

Exploring Medicinal Plants for Anti-Helicobacter Pylori Activity

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Abstract

Helicobacter pylori is a class 1 carcinogen that requires targeted therapeutic strategy. A number of drugs including proton pump inhibitors, antibiotics and antiprotozoals are available for the treatment of *Helicobacter pylori* infections like chronic gastric irritation, gastro duodenal ulcers and low grade gastric mucosa associated lymphoid tissue lymphoma. Clinical evaluation of these drugs has shown the incidence of relapses, side effects and drug interactions. Multi drug resistance to *Helicobacter pylori* has been the main reason for treatment failure. This has been the rationale for the development of new anti- *Helicobacter pylori* drugs and search for novel molecules has been extended to medicinal herbs that offer better protection, decreased relapse and undevelopment of resistance towards bacteria. The present article reviews the medicinal herbs from global perspective for their anti- *Helicobacter pylori* activity and active compounds from the plants responsible for this activity. We have highlighted some of the important plants and their active constituents reported for their anti- *Helicobacter pylori* activity. Ancient system of medicine (Ayurvedic and Unani) supported by modern science is necessary to isolate, characterize and standardize the active constituents from herbal sources for anti-*Helicobacter pylori* activity.

Index terms—

1 Exploring Medicinal Plants for Anti-Helicobacter Pylori Activity

Abstract -*Helicobacter pylori* is a class 1 carcinogen that requires targeted therapeutic strategy. A number of drugs including proton pump inhibitors, antibiotics and antiprotozoals are available for the treatment of *Helicobacter pylori* infections like chronic gastric irritation, gastro duodenal ulcers and low grade gastric mucosa associated lymphoid tissue lymphoma. Clinical evaluation of these drugs has shown the incidence of relapses, side effects and drug interactions. Multi drug resistance to *Helicobacter pylori* has been the main reason for treatment failure. This has been the rationale for the development of new anti-*Helicobacter pylori* drugs and search for novel molecules has been extended to medicinal herbs that offer better protection, decreased relapse and undevelopment of resistance towards bacteria. The present article reviews the medicinal herbs from global perspective for their anti-*Helicobacter pylori* activity and active compounds from the plants responsible for this activity. We have highlighted some of the important plants and their active constituents reported for their anti- *Helicobacter pylori* activity. Ancient system of medicine (Ayurvedic and Unani) supported by modern science is necessary to isolate, characterize and standardize the active constituents from herbal sources for anti-*Helicobacter pylori* activity.

Health Organization has categorized *H. pylori* as a class 1 carcinogen. 5 Eradication of the organism has been shown to result in ulcer healing, prevention of peptic ulcer reoccurrence and may also reduce the prevalence of gastric cancer in high-risk populations. 6 Many clinical trials involving patients with gastric and duodenal ulcers show that curing the infection is associated with a significant reduction in ulcer reoccurrence rates. [7][8] Since 1984 physicians prescribing triple therapy to treat *H. pylori* infections which includes three options.

First option includes the combination of proton pump inhibitor (PPI), clarithromycin and ampicillin. Second option includes PPI, clarithromycin and metronidazole. Third option includes bismuth subsalicylate, metronidazole and tetracycline, but the cure rate from standard triple therapy has been low as 50%. 9-10 However, eradication by the triple therapy is not always successful and acquisition by *H. pylori* resistance to antibiotics could present a serious problem that may reduce treatment efficiency. 11 Quadruple therapy, where three antibiotics are taken alongside the PPI, has also been used in cases where triple therapy has not been successful. But the success rate was only 67%. 12 Many strains of *H. pylori* are now developing resistance to commonly used antibiotics. *H. pylori* acquires resistance by mutations to all the antibiotics used in the treatment regimens. The mechanism of resistance involves point mutations which are transmitted vertically, however transformation may be possible if two strains are present simultaneously in the stomach. Drug efflux proteins also can contribute to natural insensitivity to antibiotics and to emerging antibiotic resistance. Efflux pump gene hef A of *H. pylori* play an important role in multidrug resistance. Global resistance of *H. pylori* to metronidazole, clarithromycin, amoxicillin and tetracycline was also reported. One person may have more than one strain of *H. pylori*. Here the antibiotics may kill one strain, but not the other. [13][14] Furthermore, undesirable side effects of the drugs and the significant cost of combination therapy require the

