



GSJ: Volume 8, Issue 6, June 2020, Online: ISSN 2320-9186

www.globalscientificjournal.com

Pakistani Medicinal Plants Used in Treatment of Helicobacter Pylori

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ABSTRACT

Helicobacter pylori is one of the class 1 carcinogen due to its ability to cause infections like chronic gastritis, gastro duodenal ulcers and MALT lymphoma. Historically H.Pylori has been treated with antibiotics, proton pump inhibitors and antirpotozoal but due to evolving multi drug resistance incidence of relapses, side effects and drug interactions are increasing by day and its a major reason for treatment failure. Search for novel molecules and innovative therapies have since been underway ranging from herbal therapy to ancient Ayurvedic system of medicine. The present article would give a perspective of medicinal herbs for treatment of H. Pylori from Pakistan's point of view, which provides better protection,less side effects and even lesser prolapse rates. It will highlight the active plant compounds responsible for this effect duly supported by modern science which makes it necessary to standardize the constituents responsible.

Key Words: H Pylori, Gastric Irritation, Drugs, Herbs

INTRODUCTION

World Health Organization (WHO), reported up to 80% of the world's population relies on the traditional medicine (Mostly from medicinal plants) for their primary health care needs(Organization, 1993). Meaning that, only 20% of the world's population depends on Modern medicine (Mostly synthesized or semi-synthesized compounds). Moreover Modern drugs can be categorized as synthetic,semi synthetic or derived from natural sources, up to 25% of drugs are derived from plants, 11 percent of basic drugs are plant based and more than half (60%) of antitumor and anti-inflammatory drugs are naturally derived (Rates, 2001). Although the dominant antibiotics have always been synthetic since long but we are increasingly identifying infectious diseases both new and old with new properties most of them are zoonotic in origin. Atleast 30 new infections have been identifies during last three decades, among them are *Helicobacter pylori* which may cause Duodenal, gastric ulcer and stomach cancer (Dikid et al., 2013) Eradication of H. pylori by various drug regimens have been prescribed with different combinations of therapeutic agents such as antibiotics, proton pump inhibitors, bismuth subsalicylate, and H2 blockers (Brandstatter G et al., 2001). However, gastric inflammation persists even after eradication of H. pylori. The success of commercially available drugs in the treatment of gastric ulcers is overshadowed by the various side

effects associated with these drugs. There is also the resistance problem coming up by inappropriate and extensive use of such drugs (Mégraud et al., 2012).

Furthermore, alarming increase in resistance to antibiotics, especially clarithromycin and metronidazole confines their use in the treatment of infections (Lind T et al., 2006). Cost effectiveness and reduction of side effects has always been a challenge necessitating the need for a new better drug or alternative therapy (O’Gara et al., 2004). This results in an emerging surge in alternative approaches such as anti-inflammatory agents, antioxidants, probiotics, vitamins, plant extracts and phytochemicals in controlling *H. pylori* related inflammation and disorders (Lee SY et al., 2004). Plants have always been the main source of new drugs and folk medicines. Plants are well known to contain active metabolites, which are useful in treating various infectious diseases with no or less toxicity (Cowan et al., 1999). Several naturally occurring medicinal plants, herbs, and fruit extracts have been shown to possess antimicrobial activity against *H. pylori* (Tabaka et al., 1999). Awareness is now growing regarding the preferred use of medicinal plant materials as prophylaxis and therapeutics over the synthetic drugs (Rojas et al., 2006). Anti-*H. pylori* activity of *A. nilotica* leaves may be attributed to the hydrolysable tannins, saponins, glycosides, phenols, terpenes and flavonoids isolated from its leaves (Dabur et al., 2007). Amongst the plants tested, the extracts from *A. nilotica* and *C. procera* were found to be superior anti-*H. pylori* and urease inhibitory agents as compared to those from *A. vasica*, *F. arabica* and *C. equisetifolia* (Malviya et al., 2011). Antibacterial activity of *C. procera* against Gram +ve and Gram -ve bacteria has already been demonstrated (Amin et al., 2013)

Current Treatment Regimens

Since three decades (1984) triple therapy is the mainstay for treatment of *H. Pylori*, used in different set of combinations, at least three of which is standard for a long time. One option is PPI in combination with Clarithromycin and Ampicillin. Second uses Metronidazole instead of Ampicillin. Third option makes use of a tetracycline in combination with bismuth subsalicylate and Metronidazole but the cure rate from these standard therapies has been as low as 50% (Usta Y et al., 2008) -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. (Glupczynski Y et al., 1998). 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%. (Saltik-Temizel et al., 2007).

