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Review Article

A REVIEW ON *HELICOBACTER PYLORI*: ITS BIOLOGY, COMPLICATIONS AND MANAGEMENT

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ABSTRACT

Helicobacter pylori (HP) emergences in gastro intestinal tracts of human beings are one of the major health concerns in recent times. The infection in the later stages can lead to peptic ulcers and gastric cancers. HP is second commonly encountered pathogen in humans next only to *Streptococcus.* The virulence of the pathogen is further strengthened by its capability in forming biofilms. There are various therapies to treat this infection which are classified as first line, second line and third line, but are not free from the serious antibiotic resistances which normally are encountered in treating bacterial diseases. Vowing to above reason, it is necessary to search for alternative management strategies with lesser side effects and complications like plant based drugs and designer nutraceutical products which includes herbal extracts, probiotics, phytomedicines, antioxidants, essential oils, flavonoids so-on. In the present study, we have reviewed on the thorough understanding on biology, complications and management of *H. Pylori* and its infections.

Keywords: Peptic ulcers, *H. Pylori,* Biofilms, Cag A, Vac A, Phytomedicines.

INTRODUCTION

Helicobacter pylori a microaerophilic, gram negative bacteria belonging to the family Helicobacter, is found mainly in the gastro intestinal tract of human beings. It infects about 50% of world population, out of which 10% develop peptic ulcer and around 1% develop gastric cancer [1]. Studies done by Marshell and Robin have provided vital hints in its role in the development of gastritis and peptic ulcer diseases. *H. pylori* infection varies according to the geographical conditions and different population. Among infected people only few develop gastritis depending upon expression of specific virulence factor by bacteria and host immune response [2]. *Helicobacter pylori* infection is mediated by the number of factors such as flagella, heamagglutin, BabA gene expression and virulence factors (CagA, Vac) [3]. *H. pylori* can form a biofilm on gastric epithelial cells which contribute in adapting to the changing environment in gastric mucosa, helping in longer survival and fight against immune system [4] *Lux S* gene helps in quorum sensing in biofilm [5]. These are the reasons for an initiation of gastritis which if not treated may lead to clinical complications like peptic ulcer, gastric cancer, gastro-oesophageal diseases, non-ulcer dyspepsia and extra-intestinal diseases [6]. Numerous diagnostic methods exist to detect infection that includes endoscopic and non-endoscopic methods, Technique used may be direct (culture, microscopic demonstration) or indirect methods (urease test, stool culture, PCR) [7]. To overcome this infection, different treatment regimes are used which includes the first line therapy (concomitant therapy and hybrid therapy), second line therapy bismuth-containing quadruple therapy and levofloxacin-containing therapy and third line therapy(culture-guided therapy) [8]. Severe genetic variability shown by *H. pylori* bestows it with antibiotic resistance owing to search for alternative safer drugs.

Morphology

The basic morphology of *H. pylori* have specific feature of S-shape with polar, sheathed flagella, which are varied by its size and the number of spirals/turns [9]. Certain aspects of the ultra-structural detail of the *Helicobacter*, e. g., sheathed flagella and surface urease, have been implicated in their ability to survive in hostile environments such as the acidic gastric mucosa and ability to induce disease. *Helicobacter pylori in vivo* and under optimum *in vitro* condition is an S-shaped bacterium with 1 to 3 turns, 0.5 ×5 µm in length, with a tuft of 5 to 7 polar sheathed flagella [10].

Biofilm formation by *H. pylori*

Biofilms are formed when bacteria transform from planktonic type to a form, in which organisms are firmly adhered to abiotic and biotic surfaces and these biofilms play an important role in bacterial virulence. *H. pylori* has the ability to form biofilm in the gastrointestinal tract. It is the second most common organism to cause human infection next to *Streptococcus* mutants [4]. Flagella help in adherence of *Helicobacter pylori* to gastric epithelial cells, *LuxS* gene is responsible for the production of auto inducer2(AI-2) which is the quorum sensing molecule helping the organism to communicate with each other to know about their cell density and an external environment. Vir B protein helps bacteria to spread and form biofilm over the surface [11].

