Helicobacter pylori Eradication: Are there Alternatives to Antibiotics?

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Abstract

It is now generally accepted that infection with *Helicobacter pylori* is an important cause of peptic ulcer disease and that eradication of this organism greatly reduces the recurrence rate of ulcers. *H. pylori* also can cause chronic gastritis and hypochlorhydria and is a risk factor for gastric cancer. Conventional eradication therapies, which consist of two antibiotics plus either a proton-pump inhibitor or a bismuth compound, are highly effective, but can cause significant side effects in some cases. Alternative methods of eradicating *H. pylori* are therefore being investigated. To date, the research in this area is still preliminary, and no treatment has emerged as a clear alternative to the conventional triple-therapy regimens.

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Introduction

In the early 1980s, Warren and Marshall, two Australian physicians, reported the presence of an unidentified gram-negative curved and spiral-shaped bacillus in gastric epithelial tissue of patients with chronic gastritis. Originally called *Campylobacter pylori*, this organism was later renamed *Helicobacter pylori* when the organism was found to have characteristics that differed from those of true Campylobacters.

H. pylori and Peptic Ulcer

Marshall et al demonstrated that gastric antral mucosa can be present in the duodenum and that this tissue could also be infected with *H. pylori*. Although the medical community was initially skeptical, subsequent research strongly supports the proposition that *H. pylori* infection plays an etiologic role in both chronic gastritis and peptic ulcer (gastric and duodenal).

H. pylori infection is quite common, even among asymptomatic individuals. It occurs in about 10 percent of healthy individuals younger than age 30, and in nearly 60 percent of those over age 60. However, *H. pylori* is substantially more prevalent in people with peptic ulcer, occurring in virtually all patients with duodenal ulcer and about 80 percent of those with gastric ulcer.[1]

While some argue that *H. pylori* is merely an opportunistic organism that thrives on inflamed or ulcerated gastroduodenal tissue and plays little or no causative role in peptic ulcer,[2,3] clinical trials of *H. pylori*-eradication regimens indicate otherwise. A review of 60 studies

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that included a total of 4,329 patients demonstrated that *H. pylori* eradication accelerates the healing of peptic ulcers.[4] Even more important, appropriate antimicrobial therapy reduces the recurrence rate of the disease. Whereas 60-70 percent of *H. pylori*-infected ulcer patients develop a recurrence after initial healing, ulcers recur in only 5-10 percent of patients in whom *H. pylori* has been successfully eradicated.[5]

Because of strong evidence that *H. pylori* eradication facilitates ulcer healing and decreases recurrence rates, antibiotic therapy is now generally accepted as an important component of the overall treatment of peptic ulcer disease. Practice guidelines formulated by the American College of Gastroenterology state that, "antibiotic therapy is indicated for all *H. pylori*-infected ulcer patients."[6] This approach is widely considered to be a breakthrough in the treatment of peptic ulcer disease. However, the recommendation to administer antibiotics to all *H. pylori*-infected ulcer patients may be premature. There is a subset of ulcer patients – those taking non-steroidal anti-inflammatory drugs (NSAIDs) – who may not benefit from antibiotic therapy. On the contrary, according to one study, *H. pylori* eradication in long-term NSAID users inhibited the healing of gastric ulcers.[7] However, with the exception of patients who are unable to discontinue NSAIDs, eradicating *H. pylori* infection appears to be an important goal in the treatment of peptic ulcer.

Other Gastrointestinal Conditions Associated with *H. pylori*

It is generally accepted that *H. pylori* infection causes chronic gastritis and is responsible for most cases of gastritis not associated with other known causes (e.g., autoimmune gastritis or eosinophilic gastritis). Virtually all people who harbor this organism acquire chronic superficial gastritis, which can persist for decades if left untreated. In most cases, however, the chronic gastritis causes no symptoms.

