinone |  |  |  |
| Emodin | Rhei Rhizoma | MIC86-99: 250 μg/mL | Wang and Chung[[98](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B98)] |
| Coumarins |
| Benzoyl aegelinol, aegelinol | *Ferulago campestris* (Apiaceae) roots | MIC: 5-25 μg/mL | Basile et al[[99](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B99)] |
| 24 Synthetic coumarin derivatives |  | MIC: 10-40 μg/mL | Jadhav et al[[100](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B100)] |
| 23 Synthetic coumarin derivatives |  | MIC50: 23->100 μg/mL | Kawase et al[[101](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B101)] |
| Terpenoids |  |  |  |
| Arjunglucoside I | *Pteleopsis suberosa* | MIC: 1.9-7.8 μg/mL | De Leo et al[[102](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B102)] |
| Trichorabdal | *Rabdosia trichocarpa* | MIC: 2.5-5 μg/mL | Kadota et al[[103](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B103)] |
| Sivasinolide, altissin, 1-epi-tatridin B, desacetyl-β-cyclopyrethrosin, | *Anthemis altissima* | MIC: 12.5-50 μg/mL | Konstantinopoulou et al[[92](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B92)] |
| tatridin-A |  |  |  |
| (Z)-R-santalol (7), (Z)-β-santalol, (Z)-lanceol | *Santalum album* | MIC: 7.8-31.3 μg/mL | Ochi et al[[104](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B104)] |
| Stigmasta-7,22-diene-3β-ol | *Impatiens balsamina* L. | MIC: 20-80 μg/mL | Wang et al[[95](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B95)] |
| MBC: 20-80 μg/mL |
| Plaunotol | Plau-noi | MIC90: 12.5 mg/mL | Koga et al[[105](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B105)] |
| Terpinen-4-ol | *Sclerocarya birrea*(Anacardiaceae) | MIC50: 0.004-0.06 μg/mL | Njume et al[[106](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B106)] |
| Alkaloids |
| 1-Methyl-2-[(Z)-8-tridecenyl]-4-(1H)-quinolone, | *Evodia rutaecarpa* fruits | MIC: < 0.05 μg/mL | Hamasaki et al[[107](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B107)] |
| 1-Methyl-2-[(Z)-7-tridecenyl]-4-(1H)-quinolone |  |  |  |
| Tryptanthrin | *Polygonum tinctorium* Lour. | MIC: 2.5 μg/mL | Hashimoto et al[[108](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B108)] |
| Other compounds |
| Pyrrolidine | *Sclerocarya birrea*(Anacardiaceae) | MIC50: 0.05-6.3 μg/mL | Njume et al[[106](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B106)] |
| Diallyl disulfide, diallyl trisulfide, diallyl tetrasulfide, allicin |  | MIC: 3-100 μg/mL | O’gara et al[[109](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B109)] |
| MBC: 6-200 μg/mL |
| Palmitoyl ascorbate |  | MIC: 40-400 μg/mL | Tabak et al[[110](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B110)] |
| Capric acid, lauric acid, myristic acid, myristoleic acid, |  | MBC: 0.5-5 mmol/L | Sun et al[[111](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B111)] |
| palmitoleic acid, linolenic acid, monolaurin, monomyristin |  |  |  |

MIC: Minimum inhibitory concentration; MBC: Minimum bactericidal concentration.

In one study it was shown that ethanolic extracts show a higher efficacy than essential oils due to their anti-mutagenic properties (Wei 2010).

 **Anti-*H. pylori a*ction mechanisms**

The action mechanism that show anti-*H. pylori* action mechanisms include the inhibition of enzymatic and adhesive activities, high redox potential, and hydrophilic/hydrophobic nature of compounds. Inhibition of enzymatic activity includes urease, DNA gyrase, dihydrofolate reductase, N-acetyltransferase, and myeloperoxidase. These mechanisms have all been discussed in detail (Wang 2015).