Biofilm biomass mainly consists of extracellular polymeric substances (EPS) matrix up to 90% and is a mixture of EPS, cDNA, proteins and some amount of other macromolecules [12]. The EPS helps *Helicobacter pylori* in protecting itself against adverse conditions particularly pH changes [13]. According to studies done by Hideoyonizawa *et al.* [12] 'TK1402' strain of *H. pylori* showed significantly higher level of biofilm formation compared to other strains and Percival *et al.*, referred biofilm's role in longer survival of the bacterium by fighting against an immune system of host and chemotherapeutics [5].

Gastric *Helicobacter* species

Gastric *Helicobacter* species have adjusted to the harsh condition found in gastric mucosal surface, the stomach of all mammals can be colonized by members of genus *Helicobacter* [14] as indicated in table 1.

Pathogenesis of *Helicobacter pylori*

Colonization of *H. pylori* alone will not cause diseases by itself, but several factors contributes to this like smoking, alcohol, Non-steroidal Anti-inflammatory drug, Proton Pump Inhibitors and host factors like gene polymorphism and immune response[16]. *H. pylori* infection can be transmitted form one person to other by three basic mode *viz.,* iatrogenic mode, faecal-oral mode, oral-oral mode [17]. Adhesion of *H. pylori* is highly specific to gastric epithelium [18].

Outer membrane protein BabA encoded by gene *babA2* binds to blood group antigen lewis^b present on an epithelial cell membrane. *H. pylori* with babA2$^+$ strain associated with the increase in risk of duodenal ulceration and gastric adenocarcinoma in association with VacAS1 and Cag A strains increasing the risk of peptic ulcer and gastric cancer [19].

Virulence factors of *H pylori*

Cag A

The main virulence determinant of *H. pylori* is a pathogenicity island called Cag. Its pathogenicity island-positive strains have been closely associated with peptic ulcer and gastric ulcers [15]. Genes in the *cag* pathogenicity island encode a type IV secretion system through effector protein and CagA is translocated into the host cell cytoplasm [20].

Vac A

Vac A, the vacuolating cytotoxin encoded by the Vac A gene, a strong marker for *H. pylori* virulence which causes vacuolization of epithelial cells, disruption of the endo somal/lysosomal pathway, interference with cell signalling and the inhibition of T-cell proliferation [21]. Vac A, has mature 87-KDa monomer in *different H pylori* strains, but its cytotoxic activity has been shown to occur in only 50% of *H pylori* strains [20]. Patients identified as VacA seropositive were shown to have an increased risk of gastric carcinoma that occurred in conjunction with the s1m1 polymorphism [22].

Biochemical characteristics of *H. pylori*

H. pylori infection is usually life long as it has the capacity to adjust to natural habitat like mucus layer over the gastric epithelial cell. *H. pylori* lack several pathways which are commonly present in less specialized bacteria like enteric bacteria [23]. The organism can be cultured only in specific chemically defined medium containing amino acids arginine, histidine, iso leucine, methionine, phenylalanine and valine [24]. *H. pylori* are urease, catalase, oxidase positive [25] and is microaerophilic utilizing O_2 as terminal electron acceptor [24]. Ammonia plays very important role in both nitrogen metabolism and acid resistance. Ammonia production is mainly through high urease activity, which acts as key component in nitrogen metabolism, acid resistance and virulence factor [26, 27]

Diagnosis of *H. pylori*

Diagnostic tests for *H. pylori* infection include endoscopic and nonendoscopic methods. The techniques used may be direct (culture, microscopic demonstration of the organism) or indirect methods (using urease, stool antigen, or an antibody response as a marker of disease)[7]. The choice of test depends to a large extent on availability, cost and includes a distinction between tests used to establish a diagnosis of the infection and those used to confirm its eradication.

Culture methods

H. pylori may be routinely isolated by culture from human gastric biopsy samples. The organism requires a microaerophilic environment and complex media. Variety of basal media and different supplements has been proposed for isolation of the organism. However, Columbia Agar Base or Brain Heart Infusion (BHI) broth supplemented with blood or serum has been found adequate for culturing [7]. They typically grow best in freshly prepared moist media incubated in a warm (37 °C) atmosphere with 5%-10% CO_2, 80%-90%N_2 and 5%-10% O_2. The best specimens for isolation of *H. pylori* are biopsy samples obtained during endoscopy.