Multidrug Resistance to H. Pylori

Many strains of microorganisms are developing resistance to traditionally used antibiotics and H.pylori is no exception, it undergoes mutations which imparts it with resistance to almost all antibiotics used in its treatment. Common mechanism of resistance is thought to be point mutation which are transmitted vertically, however transformation is also believed to be possible with two strains inhabiting stomach at the same time. Drug efflux pumps may also add to the already emerging resistance. Pumps like hef A of H. Pylori is mainly indicted in such scenarios. Global resistance of H. Pylori to all the antibiotics used in standard therapy has been reported which makes it very difficult to eradicate if a person is having two different strains at the same time and one of which is already resistant (Kivi M et al., 200))(Torres J, et al., 2000). Furthermore, undesirable side effects of the drugs and the significant cost of combination therapy require the mice as well as restoration of H.pylori induced gastric damage.

Curcuma Extract Commonly Known As Turmeric In Paksitan Used In Treatment Of H.Pylori

Curcuma leaf extract was the most efficient in killing the seven strains of H.pylori within 15 minutes followed by chilli and ginger (Di Mario et al., 2007). Mallotus phillipinesis is (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 (zaidi et al., 2009). 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. Thiosulfinates play an important role in the antibiotic activity of garlic. Further clinical evaluation seems warranted (SivamGP et al 1998). 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 (Ruggiero P et al., 2006).

Similarly Curcuma species are widely known for their broad range of pharmacological activities. In Pakistan, three varieties of Curcuma species namely Curcuma amadaRoxb.(CAR), Curcuma caesiaRoxb. (CCR), and Curcuma longa L. (CLL) are available. CAR and CLL are commonly used as a spice in daily life while CCR is mainly employed for medicinal purposes especially as an alternate of turmeric or CLL (Usmanghani et al., 1997). Among these three species, CAR (31.2–62.5 g/ml) and CLL (62.5 g/ml) showed strong inhibition on Helicobacter pylori growth in all strains while CCR (250 g/ml) exhibited weak bactericidal activity in contrast with the other two. Anti-Helicobacter pylori activity of CLL and its major polyphenolic chemical constituent, curcumin, has been documented earlier (Mahady et al., 2002) whereas, Siddaraju and Dharmesh (2007) recently reported the anti-Helicobacter pylori activity of CAR. However, no comparative study between the three species against Helicobacter pylori has been reported previously. Our results displayed the different bactericidal potential in the above mentioned species which might be due to the difference in antibacterial chemical constituents in them. The MBC value of curcumin revealed from our study is ranged from 25.0 to 50.0 g/ml which is also comparable with amoxicillin.



Medicinal Importance Of Garlic (Allium Sativum) In Treatment Of H.Pylori

One of the major cancer in developing country is gastric cancer cause due to H.pylori (Fuchs and Mayer 1995).). Antimicrobial activity of garlic against H. pylori was investigated Because allium vegetables, particularly garlic, have antibiotic activity. (Sivam et al. 1997). was found to be Thus H. pylori is more susceptible to garlic extract at 40 mg/mL this is its minimum inhibitory concentration but At this concentration, the control organism Staphylococcus aureus was not inhibited by the garlic extract. It is clear that the sensitivity of H. pylori to garlic extract at such a low concentration may be related to the reported lower risk of stomach cancer in those with a high allium vegetable intake (Sivam. 2001).

How Garlic Work Against H. Pylori

Thisulfates like allicin paly important in antimicrobial activity of garlic it totally inhibit RNA synthesis while partially inhibit DNA and protein synthesis and its activity is also depend the lipid

content of the bacterial membrane that is why susceptibility observed between gram-negative *H. pylori* (40 mg/mL) and gram-positive *Staphylococcus aureus* (160 mg/mL) to garlic extract (Sivam. 2001).

Anti *h. Pylori* of *Acacia Nilotica* Commonly Known As Kikar Or Babul Tree In Pakistan

As compare to metronidazole methanol and acetone extracts of *A. nilotica* (flowers) showed stronger but less potent activity than amoxicillin and clarithromycin against *H. pylori* , and tetracycline has almost the same activity as methanol and acetone extracts of *A. nilotica*. By a competitive mechanism Methanol and acetone extracts of *A. nilotica* inhibit urease activity (Amin et al., 2013).