A condition that is related to and overlaps chronic gastritis is so-called "non-ulcer dyspepsia," which affects as much as 25 percent of the U.S. population. Non-ulcer dyspepsia is a syndrome characterized by recurrent upper abdominal pain or discomfort in the absence of definite gastrointestinal disease. Although some studies have shown that the prevalence of *H. pylori* infection is higher in patients with non-ulcer dyspepsia than in asymptomatic individuals, the potential benefit of curing the infection in such patients is questionable. While some studies have reported benefit,[8] three recent double-blind trials have failed to demonstrate any effect of eradication therapy on symptoms of non-ulcer dyspepsia.[9,10,11]

H. pylori infection is also a known risk factor for gastric cancer, although the disease develops in only one percent of infected individuals.[12] While the association between *H. pylori* and gastric cancer has not been proven to be causal, there is a theoretical mechanism by which the organism could be carcinogenic. It has been demonstrated that the concentration of vitamin C in gastric juice is significantly lower in patients with *H. pylori* infection than in healthy controls.[13] The reduction in gastric ascorbate concentrations appears to be due to inhibition by *H. pylori* of the secretion of vitamin C into gastric juice. When *H. pylori* was successfully eradicated, gastric-juice ascorbate concentrations increased; however, in patients in whom eradication therapy was unsuccessful, ascorbate concentrations did not increase.[14] As the presence of vitamin C in gastric juice is believed to prevent the development of gastric cancer (presumably by inhibiting the conversion of nitrites to carcinogenic nitrosamines),[15] the reduction in ascorbate levels by *H. pylori* infection may enhance carcinogenesis.

H. pylori, Gastric Acidity, and Nutritional Status

There is evidence that *H. pylori* infection can exert variable effects on gastric acid secretion. While some infected persons have increased amounts of gastric acid, a subset of individuals without duodenal ulcer develops hypochlorhydria as a result of *H. pylori* infection. In this latter group, eradication of the infection has been reported to increase gastric acid secretion toward normal.[16] This observation is consistent with reports of transient achlorhydria occurring in patients with acute *H. pylori* gastritis,[17] and with evidence that *H. pylori* produces a protein that inhibits the secretion of gastric acid as effectively as cimetidine.[18] Although some hypochlorhydric patients may experience an improvement in hydrochloric acid secretion after treatment of *H. pylori* infection, it has been hypothesized that long-standing *H. pylori*-induced chronic gastritis may eventually lead to gastric atrophy and permanent hypochlorhydria, even if the organism is subsequently eradicated.[19]

The production of hydrochloric acid by the stomach serves two main physiological functions: (1) it enhances the digestion and absorption of various nutrients, including protein, iron, folic acid, vitamin B12, copper, and possibly calcium, and (2) it functions as a barrier against infection by various bacteria, viruses, fungi, and parasites. While some people with impaired gastric acid secretion do not seem to suffer adverse consequences, many practitioners have observed clinical benefits (ranging from a reduction in gastrointestinal symptoms to increased energy) when hypochlorhydric patients take hydrochloric acid supplements (such as betaine hydrochloride) with meals. Thus, *H. pylori*-induced hypochlorhydria may be a clinically important problem in certain individuals.

It was recently shown that serum ferritin concentrations were significantly lower in presumably healthy people with *H. pylori* infection than in uninfected individuals.[20] That finding is consistent with the possibility that iron absorption is impaired by *H. pylori*-induced hypochlorhydria.[21] In addition, *H. pylori* infection has been shown to play a role in the malabsorption of vitamin B12 from food, a process that requires the presence of gastric hydrochloric acid. In a study of 159 patients (mean age, 57 years) with low vitamin B12 levels and 43 volunteers (mean age, 52 years) with normal hydrochloric acid levels, *H. pylori* infection was significantly associated with food-vitamin B12 malabsorption ($p = 0.0001$), as determined by an egg yolk-cobalamin absorption test. This association was independent of age.[22]