Urease test

H. pylori are known for the production of urease enzyme. The test involves utilization of *H. pylori* urease to identify active organisms [28]. Sensitivity of greater than 93% and specificity of 98% is reported for urease testing.

Urea breath test

Urea breath test is considered as the gold standard for the diagnosis of *H. pylori*. This test gives accurate and proper result compared to other tests. In this test ^{13}C or ^{14}C urea is fed to patient where in stomach it's broken down by urease enzyme of *H. pylori* [29]. Inactive coccoid form of *H. pylori* in stomach will not give the positive urea breath test.

Stool culture

One of the suspected routes of transmission of *H. Pylori* is oro-fecal making it a candidate to be isolated from faecal sample. *H. pylori* are susceptible to biliary salts and there is a great competition with other numerous bacteria present in the stool. Dore *et al.*[30] have reported successful isolation of *H. pylori* after treating with bile sequestering agent cholestyramine before plating on culture medium. A meta-analysis revealed that the global sensitivity and specificity of stool antigen tests are 94% (95%CI: 93-95) and 97% (95%CI: 96-98), respectively.

PCR

PCR is used not only for the detection of bacterium but also for characterization of pathogenic genes and specific mutations associated with antimicrobial resistance. The highly conserved 16S rRNA gene in bacteria exhibits sequences which are shared by different species of *Helicobacter*. *H. pylori* specific DNA in these specimens, target genus specific gene (C97 and C98) and conserved region of Vac A gene. Rocha *et al.* and Cirak *et al.* suggested that any specimens should be designated positive for *H. pylori* when there is amplification of two different conserved target genes [31, 32].

Complications of *H. pylori* infection

Gastritis: is a condition where stomach lining is inflamed. There are three stages of gastritis acute, chronic and atrophy phase. Acute phase is subclinical stage, where *H. pylori* penetrate through viscid mucous layer reaching epithelial cell where it multiplies. Epithelial cells react to this by mucus depletion, cell exfoliation and compensatory regenerative changes [33] If immune response fails to eradicate the infection, in next 3 or 4 weeks there will be change from acute phase to chronic phase. In this phase the production of cytokine and specific anti-*H. pylori* antibodies by B-cell proliferation and plasma cell differentiation results in production of Ig-M antibodies and complement fixing antibody. But still if it fails to eliminate infection [34]. Atrophy is the last stage of gastritis where loss of glandular tissue takes place due to repeated or continuous mucosal injury leading to progressive mucosal damage, leading to erosion or ulceration of the mucosa [35].

Peptic ulcer

H. pylori causes an inflammatory response in gastric mucosa by inducing epithelium derived cytokines mainly interleukin 8 (IL8) and IL 1β [36] by the action of neutrophils, macrophages, lysosomal enzymes, leukotrienes (LT), and reactive oxygen species hampering mucosal defence and initiating the immuno pathogenetic process of ulcer formation. Urease catalyses production of ammonia, when there is an increase in concentration leading to the formation of toxic complex such as ammonic chloride, along phospholipases A and C impairs the phospholipid-rich layer in the mucosa that maintains mucosal hydration and integrity of the gastric epithelial barrier leading to ulcers [37].

Gastric cancer

GC is the second cause for cancer related death worldwide, accounting nearly 11% of cancers in male and 7% in female [38]. *H. pylori* infection is recognized as type 1 carcinogen by International Agency of Research on cancer [39]. Multiple mechanisms are involved in carcinogenesis, among them important are production of relative oxygen species that causes DNA damage and mutation. Hypermethylation of gene promoter (CpG) island is associated with *H. pylori* infection and deregulation of many pathways; among them some are important pathways such as p53 pathway,PI3 kinase/Akt pathway, Wnt pathway and NF-κB pathway [40].

Gastroesophageal reflux diseases (GERD)

Is a multifaceted disorder where gastric acid coming up from the stomach into the oesophagus [41]. The Montreal consensus

conference defined (GERD) as "a condition which develops when the reflux of gastric contents causes troublesome symptoms and/or complication" [42]. GERD symptoms are seen in 25-40% of the general population, the relationship between GERD and *H. pylori* are documented by many researchers and infection varies by geographic location [43].

