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Review Article

**PEPTIC ULCER DISEASE: A BRIEF REVIEW OF
CONVENTIONAL THERAPY AND HERBAL TREATMENT
OPTIONS**

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Article Received: April 2020**Accepted:** May 2020**Published:** June 2020**Abstract:**

Peptic ulcer is a chronic disease and up to 10% of the world is affected by it. Peptic ulcers are formed due to abnormal changes in gastric juice, its pH and decline in mucosal defenses. Two major factors; non-steroidal anti-inflammatory drugs (NSAIDs) and Helicobacter pylori (H. pylori) infection, play a disrupting role that causes mucosal injury. Conventional treatments like proton pump inhibitors (PPIs) and histamine-2 (H2) receptor antagonists have shown adverse effects, drug interactions and relapses.

On the other hand, some medicinal plants are very helpful and useful along with their chemical compounds in the prevention and treatment of different diseases. However, this review paper only encompasses some medicinal plants that are found useful for the prevention and treatment of peptic ulcers.

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INTRODUCTION:

In the digestive tract, at the site of the stomach or proximal duodenum, acid induced lesions sometime develops which are characterized by the denuded mucosa with the abnormal or defected extending into the muscularis propria, these lesions are called peptic ulcer.³ The estimated prevalence of this disease around the globe is up to 10%, but recent evidence has shown a decline in mortality rate and hospital admissions. This situation is owing to better hygienic conditions, improved therapies and decline in *Helicobacter pylori* infections.⁴

Usually, disruption in stomach acid along with acid peptic disease in patients occurs due to hypersecretory acidic environment, stress and dietary factors.⁵ Risk factors for this disease include alcohol, tobacco, *H. pylori* infection, Zollinger-Ellison syndrome and non-steroidal anti-inflammatory drugs. The main factors for duodenal and gastric ulcers are NSAID use and *H. pylori* infections.⁶ However, only a small proportion of people who are exposed to *H. pylori* infections develop peptic ulcers, this means the individual's susceptibility matters a lot in the beginning of mucosal damage.⁷

The risk of complications in patients with peptic ulcer increases four folds with the use of aspirin and NSAID. The auxiliary use of aspirin or NSAID with corticosteroids, anticoagulants, and selective serotonin reuptake inhibitors aggravates the risk of gastrointestinal bleeding. A meta analysis of observational studies has shown that *H. pylori* infection, aspirin and NSAID, these all independently contribute to worsening the peptic ulcer disease.^{8,9}

Treatment: Conventional Therapy

- **Helicobacter pylori Eradication**

The successful eradication of *H. pylori*, is alone a paramount for healing in peptic ulcer and preventing its recurrence, but the growing antibiotic resistance is becoming a global challenge. The very first effective therapy was introduced in 1980s, it consisted of tetracycline, metronidazole, and bismuth which was given for two weeks. Then triple therapy, a first line therapy was introduced which consisted of proton pump inhibitor (PPI) and 2 antibiotics like amoxicillin plus clarithromycin or metronidazole. However, the increasing antibiotic resistance, especially for clarithromycin became a new challenge and it declined the success of triple therapy. In-depth studies showed that the use of antibiotics should be based upon the local prevalence of antibiotic resistance and individual susceptibility.^{10,11}

At present, the recommended first line therapy includes, either a 14 day bismuth containing quadruple therapy or a 14 day concomitant therapy for bismuth intolerant patients, containing PPI, amoxicillin, metronidazole and clarithromycin. Both these therapies are successful in 90% eradication of the *H. pylori*.

The second line therapy is prescribed upon the failure of first line therapy, and it must not include clarithromycin or metronidazole. In addition, Levofloxacin triple therapy which includes amoxicillin, levofloxacin and PPI, seems to be effective in achieving 75 to 82% eradication rates. If a patient has already received a first line therapy with clarithromycin based regimen, then the next preferable treatment is with bismuth quadruple therapy, which has up to 93% eradication rate. Another option is the high dose dual therapy with PPI and amoxicillin, because *H. pylori* scarcely develops amoxicillin resistance.^{12,13}

Despite great care and well developed recommendations, some patients still show persistent infection. The failure might be based upon two possible factors, either the *H. pylori* is resistant to one or more antibiotics or two treatments are suboptimal compliance, that's why susceptibility testing is recommended.

However, when at least three recommended treatment options gave unsuccessful results, then the most recommended salvage regimen is rifabutin based triple therapy. This is given for 10 days and have almost 70% eradication rates, but rifabutin has adverse effects as well.

- **NSAID Associated Ulcer**

Many therapies are present to prevent aspirin and NSAID associated ulcer and its complications. One of them is the use of PPI, H₂ antagonist or misoprostol. PPIs are the most effective prophylactic agents. Their mechanism of action includes the irreversible binding of potassium/hydrogen ATPase enzyme to reduce gastric acid production. However, the COX-2- selective NSAIDs and its combination with PPI offers the best therapy against peptic ulcer complications. Abortifacient actions and gastrointestinal upset limit the misoprostol use for gastric protection, despite its effective results against the disease. With PPIs therapy, more than 85% patients heal within 6 to 8 weeks of therapy if the offending agent is reduced/ discontinued. If the disease continues, then it is important to check the drug compliance.¹⁴

Despite the fact that the PPIs are the most commonly prescribed and used drugs around the globe, these have side effects like headache,

diarrhea, constipation, and abdominal discomfort. Suppression of gastric acid secretion is another side effect, it allows various ingested pathogens to colonize the upper GIT tract and cause infections, which would otherwise be killed by the gastric acid. Studies are showing that the PPI use might increase the risk of enteric infections such as *Campylobacter*, *Salmonella*, and spontaneous bacterial peritonitis.