**Anti-*H. pylori* Medicinal Plants**

There are many natural products that have anti-*H. pylori* induced inflammation activity and have relevant mechanism that allow for the suppression of nuclear factor- κB and mitogen-activated protein kinase activation and inhibition of oxidative stress (Wang 2015). Some plant products that have been seen to reduce these effects include quercetin, apigenin, carotenoids-rich algae, tea product, garlic extract, apple peel polyphenol, and finger root extract. In one research review, 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. (Safavi 2015). In another study (medicinal plants) 80 plant species had been investigated and their MIC (minimum inhibition concentration) was taken to show their impact on *H. pylori.*  The following is a table showing plant species with anti-*H. pylori* properties:

Anti-*Helicobacter pylori* activity of medicinal plant extracts and fractions

| **Plant** | **Test sample** | **MIC/MBC** | **Ref.** |
| --- | --- | --- | --- |
| Strong activity (MIC: < 10 μg/mL) |  |  |
| *Impatiens balsamina* L. | Pod acetone/95% ethanol/ | MIC: 0.625-2.5 μg/mL | Wang et al[[52](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B52)] |
| ethyl acetate extracts | MBC: 1.25-2.5 μg/mL |
| Strong-moderate acticity (MIC: 10-100 μg/mL) |
| *Persea americana, Annona cherimola, Guaiacum coulteri, Moussonia deppeana* | Methanol extract | MIC: 7.5-15.6 μg/mL | Castillo-Juárez et al[[53](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B53)] |
| *Myristica fragrans (seed), Rosmarinus officinalis* (rosemary leaf ) | Methanol extract | MIC: 12.5-25 μg/mL | Mahady et al[[54](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B54)] |
| *Curcuma amada* Roxb., *Mallotus phillipinesis* (Lam) Muell., *Myrisctica fragrans* Houtt.,*Psoralea corylifolia* L. | 70% Ethanol extract | MIC: 15.6-62.5 μg/mL | Zaidi et al[[55](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B55)] |
| *Achillea millefolium, Foeniculum vulgare* (seed), *Passiflora incarnata* (herb), *Origanum majorana* (herb) and a (1:1) combination of *Curcuma longa* (root), ginger rhizome | Methanol extract | MIC: 50 μg/mL | Mahady et al[[54](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B54)] |
| *Carum carvi* (seed), *Elettaria cardamomum* (seed), *Gentiana lutea* (roots), *Juniper communis*(berry), *Lavandula angustifolia* (flowers), *Melissa officinalis* (leaves), *Mentha piperita* (leaves),*Pimpinella anisum* (seed) | Methanol extract | MIC: 100 μg/mL | Mahady et al[[54](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B54)] |
| *Abrus cantoniensis, Saussurea lappa, Eugenia caryophyllata* | Ethanol extract | MIC: 40 μg/mL | Li et al[[56](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B56)] |
| *Hippophae rhamnoides, Fritillaria thunbergii, Magnolia officinalis, Schisandra chinensis, Corydalis yanhusuo, Citrus reticulata, Bupleurum chinense, Ligusticum chuanxiong* | Ethanol extract | MIC: 60 μg/mL | Li et al[[56](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B56)] |
| *Myroxylon peruiferum* | Methanol extract | MIC: 62.5 μg/mL | Ohsaki et al[[57](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B57)] |
| Weak-moderate acticity (MIC: 100-1000 μg/mL) |
| *Aristolochia pauciner6is* | Rhizome/leave fraction | MIC: 4-128 μg/mL | Gadhi et al[[58](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B58)] |
| *Cistus laurifolius, Spartium junceum, Cedrus libani, solstitialis, Momordica charantia, Sambucus ebulus, Hypericum perforatum* | Solvent extract and hexane fraction | MIC: 1.95-250 μg/mL | Yeşilada et al[[59](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B59)] |
| *Larrea divaricate Cav* (leaves and tender branches) | Aqueous extract | MIC: 40-100 μg/mL | Stege et al[[60](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B60)] |
| *Acacia nilotica* (L.) Delile, *Calotropis procera* (Aiton) | Methanol/acetone extract | MIC: 8-256 μg/mL | Amin et al[[61](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B61)] |
| W.T. Aiton, *Fagonia arabica* L., *Adhatoda vasica* Nees, *Casuarina equisetifoli*a L. |
| *Zingiber officinale* | 95% Ethanol extract | MIC: 10-160 μg/mL | Nostro et al[[62](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B62)] |
| *Tephrosia purpurea* (Linn.) Pers. | Methanol extract and fraction | MIC: 25-400 μg/mL | Chinniah et al[[63](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B63)] |