Camellia Sinensis Commonly Known As Tea Shrub In Pakistan Has Potential Anti H. Pylori Activity

on the vivo and in vitro antibacterial effects of *c. sinensis* extracts there are several reports.(hamilton-miller, 1995; toda et al., 1991). in 1994, diker et al. growth of six clinical isolates of *h. pylori* is inhibited by extracts of black and green in vitro in an agar diffusion assay (diker & hascelik, 1994). green tea posses protective effect against stomach cancer (setiawan et al., 2001). *h. pylori*-induced gastric lesions in mongolian gerbils is greatly suppressed by green tea extract (matsubara et al., 2003)

Chamomilla Recutita Commonly Known As Gul-E-Baboon Posses Anti H.Pylori Activity

Study found that urease production of *H. pylori* was inhibited by the *C. recutita* oil extract . also the oil extract demonstrates anti-*H. pylori* activity by inhibiting the reference strain. (Shikov et al., 2008)

Cinnamomum verum (c. Zeylanicum) as Anti H.Pyloric Agent In Pakistan

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 Commonly Known As Broom Creeper Or Patalgarudi (Sanskrit) In Pakistan Is Use Against H.Pylori

In both traditional and folk medicines Cocculus hirsutus extracts is a reputed medicine for the treatment of various common diseases . The extracts of this plant i.e. ethanol and acetone have high antimicrobial activity against H. pylori (Safavi et al. 2015).

Daucus Carota Commonly Known As Carrot In Pakistan Has Potential Activity Against H.Pylori

The in vitro anti-H. pylori properties of 60 different commercial essential oils were examined in a study. bacteria treated with carrot seed oil shows marked inhibition of H. pylori viability. different tested essential oils which exhibited the strong anti-H. pylori activities contains Carvacrol, isoeugenol, nerol, citral and sabinene as pure constituents. In the group of treated animals infected with H.pylori mice did not result in significant decreases in the bacterial loads after treating with carrot seed oil compared with those in the control group (Bergonzelli et al., 2003).

Eucalyptus toerellina commonly known blue gum in pakistan posses high anti H.Pylori Activity

When the susceptibility of H.pylori to E.toerellina was measure it shows that six strains of H.pylori is susceptible to it and it follow-up the gastroprotection. The data of this work indicate that the hexane extract of the leaves showed the most potent activity against H. pylori. Tannins and saponins found in e. torelliana posses potent anti-h. pylori properties and offer protection against ulcers (Adeniyi et al., 2009).

Table 1: List of the tested plant Botanical names, tested parts and Extract uses in Pakistan for medical use.

Botanical name	Source	Part used	Extract
<i>Mallotus philippinesis</i>	Pakistan	Covering fruit	Aqueous ethanol 70 %
<i>Curcuma amada</i> Roxb	Pakistan	Rhizum	Ethanol
<i>Myristica fragrans</i> Houtt.	Pakistan	Seed	Ethanol/methanol
<i>Psoralea corylifolia</i>	Pakistan	Seed	Ethanol
<i>Terminalia chebula</i>	Pakistan	Fruit	Ethanol
<i>Berginia ciliata</i> (Haw.) Sternb./Schapur/SP-43	Pakistan	Root	Decotion
<i>Polygonum tataricum</i> L./Khobro/SP-144	Pakistan	Seed	Powder
<i>Fagopyrum esculentum</i> Moench, Meth. /Bro/SP-	Pakistan	Seed	Powder
<i>Hordeum vulgare</i> L./Nus/SP-154	Pakistan	Seedlings	Decotion
<i>Acantholimon lycopodioides</i> (Girad) Boiss./Choqmandoq/SP-68	Pakistan	Flowers	Decotion
<i>Vicia faba</i> L./Naqstarn/SP-82	Pakistan	Seed	Seed is cook
<i>Hippophae rhamnoides</i> subsp. <i>turkestanica</i> Rousiss/Karsoq/SP-70	Pakistan	Fruit and leaves	Fresh fruit is eaten

CONCLUSIONS

Resistance to synthetic drugs among strains of *H.pylori* is a global concern for healthcare stakeholders. Use of alternative therapy such as plants based active components may hold the key to this in addition to providing more benefits which and less side effects, which definitely warrants more research and standardization of such therapy. Present investigation shows promise in such an untapped field provides scientific support and evidence towards the use of such compounds in treatment of stomach related diseases. It is therefore viable to conclude that such plants can be explored to be used as therapy against *H. Pylori* and to isolate other urease inhibitory agents we reported here in potential in vitro anti *Helicobacter pylori* activity of medicinal plants from Pakistan that are used to cure GI disorders. As *Helicobacter pylori* is widely accepted to be the causative agent for numerous GI diseases including dyspepsia, our study not only partially validates the idea of exploring and using plant based compounds in gastric disease but lays stress on further scientific research to tap this territory for potential life changing drugs for future development and to provide rationale for its use.



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