Another study demonstrated that eradication of *H. pylori* infection as sole therapy (without concomitant vitamin B12 administration) can correct vitamin B12 deficiency in selected cases. In that study of 138 patients with anemia and vitamin B12 deficiency (without classic causes of B12 deficiency, such as pernicious anemia or gastrectomy), 77 (56%) were found to have *H. pylori* infection.[23] The organism was successfully eradicated in 31 (40%) of the 77 infected patients. In all 31 patients (mean age, 51.2 years), hematologic parameters and serum vitamin B12 levels improved without vitamin B12 therapy. Improvement was evident after four weeks, and became maximal after three to six months. In these patients, the mean hematocrit increased from 29 percent to 40 percent, and the mean serum vitamin B12 level increased from 63 pmol/L to 223 pmol/L. Hematologic parameters and serum vitamin B12 levels did not improve in the patients in whom *H. pylori* eradication was unsuccessful.

These studies suggest *H. pylori* infection can result in malabsorption of some nutrients, presumably as a consequence of hypochlorhydria. Eradication therapy should therefore be considered in *H. pylori*-infected patients who have either documented hypochlorhydria or malabsorption of nutrients requiring

Table 1. Conditions having Possible Association with *H. pylori*

Condition	Strength of Evidence
Peptic Ulcers	strong
Gastritis	strong
Non-ulcer Dyspepsia	weak
Gastric Cancer	moderate
Hypochlorhydria	strong
Malabsorption (esp. iron, B12)	moderate
Coronary Heart Disease	weak

gastric acid for absorption. In cases in which eradication therapy is not indicated or is unsuccessful, nutritional status should be assessed periodically and deficiencies treated appropriately. In addition, it may be worthwhile to measure gastric acidity in such patients and to consider replacement hydrochloric acid therapy at mealtime for those who are hypochlorhydric.

H. pylori and Coronary Heart Disease

In a case control study of 111 patients with coronary heart disease (CHD), *H. pylori* infection (identified by the presence of *H. pylori*-specific IgG antibodies in serum) was associated with an increased risk of CHD, even after adjustment for cardiovascular risk factors and other potentially confounding variables.[24] However, other studies have failed to demonstrate such an association,[25] and a review of the relevant research concluded that the evidence supporting a relationship between *H. pylori* and CHD is weak.[26] If *H. pylori* does play a role in the pathogenesis of coronary heart disease, the effect could be due to reduced absorption of nutrients such as folic acid and copper, which appear to protect against CHD,[27,28] and which require gastric acid for optimal absorption.[29,30] However, it is not presently known whether eradicating *H. pylori* would provide any protection against CHD.

Table 1 outlines conditions with potential associations with *H. pylori.*

Conventional Eradication Therapy

Treatment of *H. pylori* with a single antibiotic has been found not only to be ineffective in curing *H. pylori* infection, but also to promote the emergence of resistant strains of the organism. Therefore, single-antibiotic therapy should not be used to treat this infection. The most effective eradication regimens identified to date involve a triple therapy (Table 2), which combines two antibiotics with either a proton-pump inhibitor (e.g., lansoprazole, omeprazole, pantoprazole, or rabeprazole) or a bismuth compound (such as bismuth subsalicylate). Currently recommended protocols include a 10-14 day treatment with one of the following: (1) a proton-pump inhibitor (PPI) plus clarithromycin and amoxicillin; (2) a PPI plus clarithromycin and metronidazole; or (3) bismuth subsalicylate plus metronidazole and tetracycline.[31] The PPI-

Table 2. Conventional Triple Therapy for *H. pylori*

One of the Following Combinations for 10-14 Days		
Proton pump inhibitor (PPI)	PPI	Bismuth subsalicylate
Clarithromycin	Clarithromycin	Metronidazole
Amoxicillin	Metronidazole	Tetracycline

based triple therapy has produced a cure rate of 90 percent or better, whereas the cure rate with the bismuth-based triple therapy is slightly less – approximately 85-90 percent.