| *Terminalia macroptera* (*root*) | Root solvent fraction | MIC: 100-200 μg/mL | Silva et al[[64](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B64)] |
| Black myrobalan (*Teminalia chebula* Retz) | Water extract | MIC: 125 μg/mL | Malekzadeh et al[[65](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B65)] |
| MBC: 150 μg/mL |
| *Rubus ulmifolius leaves* | Ethyl acetate/methanol | MIC: 134-270 μg/mL | Martinia et al[[66](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B66)] |
| *Amphipterygium adstringens* | Bark petroleum ether fraction | MIC: 160 μg/mL | Castillo-Juárez et al[[67](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B67)] |
| *Lycopodium cernuum* | Hexane fraction | MIC: 16-1000 μg/mL | Ndip et al[[68](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B68)] |
| MBC: 125-1000 μg/mL |
| *Ageratum conyzoides, Scleria striatinux, Lycopodium cernua* | Methanol extract | MIC: 63-1000 μg/mL | Ndip et al[[69](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B69)] |
| MBC: 195-15000 μg/mL |
| *Sclerocarya birrea* | Acetone/aqueous stem bark extract | MIC: 80-2500 μg/mL | Njume et al[[70](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B70)] |
| Including *Artemisia ludoviciana subsp.mexicana* 43 plants | Methanol/aqueous extract | MIC: 312-500 μg/mL | Castillo-Juárez et al[[53](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B53)] |
| *Pteleopsis suberosa* | Stem bark methanol extract | MIC: 313-500 μg/mL | Germanò et al[[71](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B71)] |
| *Ageratum conyzoides, Scleria striatinux, Lycopodium cernua* | Methanol extract | MIC: 32-1000 μg/mL | Ndip et al[[69](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B69)] |
| *Including Cuminum cyminum L., Cynara scolymus L., Origanum vulgare L*. 17 plants | Ethanol extracts | MIC: 600-10000 μg/mL | Nostro et al[[72](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B72)] |
| *Allium sativum* | Aqueous extract | MIC: 2000-5000 μg/mL | Cellini et al[[73](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B73)] |
| Weak acticity (MIC: > 1000 μg/mL) |
| *Mentha* × *piperita*, Peppermint Oil, *Origanum vulgare, Pimpinella anisum*, Aniseed Oil,*Syzygium aromaticum* | Essential oil | IC50: 160-1460 μg/mL | Cwikla et al[[74](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B74)] |
| *Chamomila recutita* L., *Ilex paraguariensis* A. St.-Hil. | 96% Ethanol extract | MIC: < 625-1250 μg/mL | Cogo et al[[75](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B75)] |
| *Allium ascalonicum* Linn. (leaf) | Methanol extract | MIC: 625- 1250 μg/mL | Bolanle et al[[76](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B76)] |
| Sclerocarya birrea | Stem bark acetone/aqueous extracts | MIC90: 60-2500 μg/mL | Njume et al[[70](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B70)] |
| *Punica granatum, Quercus infectoria* | Ethanol extract | MIC: 160-> 2500 μg/mL | Voravuthikunchai et al[[77](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B77)] |
| *Mentha* × *piperita*, Peppermint Oil, *Origanum vulgare, Pimpinella anisum*, Aniseed Oil,*Syzygium aromaticum* | Essential oil | IC50: 160-1460 μg/mL | Cwikla et al[[74](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B74)] |
| Including *Anthemis melanolepis* 13 plants | 70% Methanol extract | MIC: 625-5000 μg/mL | Stamatis et al[[78](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B78)] |
| Including *Cuminum cyminum* L. 17 plants | Ethanol extract | MIC: 75-10000 μg/mL | Nostro et al[[72](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B72)] |
| *Plumbago zeylanica* L. | Acetone extract | MIC: 320-10240 μg/mL | Wang and Huang[[79](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B79)] |
| MBC: 5120-81920 μg/mL |
| *Anisomeles indica* (L.) O. Kuntze, *Alpinia speciosa* (Wendl.) K. Schum., *Bombax malabaricum*DC., *Paederia scandens* (Lour.) Merr. | 95% Ethanol extract | MIC: 640-10240 μg/mL | Wang and Huang[[80](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B80)] |
| *Allium sativum* | Aqueous extract | MIC: 0.1% (v/v) | Cellini et al[[73](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B73)] |
| Including *Cymbopogon citratus* (lemongrass) 13 plants | Essential oil |  | Ohno et al[[81](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4130844/#B81)] |

MIC: Minimum inhibitory concentration; MBC: Minimum bactericidal concentration.