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Helicobacter pylori (*H. pylori*), a Gram -negative 1984 by Marshall et al, is one of the most common chronic bacterial pathogens in humans. 1 Approximately 50% of people in the world are infected with it, and its prevalence is significantly higher in developing countries than in developed countries. 2 Once a person is infected, the organism can live in the stomach indefinitely and may not cause clinical illness. It is still not clear how *H. pylori* are transmitted or why some people infected with bacteria become sick and others do not. 3 *H. pylori* infection is an important etiologic impetus usually leading to chronic gastritis, gastroduodenal ulcer and low grade gastric mucosa associated lymphoid tissue lymphoma.

Epidemiological data shows that a high *H. pylori* infection rate is related to the high incidence of gastric cancer and gastric adenocarcinoma. 4 World H spiral bacterium which was first detected in I.

3 Introduction

II.

Current Treatment Regimens As phytomedicine has proved to be an untapped treasure for the discovery of lead compounds to cure gastrointestinal disorders. Hence several studies have been aimed to evaluate the anti-*Helicobacter pylori* activity of medicinal herbs. 15 To the best of our knowledge, there is no extensive global view on exploring medicinal plants for anti-*Helicobacter pylori* activity. List of medicinal herbs with anti-*Helicobacter pylori* activity including their source and active extracts are given in table ??.

The insolubility of non-polar extracts makes it very difficult for the investigators to be used in an aqueous medium during the study of anti-*Helicobacter pylori* activity. 26 Water or alcohol (methanol/ethanol) are used mainly for a large number of crude extract preparations. 27 The type of solvent used may have an effect on the nature of the compounds extracted and the resulting bioactivity of the extract. 28 To estimate the value of each extract therefore, several factors, including the rate of extraction, the quantity extracted (yield), the diversity of compounds extracted, the diversity of inhibitory compounds extracted, the ease of subsequent handling of the extracts, toxicity of the solvent in the bioassays and the potential health hazards of the extractants have to be evaluated. In many research works, methanol/ethanol is used for alkaloid extraction; acetone for flavonoids and steroids; hexane, diethyl ether and chloroform for fat soluble oils, wax, lipids and esters. Dichloromethane for terpenoids, ethylacetate for esters, ethanol may be used for sterols, poly phenols, tannins and water for water soluble components like glycosides, polysaccharides, polypeptides and lectins. 29 Hundreds of plants with antimicrobial compounds have been reported. However, very few of these studies have reported the in vivo anti-*Helicobacter pylori* activity of these compounds. It is very important to know whether these compounds will still maintain their maximum activity in the gastric mucus niche of *H. pylori*. Anti-*Helicobacter pylori* compounds from plants and their mechanism of action are given in table 2.

Curcumin, biologically active poly phenolic from *Curcuma longa* has recently been shown to arrest *H. pylori* growth. The anti-*Helicobacter pylori* activity of curcumin against 65 clinical isolates of *H. pylori* in vitro was examined. Minimum inhibitory concentration ranging from 5-50 µg/ml, showing its effectiveness against *H. pylori* growth in vitro irrespective of genetic makeup of strains. Curcumin showed immense therapeutic potential against *H. pylori* infection as it was highly effective in eradication of *H. pylori* from infected mice as well as restoration of *H. pylori* induced gastric damage.

Curcuma longa extract was the most efficient in killing the seven strains of *H. pylori* within 15 minutes followed by chilli and ginger. [46][47][48] *Mallotus philippinensis* (Lam) Muell. Exhibited the most potent bactericidal activity against *H. pylori* which completely killed the bacteria at the concentration of 15.6-31.2 µg/ml. 16 There is no evidence of in vivo effectiveness of this plant. Antibacterial activity of *Allium sativum* L(garlic) against *H. pylori* is well documented (40 µg/ml) and resistance has not been reported. The synergistic action of garlic and omeprazole against *H. pylori* was also reported.