Bismuth, although not an antibiotic per se, is capable of suppressing the growth of *H. pylori*. In addition, antibiotic resistance does not occur with bismuth therapy, as it can with metronidazole and clarithromycin. It has been suggested that its antibacterial effect may explain the lower relapse rates in ulcer patients treated with bismuth, compared with the rates in those treated with H2-antagonists. For example, an analysis of the combined results of six studies showed that 85 percent of patients treated with H2-antagonists relapsed within 12 months, compared with only 59 percent of those treated with bismuth.[32]

However, bismuth mono-therapy is much less effective than triple therapy, which is associated with ulcer-recurrence rates of 10 percent or less. It has been pointed out[33] that bismuth alone does not eradicate *H. pylori* but merely suppresses the organism temporarily. In one study, only two of 21 duodenal-ulcer patients were *H. pylori*-negative one month after receiving a 28-day course of bismuth therapy.[34] It is possible that the anti-ulcer effects of bismuth are due primarily to other mechanisms, such as its capacity to form a protective coating on the gastric mucosa and to stimulate the synthesis of prostaglandins.

Whatever the advantages of bismuth are over H2-antagonists, bismuth is no longer recommended as the sole therapy for peptic ulcer. With short-term treatment, bismuth alone is considerably less effective than triple therapy at preventing recurrences; with long-term administration (i.e., years), bismuth accumulates in certain tissues and has the potential to cause neurotoxicity.[35]

Risks of Conventional Therapy

Antibiotic treatment of *H. pylori* infection is not without risk. Antibiotic therapy can lead to the development of pseudomembranous colitis, a potentially severe infection caused by *Clostridium difficile*. In addition, antibiotics frequently enable the overgrowth of *Candida albicans*, which can result in vaginitis, gastrointestinal disturbances, or other complaints. Moreover, antibiotic treatment could lead to the overgrowth of antibiotic-resistant strains of *H. pylori*, making further attempts at eradication more difficult.

Because of these risks, most physicians elect to treat *H. pylori* infection only in situations in which the benefits of doing so have been proven (e.g., peptic ulcer). If safer alternatives were available to eradicate *H. pylori*, then a case could be made that all such infections should be treated because of the

possibility that the risk of gastric cancer would be reduced or that nutritional status would be improved.

Alternative Treatments: Criteria for Efficacy

Several naturally occurring substances have been investigated as potential alternatives for the treatment of *H. pylori* infection. Although there are several promising leads, the research is for the most part preliminary, and additional work is needed before any of these treatments can be considered viable alternatives to conventional therapy.

It should be noted that *in vitro* activity against *H. pylori* does not necessarily imply an effect *in vivo*. In order for a compound to exert an antibacterial effect *in vivo*, it must achieve a bactericidal concentration in the gastric contents, penetrate the protective mucus layer of the gastroduodenal lining, and maintain its biological activity at the extant pH of the gastric milieu. Furthermore, the absence of detectable *H. pylori* at the end of a course of treatment is not sufficient evidence the infection has been cured. *H. pylori* is relatively easy to suppress, but difficult to eradicate completely. Most researchers require a negative *H. pylori* test four weeks after completion of treatment before concluding that the infection has been cured.

Vitamin C

At a concentration of 128 mcg/mL, vitamin C inhibited the growth of *H. pylori* incubated *in vitro* at pH 5.5.[36] Oral administration of vitamin C (10 mg/day for 7 days) reduced the number of *H. pylori* colonies in gerbils inoculated orally with the organism.[36] A preliminary human study suggests high-dose vitamin C may be capable of inhibiting *H. pylori* in selected cases. Sixty patients with dyspepsia, chronic gastritis, and *H. pylori* infection were randomly assigned to receive antacids (control group) or 5 g/day of vitamin C, administered in four divided doses (2 g, 1 g, 1 g, 1 g), for four weeks.[37] Fifty-one patients completed the study. At the end of the treatment period, *H. pylori* infection remained unchanged in all 24 patients in the control group, whereas there was no evidence of infection (as determined by histological examination and urease testing of gastric biopsy samples) in 8 of 27 patients (30%) who completed vitamin C therapy ($p = 0.01$).