Anti-*Helicobacter pylori* studies have been performed in many places around the world such as Mexico, Pakistan, Iran, India, and the United States. In an Iranian study four plants by the names of Mirtus communis, Teucrium polium, Achillea millefolium and Thymus vulgaris extracts were used to monitor the eradication of clarithromycin susceptible *H. pylori*. The eradication rate was 97.4%, 95.2%, 63.7% and 19.6% respectively. (Tadjrobehkar 2015). In the past different eradication regimens such as triple therapy were used as recommended first-line attempts of *H. pylori* treatment but were not nearly as effective. (Malfertheiner 2012). That is why this study and other phytocomounds treatments against *H. pylori* are important to be studied.

**In vivo studies:**

There have been studies done both in-vitro and in-vivo for few medicinal plants that have anti-*H. pylori* properties. One in-vivo study been performed was done with extracts of tea catechins on Mongolian gerbils. This study showed a 10%-36% reduction of *H. pylori* and a significant decrease in gastric mucosal injury. (Mabe 1999) On another study of Mongolian gerbils, it was shown that Kaempferol and tryptanthrin showed significant decrease in *H. pylori*. (Katoka 2001). In a study done with Quercetin, a flavonoid that is present in fruits and vegetables widely, there was decreased neutrophil leukocyte infiltration, *H. pylori* colonization and lipid peroxide concentration in the pylori nitrium. (Gonzalez 2008). Algae meal of extracts from Cholorococcum used the compound carotenoid-rich acetone to decrease the *H. pylori* density, the INF-y and IL-4 levels in splenocytes and the *H. pylori-*induced inflammation in mice with the gene BALB—c was effectively inhibited. (Liu 2003). In another study a garlic ethanol extract was sown to decrease hemorrhagic spots in glandular stomach and gastritis scores as well as decreased stomach weight, which could be useful in fighting *H. pylori.* (Jimuro 2002).In a 4-week study on C57BL6-J mice, apple peel polyphenol was shown to significantly decrease pylori colonization, gastritis scores and malondialdehyde levels in the animals. (Jimuro 2002). On the other hand when finger-root turmeric rhizome with 96% ethanol extracts were given to Mongolian gerbils, the turmeric extract only reduced chronic inflammation scores without anti-acute inflammation effects. (Mahady 2006). This could be due to the solution that it was prepared with. In another study it was found that when extracts mixed with hexane and the same extracts mixed with acetone, there was a significantly different MIC shown. Depending on the plant species the MIC was different for each plant species. (Guzeldag 2014).

In a study measuring the anti-inflammatory effects of Pakistani medical plants in *Helicobacter pylori*-infected gastric epithelial cells showed promising results. (Zaidi 2012)

 Inhibitory IL-8 secretion:

Alpinia galangal, Cinnamomum cassia, Cinnamomum tamala, Mentha arvensis, Myrtus communis, Oligochaeta ramose, Polygonum bistorta, Rosa damascena, Ruta graveolens, Syzygium aromaticum, Tamarix dioica, and Terminalia chebula

 Reactive Oxygen Specie inhibition:

Chillea millefolium, Berberis aristata, Coriandrum sativum, Foeniculum vulgare, Matricaria chamomilla and Prunus domestica

**In vitro studies**

Contrary to in-vivo studies, many in-vitro studies have been performed. Here is a list published by Takeuchi about natural foods and products possessing anti-*Helicobacter pylori* potential. (Takeuchi 2014):