Alternative Therapy for Peptic Ulcer: Herbal Treatment

Several factors influence the failure of conventional therapy: poor bioavailability of antibiotics; the stomach pH ranging from acidic to neutral; patient lifestyle and diet; deficiency of the patient permissiveness; bacterial resistance to antibiotics. Studies have reported that numerous medicinal plants and their anti-*H. pylori* activities are quite effective in treating peptic ulcers.

Medicinal plants play a different therapeutic role than conventional therapy. Plants like *Allium sativum*, *Zingiber officinalis*, and *Cistus laurifolius* are well known to suppress the colonization of *H. pylori*, inhibit cytokine, suppress precancerous changes by binding nuclear factor kappa B DNA, reducing gastric inflammation by chemokine release and suppresses mutagenesis along with abundant apoptosis production.¹⁵

Some of the medicinal plants and their roles are given below:

- **Allium Sativum**

History is full of health benefits and medicinal use of garlic. The organosulfur components of *Allium sativum* like δ -glutamyl S-allyl-L-cysteine, and S-allyl-L-cysteine (SAC) sulfoxides are famous for their bioactivities.¹⁶

Numerous kind of extracts of ginger can be used with combination of different bioactive components. The main function of *Allium sativum* is observed as its antioxidant effect by inhibiting lipoprotein oxidation, scavenging reactive oxygen species, and lowering the serum glucose induction of antioxidant enzymes.

It also suppresses the *H. pylori* growth, its induced gastric inflammation and promotes apoptosis to induce an anti-tumorigenic effect.¹⁷

- **Cistus Laurifolius**

The most important components in human diet are flavonoids, which play a key role in various biological activities, specifically as an antioxidant. Due to their high cost, a rapid synthesis of flavones that are accessible and inexpensive have been developed.

By bromination protocol 3-demethoxysudachitin and methoxylation, a flavone component with antimicrobial activity has been designed against *H. pylori*. Numerous flavonoids were designed with an

extract from *Cistus laurifolius*. The experiment evaluated a series of metronidazole-flavonoid extracts which showed excellent results against *H. pylori* suppression. It was found that how one compound can remarkably aid in achieving great results with enhancement in IL-8 levels in gastric cancer cells induced with water extract of *H. pylori*.^{18,19}

Similarly, studies also discovered that a chloroform extract of *Cistus laurifolius* has strong anti-*H. pylori* effects. So, isolated flavonoids can be used as a treatment for peptic ulcer, in which the main target is the *H. pylori* eradication.

- **Zingiber officinalis**

Zingiber officinalis is also known as ginger. This plant extracts showed anti-tumor effects on colon cancer by increasing DNA synthesis, inhibiting cancer cell growth and apoptosis production. The main pungent phenolic components of *Zingiber officinalis* are 6-gingerol and zingerone, and these have numerous health benefits. These active compounds of ginger inhibit parietal cell K^+ -ATPase, H^+ . Owing to this zingerone and gingerol plays two important roles; reduction of excessive gastric acid secretion and proton pump inhibition. In addition, its anti-*H. pylori* effects are also observed.²⁰

Zingiber officinalis is a natural antioxidant against peptic ulcer. These have limited solubility in gastric juice, which prevents its transport to high acidic pH regions of duodenum and ileum, therefore it has more transit time in the stomach which helps it in playing its anti-*H. pylori* role effectively.

- **Camellia Sinensis (Green Tea Polyphenols)**

Green tea has gained immense importance these days. The chemopreventive effects of green tea depend upon its antioxidant properties, regulatory functions on cell growth, apoptosis, development, positive impacts upon the intestinal microflora. Green tea has many components, and among them, polyphenols and EGCG are well known for anti-tumor necrosis factor-alpha gene expression. Urease is important for *H. pylori* colonization, and studies have shown negative impacts of *Camellia sinensis* on this enzyme. Thus, it results in inhibition of *H. pylori* colonization and helps the patient to recover from peptic ulcer.²¹

Herb-Drug Interactions

The trend of herbal supplements and drug usage is rising worldwide. Interactions between these both therapies can manifest pharmacodynamic or pharmacokinetic interaction. Pharmacokinetic interaction occurs owing to simultaneous use of herbal supplement following same mechanism of absorption, distribution, metabolism, or excretion

and a conventional drug. This interaction leads to change of drug concentration in the patient's blood. This can might exacerbate or antagonize the drug's clinical effects.

Allium sativum extracts declines the drug concentration such as, digoxin, rosuvastatin, verapamil and doxorubicin. Zingiber officinalis interfares with the thromboxane synthetase and prolongs the bleeding time. Green tea extracts have been shown to exacerbate the simvastatin amount or inhibit the actions of various drug transporting proteins.

CONCLUSION:

The combination of medicinal plants and standard anti-gastric ulcer drugs might help in synergistic effects against *H. pylori* and peptic ulcer disease. But, it is imperative to use carefully. It is found that medicinal plants have minimum to zero side effects on the gastrointestinal tract and plays a positive role in the fight against certain infections and ulcers.

No doubt, conventional therapy also plays positive role in treating peptic ulcers, but issues like antibiotic resistance, patient's susceptibility and therapy duration are troublesome and challenging.

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