Unfortunately, all of the patients in the study underwent conventional eradication therapy shortly after the trial was completed, so it was not possible to determine whether the effect of vitamin C on *H. pylori* infection was transient or long-lasting. Additional research is needed to determine whether vitamin C can eradicate *H. pylori*, what the optimal dosage and duration of therapy is, whether high-dose vitamin C would be tolerated by patients with active peptic ulcers, and whether buffered vitamin C (which would presumably cause less gastric irritation than ascorbic acid) is as effective as the acidic form of the vitamin. On the other hand, even a suppressive effect of vitamin C against *H. pylori* might have clinically important implications, since most people can safely ingest moderate doses of vitamin C indefinitely.

Polyunsaturated Fatty Acids

Alpha-linolenic acid at a concentration of 1.8×19^{-4} M reversibly inhibited the growth of *H. pylori in vitro*, while concentrations of 10^{-3} M killed virtually all of the organisms.[38] Similar inhibitory effects were seen with other polyunsaturated fatty acids including linoleic acid, gamma-linolenic acid, and eicosapentaenoic acid. To determine whether the same effect would occur *in vivo*, investigators studied 15 patients (aged 30-58 years) with mild non-ulcer dyspepsia and *H. pylori* infection (documented histologically from gastric biopsy samples and by rapid urease test).[39] The patients were treated with 2 g/day of a 1:1 mixture of fish oil and black currant

seed oil for eight weeks. This mixture contained each of the fatty acids shown to inhibit *H. pylori in vitro*. At the end of the treatment period, eight patients (53%) showed complete histological clearance of the infection. However, six months after the end of treatment, only three of the 15 patients (20%) had a negative urease test, indicating the infection had returned in the others.

The 20-percent eradication rate demonstrated in this study may turn out to be clinically important, although in the absence of a control group, it is not possible to rule out spontaneous remission of the infection. For example, in one prospective study, 12 of 188 infected patients (6.4 percent) became *H. pylori*-negative on repeat testing, even though they had not received any antibiotics or other treatment.[40] One might expect the spontaneous-remission rate to have been even higher than 6.4 percent in the fatty-acid study, since the patients were only mildly ill. Therefore, controlled trials are needed before the purported benefit of fatty acid supplementation can be considered proven.

If the results can be confirmed, it would be reasonable to attempt *H. pylori* eradication with fatty acids in asymptomatic individuals, in order to reduce the risk of gastric cancer. Fatty acids might also eventually be considered appropriate as initial therapy for patients in whom *H. pylori* eradication is not urgent (such as those with recently healed, mild peptic ulcers) or in those intolerant to antibiotics. Although the results to be expected from fatty-acid therapy would be less than those achievable with conventional triple therapy, the fatty acids used in this study are relatively innocuous and considerably safer than conventional antibiotic therapy. Fatty acids might also be considered for long-term suppressive therapy in selected cases, although the possibility that resistant strains would emerge cannot be ruled out completely. With additional research, more effective fatty-acid combinations and dosage regimens may be identified, possibly resulting in a higher eradication rate.

Lactobacilli

Lactobacilli have been shown to reduce the incidence of antibiotic-induced gastrointestinal side effects.[41] In a recent study, 120 asymptomatic individuals found to be positive for *H. pylori* infection during routine screening, and who decided to receive eradication therapy, were randomly assigned to one week of treatment with either: (1) pantoprazole (40 mg twice a day), clarithromycin (500 mg twice a day), and tinidazole (500 mg twice a day), or (2) the same regimen supplemented with *Lactobacillus* GG (*Lactobacillus casei sps. rhamnosus*).[42] The dose of *Lactobacillus* GG was 6 x 10^9 viable bacteria, given twice a day, two hours after breakfast and dinner for 14 days, during the week of eradication therapy and the following week. During the week of eradication therapy, the incidences of diarrhea (6.6% vs. 23.3%), bloating (16.6% vs. 40%), and taste disturbances (6.6% vs. 26.6%) were significantly lower by 72-, 58-, and 75 percent, respectively, in the *Lactobacillus* GG group, compared with the control group. The same pattern was observed during the week after eradication therapy. These results demonstrate that supplementation with *Lactobacillus* GG can reduce intestinal side effects resulting from conventional *H. pylori*-eradication therapy.