Non ulcer dyspepsia or functional dyspepsia

A symptom of upper gastrointestinal distress, without any identified structural abnormalities during diagnosis [15]. Uninvestigated dyspepsia is defined as presence of dyspepsia symptoms for which no further diagnostic evaluation has been performed [44].

There are many possible causes for this, like lifestyle factors, stress, altered visceral sensation, increased serotonin sensitivity, alteration in gastric acid secretion, gastric emptying and psycho-social impairment. *H. pylori* infection may be one of the factors among multifactorial etiology of the diseases [45]. Studies carried out in Kuala Lumpur by Goh *et al.* reveals that *H. pylori* was found in 31.2% of the non-ulcer dyspepsia patients [46].

Table 1: Characteristics of some selected *Helicobacter* species [15]

Species	Primary mammalian host	Pathology
Gastric Helicobacter spp. H. pylori	Human, primate	Gastritis, peptic ulcer diseases, gastric adenocarcinoma, MALT lymphoma
H. felis	Cat, dog, mouse	Gastritis in natural host; may cause peptic ulcers or gastric adenocarcinoma in mouse
H. mustelae	Ferret	Gastritis, peptic ulcer diseases, gastric adenocarcinoma, MALT lymphoma
H. acinonychis	Cheetah, tiger, other big cats	Gastritis, peptic ulcer diseases
H. heilmannii	Human, dog, cat, monkey, cheetah, rat	Gastritis, dyspeptic symptoms, MALT lymphoma
Enterohepatic Helicobacter spp. *H. hepaticus*	Mouse, other rodents	Proliferative typhlocolitis, hepatitis, hepatocellular carcinoma

Table 2: An outline of different therapeutic lines against *H. pylori* infection [8]

First line	Second line	Third line
If CLR-R*>20%		
Concomitant (10 days PPI**standard dose),clarithromycin (500 mg), amoxicillin(1g) and metronidazole(500 mg) Or Sequential (5days dual therapy: PPI(standard dose) and amoxicillin (1g) fallowed by a 5-day triple therapy with a PPI(standard dose), clarithromycin (500 mg) and metronidazole (500 mg)	Levofloxacin-based triple therapy(10 days for levofloxacin(500 mg), amoxicillin (1g) and a PPI (standard dose)	Quadruple 10 days rabeprazole(20 mg),bismuth subcitrate (300 mg), amoxicillin (500 mg) and levofloxacin(500 mg) Or Quadruple (7days lansoprazole(30 mg), tripotassium dicitratobismuthate(240 mg), furazolidone (200 mg) and tetracycline (1g).
If CLR-R<20%		
Hybrid (dual-concomitant) (7days dual therapy: PPI (standard dose) and amoxicillin (1g) followed by 7days concomitant quadruple therapy: PPI(standard dose), amoxicillin (1 g), clarithromycin(500 mg) and metronidazole (500 mg)	Levofloxacin-based triple therapy (10 days for levofloxacin(500 mg),amoxicillin(1g), and a PPI(standard dose)	Quadruple 10 days rabeprazole(20 mg), bismuth subcitrate(300 mg),amoxicillin(500 mg),and levofloxacin(500 mg) Or Quadruple 7 days lansoprazole(30 mg), tripotassium dicitratobismuthate(240 mg),furazolidone (200 mg) and tetracycline (1g)

CLR R=Clarithromycin resistance. **PPI= proton pump inhibitor. **Standard empirical third line therapy is lacking.

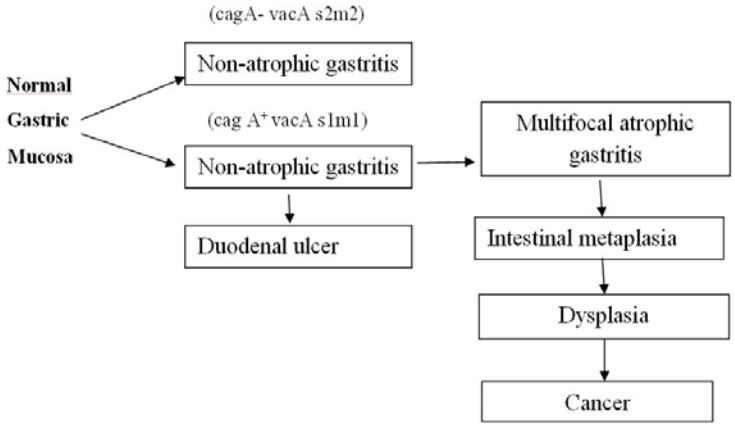

Fig. 1: Clinical manifestation of *H. pylori* infection leading to cancer [48]