| **Food** | **Putative active component** | **Stage of experiment** | **Ref.** |
| --- | --- | --- | --- |
| Bovine milk | Lactoferrin | *In vitro*, *in vivo*(animal) | [4-10] |
| *in vivo* (human) |
| Green tea | Catechin compounds | *In vitro*, *in vivo*(animal) | [11-15] |
| Ginger (*Zingiber officinale*) | 6-gingerol, 8-gingerol, 10-gingerol, 6-shogaol, phenolic acids (cinnamic, caffeic, ferulic, syringic, p-coumaric, protocatechuic, gentisic, gallic) | *In vitro* | [16-19] |
| *Curcuma amada* | Phenolic acids (cinnamic, caffeic, ferulic, syringic, p-coumaric, protocatechuic, gentisic, gallic) | *In vitro* | [20] |
| Turmeric (*Curcuma longa*) | Curcumin | *In vitro* | [21] |
| Propolis | Phenolic compounds | *In vitro* | [17,22-24] |
| *Acacia nilotica* | Unknown (phenolics, alkaloids, terpenes, flavonoids, tannins) | *In vitro* | [25,26,28] |
| *Calotropis procera* | Unknown | *In vitro* | [27,28] |
| Muscadine grape skin | Polyphenols (quercetin, resveratrol) | *In vitro*, *in vivo*(animal) | [29,30] |
| Apple peel | Quercetin glycosides | *In vitro* | [31,32] |
| Virgin oil | Phenolics | *In vitro*, *in vivo*(human) | [33,34] |
| Cranberry (Vaccinium macrocarpon) Cranbery juice | Polyphenol compound | *In vitro*, *in vivo*(human) | [35-37] |
| Plants | Tannins (tellimagrandin-I, -II) | *In vitro* | [38] |
| Broccoli sprout (*Brassica oleracea*) | Sulforaphane | *In vitro, in vivo*(animal), *in vivo*(human) | [39,40] |
| *Paeonia lactiflora* | Paeonol, benzoic acid, unknown | *In vitro* | [41-43] |
| *Decalepis hamiltonii* | 2-hydroxy-4-methoxy benzaldehyde (HMBA) Unknown | *In vitro* | [44,45] |
| (Maillard reaction products) | Melanoidin | *In vitro*, *in vivo*(animal), *in vivo*(human) | [46] |
| (Maillard reaction products) | Aminoreductone | *In vitro* | [47] |
| Milk (Maillard reaction products) | Casein polymer (FP-10), | *In vitro*, *in vivo*(animal); *in vivo*(human) | [48,49] |
| Okinawamozuku (*Cladosiphon okamuranus*) | Fucoidan | *In vitro*, *in vivo*(animal) | [50,51] |
| Garlic (*Allium sativum*) | Allicin, diallyl sulfur components | *In vitro* | [52-55] |
| Chinese chive (*Allium tuberosum*) | Unknown | *In vitro* | [56] |
| Deep seawater | Unknown | *In vitro*, *in vivo*(animal); *in vivo*(human) | [63] |
| Essential oils | Unknown (geranial in lemongrass) | *In vitro*, *in vivo*(animal) | [64-66] |

Another example of an in-vitro trial include fruits from some cultivar varieties of Rubus idaeus and Rubs Occidentals. With four varieties of red (Rubus idaeus ‘Ljulin’, ‘Veten’, ‘Poranna Rosa’) and black (Rubus occidentalis ‘Litacz’) raspberries were evaluated on their antimicrobial properties as well as their phenolic content. (Baranowska 2014). This study found that the MIC of R. occidentalis ‘Litacz’ was 32.0 and the MBC was 32.0. With R. idacus ‘Ljulin’ the MIC was 8.0 and the MBC was 16.0. R. idacus ‘Veten’ showed a MIC of 8.00 and a MBC of 16.0. R idacus ‘Poranna Rosa’ showed a MIC of 8.0 and MBC of 32.0. With Sanguiin H6 there was a less than 1 MIC and less than 1 MBC and with Ellagic acid, there was a 0.125 MIC and less than 1 MBC. The lower the MIC the better. This indicates that Ellagic acid has the highest bacterial fighting properties against *H. pylori*.

**Clinical Trials**

In a report published by World J Gastroenterol 8 herbs are used for clinical trials. These herbs include garlic oil, fresh garlic or jalapeno peppers, cinnamon, lycopene, nigella sativa, green propolis, Glycyrrhiza glabra, and Chinese patient medicine wenweishu/yanngweishu. The only significant clinical outcomes were Glycyrrhiza glabra and the Chinese patent medicine wenweishu-yangweishu. All other herbs were shown to have no difference between experimental and control group.