In addition to reducing side effects, preliminary evidence suggests Lactobacilli might increase the effectiveness of antibiotic therapy. *In vitro*, *L. acidophilus* has been shown to inhibit the growth of *H. pylori* isolated from gastric biopsy samples of patients with "acid-peptic disease."[43] In addition, administration of *L. salivarius* prevented the gastric colonization of *H. pylori* in mice.[44] In a study in humans, 120 patients infected with *H. pylori* were randomly assigned to receive a standard seven-day triple therapy of rabeprazole, clarithromycin, and amoxicillin

Table 3. Potential Alternative Treatments for *H. pylori*

Substance	Evidence	Effect
Vitamin C	*in vitro; in vivo* (gerbils; humans)	↓ *H. pylori*
α-Linolenic, Linoleic, γ-Linolenic, Eicosapentaenoic acids	*in vitro; in vivo* (humans – fish oil and black currant seed oil)	↓ *H. pylori*
Lactobacilli	*in vitro; in vivo* (mice) *in vivo* (humans)	↓ *H. pylori* ↓ antibiotic side effects ↑ antibiotic effects
Mastic Gum	*in vitro* *in vivo* (humans)	↓ *H. pylori* ↑ ulcer healing
Garlic	*in vitro* *in vivo* (humans)	↓ *H. pylori* no results
Berberine	*in vitro;* *in vivo* (humans)	↓ *H. pylori*
Flavonoids (various)	*in vitro; in vivo*	↓*H. pylori*

(control group), or the same regimen supplemented with a lyophilized and inactivated preparation of *L. acidophilus* (Lacteol Fort; Bruschetti, Genoa, Italy).[45] The acidophilus was given three times daily; each dose containing at least 5×10^9 organisms. In intent-to-treat analysis, the eradication rate was significantly greater in the group receiving *L. acidophilus* than in the control group (86.6% vs. 70%; $p < 0.05$).

These studies indicate Lactobacilli may decrease side effects and enhance the efficacy of conventional eradication therapy. However, there are no data suggesting that Lactobacillus therapy by itself would be an effective treatment for *H. pylori* infection.

Mastic Gum

Mastic gum is a resinous exudate obtained from the stem and leaves of the mastic tree (*Pistacia lentiscus*), an evergreen shrub native to the Mediterranean Basin. It is used as a food ingredient in the Mediterranean region and also to make chewing gum. In a small, uncontrolled study of six patients with gastric ulcer, mastic extract at a dose of 1 g twice daily for four weeks was said to promote ulcer healing.[46] However, because dietary changes were recommended and medical therapy was instituted, it is difficult to determine what role mastic played in the healing of the ulcers. In a double-blind trial, 60 patients with endoscopically proven duodenal ulcer were randomly assigned to

receive mastic (1 g/day before breakfast) or placebo for two weeks.[47] Among the 38 patients who completed the trial, ulcer healing (as determined by repeat endoscopy) was seen in 78 percent of patients receiving mastic, compared with 22 percent of those receiving placebo ($p < 0.01$). These studies suggest mastic promotes the healing of peptic ulcers.

Mastic has also been shown to kill *H. pylori in vitro*, with a minimal bactericidal concentration of 0.06 mg crude mastic per mL.[48] A bacteriostatic effect was seen at concentrations as low as 0.0075 mg/mL. It is possible the ulcer-healing effect of mastic is due, at least in part, to the eradication of *H. pylori*. On the other hand, the mechanism of action could be unrelated to this *in vitro* antibacterial effect. Further research is needed to determine how mastic enhances ulcer healing, and whether it is capable of suppressing or eradicating *H. pylori* in humans.