Extra-intestinal diseases

The *H. pylori* infection has association with other diseases along with intestinal diseases because proinflammatory nature of *H. pylori* inflammation could be the common and important feature of pathogenesis. The association of many diseases with *H. pylori* proposes that there would be a common pathway existing in all the conditions [47]. These includes cardiovascular diseases, hepatobiliary diseases, respiratory tract disorder like laryngeal cancer, lung cancer, dermatological disorder like chronic urticaria, haematological disorder like immune thrombocytopenic purpura, henoch-schonlein purpura, iron deficiency anaemia, cobalamin deficiency and appetite regulation [15].

However further research should be carried out in detail to draw a proper conclusion between *H. pylori* infection and above diseases [6].

Treatments for *Helicobacter pylori* infection

Presently there are three main therapies followed by clinicians in treatment of *H. pylori* infections: first line, second line and third line therapy [8].

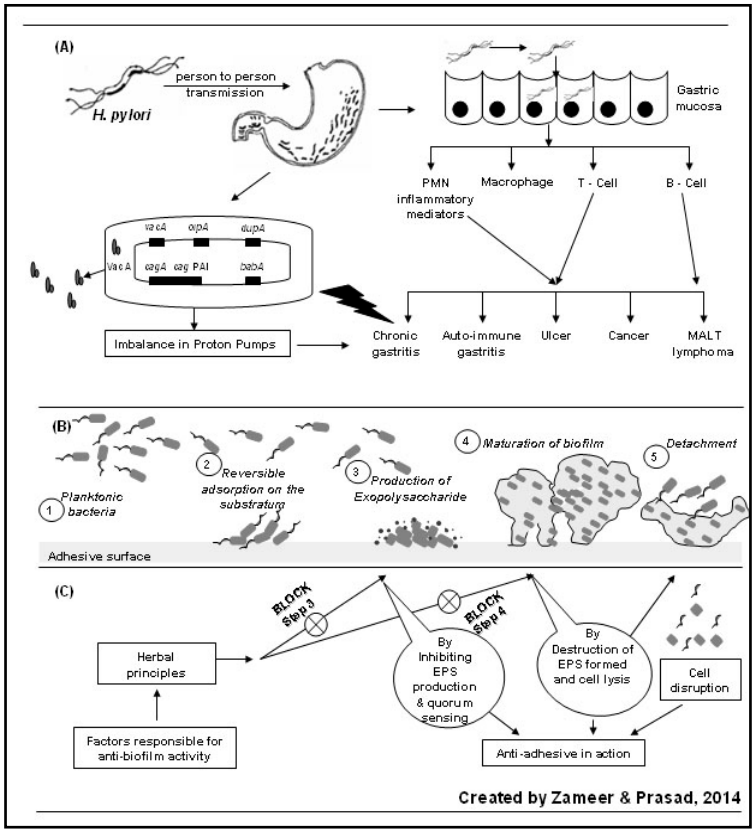

Fig. 2: Overview on *Helicobacter pylori*: Biology, Complications and Management-(A). Interaction of the *H. pylori* with host, possible consequences and complications. (B). Stages of Biofilm development. (C). Herbal management of pathogenesis and possible target mechanism [80, 81]

First line therapy

First line therapy is a combination of PPI (proton pump inhibitor) along with antibiotics amoxicillin or metronidazole and clarithromycin[49]. A study suggested that eradication rate of standard triple therapy were more than 90% [50] but recently the efficacy is decreased worldwide due to increased rate of clarithromycin resistance of *H. Pylori* [51]. This is considered as main cause for failure in first line therapy [52]. First line therapy involves three methods concomitant therapy, sequential therapy, hybrid therapy [53].