Other clinical studies have been observed from natural foods and plant compounds. A list of the clinical studies, their agents that are active and the eradication rate is shown below:

| **Food** | **Putative anti-*H. pylori* effect** | **Effect comminbed with agents in clinical trial** | **Ref.** |
| --- | --- | --- | --- |
|  |  | Agents | Eradication rate | Study design |  |
| Bovine milk | Penetration of the antibiotics to *H. pylori* | bLF + triple therapy | 100% | Open, randomized, single-center | [5] |
| (damage of cell membrane) | (rabeprazole, CAM, tinidazole) | 93% | Open, randomized, multi-center | [6] |
| Green tea | Inhibition of urease activity *via* disrupted cell membrane |  |  |  |  |
| Ginger (*Zingiber officinale*) | Blockage of Toll-like receptor 4 (TLR4) activation |  |  |  |  |
| *Curcuma amada* | - |  |  |  |  |
| Turmeric (*Curcuma longa*) | - |  |  |  |  |
| Propolis | Damage of cytoplasmic membrane |  |  |  |  |
| *Acacia nilotica* | Suppression of urease activity |  |  |  |  |
| *Calotropis procera* | Suppression of urease activity |  |  |  |  |
| Muscadine grape skin | - |  |  |  |  |
| Apple peel | Inhibition of urease activity |  |  |  |  |
| Virgin oil | - |  |  |  |  |
| Cranberry (Vaccinium macrocarpon) Cranbery juice | Inhibition of *H. pylori* adhesion to gastric mucosa | Cranbery juice +*Lactobacillus* (La1) | 22.90% | Multicentric, randomized, controlled, double-blind | [37] |
| Plants | Damage of lipid bilayer membrane |  |  |  |  |
| Broccoli sprout (*Brassica oleracea*) | - |  |  |  |  |
| *Paeonia lactiflora* | Inhibition of urease activity |  |  |  |  |
| *Decalepis hamiltonii* | Bacterial lysis (cell death) |  |  |  |  |
| (interference of DNA/protein involved in DNA protection and bioavailability) |
| (Maillard reaction products) | Inhibition of *H. pylori* urease binding to gastric mucin |  |  |  |  |
| (Maillard reaction products) | - |  |  |  |  |
| Milk (Maillard reaction products) | Blockage of interaction between *H. pylori* and gastric mucin |  |  |  |  |
| Okinawamozuku (*Cladosiphon okamuranus*) | Inhibition of *H. pylori* binding to gastric cell |  |  |  |  |
| Garlic (*Allium sativum*) | - |  |  |  |  |
| Chinese chive (*Allium tuberosum*) | Interference of the cell division process |  |  |  |  |
| Deep seawater | - |  |  |  |  |
| Essential oils | - |  |  |  |  |

As you can see the only compounds that had an effect on *H. pylori* are bovine milk and cranberry. Bovine milk used the agents bLF + triple therapy, a 100% eradication of *H. pylori* was observed. From bovine milk the active agent rabeprazole, CAM, tinidazole had a 93% eradication rate. Cranberry (vaccinium macrocarpon) Cranberry juice was much less effective against *H. pylori.* The agents Cranberry juice+ Lactobacillus only had a 22.90% eradication rate. All the other compounds had putative anti-*H. pylori* effects but once combined with agents in clinical trial, there was no eradication rate. (Wang 2015)

**Potentials of Medicinal Plants**

Medicinal plants have proven to be useful in anti-*H. pylori* treatments against inflammation, gastric ulcers as well as cancer. Flavenoid glycosides of Polygonum capitatum for example protect against inflammation associated with *H. pylori infection.* (Zhang 2015).This plant and several others that can treat gastritis and protect against gastric injuries and should be developed as a potential drug for the therapy of gastritis caused by this bacteria. Antibiotics such as tetracycline, penicillin, and others are affected by pH differences. They are not as effective as these phytocompounds due to the acidity of the stomach. *H. pylori* has a high prevalence in the human population which indicates that this microorganism has developed mechanisms for resistance against host defenses. (Zhang 2015). Medical plant products have shown to be almost equal to clinical antibiotics. (Tadjirobehkar 2015). With continued study and clinical trials of medicinal plant extracts, there is potential to find anti-*H. pylori* compounds that effectively eradicate and reduce side effects of the bacteria. According to legislation, herbs are not considered medicine, but rather dietary supplements. (Bent 2008). This means that they can be marketed without previous demonstration of safety and efficacy; that is why care must be taken and regulations need to be followed to avoid potential safety and health risks.