Garlic

An aqueous extract of garlic cloves, standardized for its thiosulfinate concentration, was found to inhibit the growth of *H. pylori in vitro*, with a minimum inhibitory concentration of 40 mcg of thiosulfinate per mL.[49] To achieve that concentration of thiosulfinate using fresh garlic would require approximately 5 g garlic (two small cloves) in a 500-mL volume of stomach contents, which is considered a fairly modest dose of garlic.

Despite the evidence of an antibacterial effect *in vitro*, clinical trials using garlic preparations have been disappointing. In one study, 15 patients who tested positive for *H. pylori* using the urea breath test were treated with a 300-mg tablet of dried garlic powder (Li 114; Lichtwer Pharma, Berlin, Germany) three times daily for eight weeks.[50] At the end of the treatment period, only one of the 15 patients had a negative breath test, and this patient was not re-tested at a later date to determine whether the organism had been eradicated or merely suppressed. In a second study, 20 patients with *H. pylori* infection and endoscopic evidence of gastritis and/or bulbitis were randomly assigned to receive capsules containing 275 mg garlic oil (providing 800 mcg of allicin) three times daily, or the same treatment plus omeprazole (20 mg twice daily) for two weeks.[51] One month after the end of treatment, compared with baseline, there was no significant change in *H. pylori* density and all of the patients were still *H. pylori*-positive. Based on these studies, garlic cannot be recommended as a treatment for *H. pylori* infection.

Berberine

Berberine, a constituent of herbs such as goldenseal, barberry, and Oregon grape, has broad-spectrum antibiotic activity.[52] *In vitro*, berberine has been found to inhibit the growth of *H. pylori*.[53] In a Chinese study, administration of 300 mg berberine three times daily for six weeks resulted in suppression of *H. pylori* in at least 40 percent of a group of peptic ulcer patients. However, as mentioned previously, *H. pylori* is relatively easy to suppress, but difficult to eradicate. Additional research is therefore needed to determine what role, if any, berberine has in the treatment of *H. pylori* infection.

Flavonoids

Although no clinical studies have been conducted on flavonoids and their potential for eradicating *H. pylori*, several *in vitro* and animal studies point to their potential benefit. *In vitro* inhibitory effects against *H. pylori* have been found for the flavonoids ponciretin (found in citrus and other plants), hesperetin, naringenin, and diosmetin, with ponciretin exhibiting the most potent inhibitory effect.[54] In another study, the flavonoid tryptanthrin and kaempferol (not a flavonoid), both isolated from *Polygonum tinctorium*, were found to inhibit *H. pylori*, both *in vitro* and in the

stomach of Mongolian gerbils.[55] More research is needed on the effect of flavonoids on *H. pylori*. Table 3 summarizes alternative treatments for *H. pylori*.

Conclusion

The search continues for alternatives to conventional triple therapy for *H. pylori* eradication, which is quite effective, but which can cause significant side effects in some patients. At present, the most promising natural treatment is a mixture of black currant seed oil and fish oil, although controlled trials are needed to confirm a preliminary report that this mixture can eradicate *H. pylori* in 20 percent of cases. In addition, Lactobacillus therapy, although not effective by itself, may increase the efficacy of conventional treatment, while reducing its side effects. Mastic gum has been shown to promote the healing of duodenal ulcers, but its activity against *H. pylori* is supported only by *in vitro* data. Its anti-ulcer effects may, therefore, be explainable by mechanisms other than an antibacterial effect. Vitamin C and berberine appear to suppress *H. pylori* temporarily in some patients, but neither substance has been demonstrated to eradicate the infection. To date, none of the alternative therapies discussed in this article have emerged as a clear alternative to conventional antibiotic regimens.

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