Thiosulfates play an important role in the antibiotic activity of garlic. Further clinical evaluation seems warranted. [49][50][51] A mixture of tannic acid and n-propyl gallate can limit the gastric mucosa deterioration induced by H.pylori infection and vac A administration, suggest that vac A inhibition plays a role in this protective activity. So, polyphenols from plant sources may contribute to limit the pathological outcomes of H.pylori infection. 52 Successive extracts of Sapindus mukorossi and Rheum emodi inhibited the growth of 30 resistant clinical isolates of H.pylori in vitro and in vivo studies and there was no acquired resistance against these herbal extracts even after ten consecutive passages. 53 The evidence summarized above tentatively suggests possible benefits from some herbal sources with anti-Helicobacter pylori activity. Herbal science, Ayurvedic knowledge supported by modern science is required to standardize the plant extracts and to isolate, characterize and standardize the active constituents from plant sources for anti-Helicobacter pylori activity.

Extensive investigations and large scale well designed clinical trails are required to provide more conclusive proof to explore medicinal herbs for anti-Helicobacter pylori activity.

Table1 : Medicinal herbs having anti-Helicobacter pylori activity (global perspective).

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Figure 1: hydroxy- 4

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Exploring Medicinal Plants for Anti-Helicobacter Pylori Activity

Botanical name	Source	Part used	Extract	Reference
South Asian Herbs				
<i>Mallotus philippinesis</i>	Pakistan	covering fruit	Aqueous ethanol (70%)	16,17,18
<i>Curcuma amada</i> Roxb.	Pakistan	rhizome		
<i>Myristica fragrans</i> Houtt.	Pakistan	seed		
<i>Psoralea corylifolia</i>	Pakistan	seed		
<i>Glycyrrhiza glabra</i> L	India, Srilanka	root		
<i>Terminalia chebula</i>	Pakistan	fruit		
<i>Curcuma longa</i> L	India	rhizome		
<i>Cuminum cyminum</i>	Srilanka	seed		
<i>Coccinia grandis</i>	India	leaves	Ethanol	
<i>Terminalia arjuna</i>	India	bark	Methanol	
East Asian Herbs				
<i>Rhizoma coptidis</i>	China	rhizome	Aqueous	19,20
<i>Radix scutellariae</i>	China	root		
<i>Radix isatidis</i> Asasarum sieboldi	China Korea	root root	Methanol	
<i>Lindera strychnifolia</i>	Korea	root		
<i>Angelica tenuissima</i>	Korea	root		
<i>Alpinia oxyphylla</i>	Korea	fruit		
American Herbs				
<i>Zingiber officinale</i>	USA	rhizome	Methanol	21
<i>Rosmarinus officinalis</i>	USA	rosemary leaf		
<i>Foeniculum vulgare</i>	USA	seed		
<i>Nigella sativa</i>	USA	seed		
African Herbs				
<i>Terminalia spinosa</i>	East Africa	young branches	Aqueous	22
<i>Harrisonia abyssinica</i>	East Africa	root		
<i>Ximenia caffra</i>	East Africa	root		
<i>Azadirachta indica</i>	East Africa	leaves, stem bark		
<i>Combretum molle</i>	South Africa	stem bark	Acetone	23
<i>Sclerocarya birrea</i>	South Africa	stem bark		
<i>Carica papaya</i>	Nigeria	leaf	Aqueous ethanol	24
<i>Morinda lucida</i>	Nigeria	leaf		
<i>Octimum gratissimum</i> <i>Phyllanthus amarus</i>	Nigeria Nigeria	leaf leaf		
Brazilian Herbs				
<i>Bixa orellana</i> L	Brazil	seed	Aqueous ethanol (96%)	25
<i>Chamonilla recutita</i> L	Brazil	inflorescence		
<i>Ilex paraguariensis</i> A	Brazil	green leaves		
<i>Malva sylvestris</i> L	Brazil	inflorescence & leaves		

Figure 2:

Exploring Medicinal Plants for Anti-Helicobacter Pylori Activity			
Compound name		Examples	Mechanism of action reference
Quinones		Quinones, idebenone, duroquinone, menadione, juglone, coenzyme Q 1	
Flavones, flavonoids and flavonols		Quercetin, catechins, myristin, rutin	
Phenolics and polyphenols	and	Catechol, pyrogallol, curcumin	
Tannins		Polymeric phenols, hydrolysable tannins	
Coumarins		7-hydroxy-4-methyl coumarin,	
Terpenoids and essential oils	and		
Alkaloids			
Lectins and poly peptides			

Figure 3: Table 2 :

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