Second line therapy

First line therapy approximately failed in 20% of patients, making way for second line therapy [54]. Basically second line therapy is a quadruple therapy that can be divided into two different regimes, with and without bismuth salt, bismuth based quadruple therapy consisting of a PPI, bismuth, tetracycline and metronidazole [55]. Bismuth based therapy showed no significant increase in side effect other than dark stool [56]. Levofloxacin based therapy showed 81% efficacy when study was conducted in Spain with 300 patients in 10 days trial [57] but there was increase in rate of fluoroquinolones resistance among *H. pylori* strains [58] leading to limit the use of levofloxacin in *H. pylori* eradication in second line therapy (table 2).

Third line therapy

Patients who are failing in first and second line therapy are suggested for third line therapy (table 2). An international guideline recommends the culture-guided approach or an alternative therapy based on local antimicrobial resistances [59]. The most commonly used antibiotic are rifabutin and furazolidone. Furazolidone is also used in third line therapy, when study was conducted with 10 patients who failed in first-line, second-line and rifabutin-based therapy showed 60% eradication used along with amoxicillin and PPI [60]. A study among 94 consecutive population showed>90% treatment efficacy when they prescribed regimen after carrying out susceptibility test [61]. Currently this approach is carried out in specialist centres with research interest and expertise in treatment.

Adjuvant therapy

Adjuvant therapies may show added benefits in eradication of *H. pylori* infections. One of the studies conducted in 2008, using probiotics along with *H. pylori* eradication therapy showed no side effects and increased the rate of eradication [62]. Vaccination has been proposed for eradication of *H. pylori* infection which is still in phase I trial with relatively good success [63]. So to overcome the problem of antibiotic resistance of *H. pylori* new therapeutical strategies should be developed [8].

Herbal drugs for the management of *H. Pylori*

Many infections can be treated by non-antibiotics. These non-antibiotic therapies for treating *H. pylori* infections includes herbal extracts, probiotics, phytomedicines, antioxidants, flavonoids, essential oils, terpenoids so-on [64]. Many medicinal plant products, including apple peel polyphenol, tea product, garlic extract, finger root extract possess *anti-H. pylori* activity and management of induced gastric inflammatory effect [65]. The entire mechanism is been depicted in fig. 2.

Natural antioxidants are of immense nutraceutical value. The medicinal properties of many herbal plants are because of presence of natural antioxidants. Polyphenols and flavonoids which are present in plants decreases acid mucosal secretion, inhibits the production of pepsinogen, promotes gastric mucosa formation and decrease ulcerogenic lesions [66]. Some of the herbal plants, berries, fruits which are widely used against *H. pylori* induced gastric ulcers are listed below.

Fruits

Apple (*Malus domestica)*

M. domestica fruit and its extracted phenolic acids possess gastroprotective activity by reducing neutrophil infiltration in gastric tissue and antioxidant activity by reducing gastroendothelial cell injury. Apple peel and fruit which contains polyphenols shows gastroprotective activity and also inhibit production of inflammatory cytokines and lipid peroxidation [67].

Cranberry *(Vaccinium macrocarpon)*

As per Anna *et al.*, cranberry juice at 20% concentration fortified with sodium hydrocarbonate or calcium have shown promising results in the elimination of *H. pylori* [64].

Gooseberry *(Phyllathus emblica)*

Phenolic present in the fruit of P. emblica possesses antioxidant activity and cryoprotective activity through which it protects against gastric ulcer. Gallic acid rich extract have been reported with excellent healing property on gastric ulcer. Fruit ethanol extract have shown anti *H. pylori* activity in *in vitro* conditions [68].

Pomogranate (*Puccinia granatum)*

The peel extract of *P. granatum* has antioxidant activity which protects gastric mucosa & gastric ulcer. The tannins from fruit of *P. granatum* are known to prevent the formation of gastric ulcer [69].

Raspberries *(Rubus idaeus)*

Ellagic acid, the main constituent of raspberries is a powerful disease fighting substance and it was demonstrated that it could kill several *H. pylori* strains. Ellagic acid is very stable substance which does not degrade while storage or cooking [68].

Red wine

Red wine possesses antibacterial activity against *H. pylori* because of the presence of resveratrol. Resveratrol has shown a remarkable inhibitory effect on *H. pylori* urease activity with MIC range of 6.25-25ug/ml [69].

Plants

Berberines

An active constituent of *Berberis vulgaris* is an alkaloid isolated from root and bark, has been effective in preventing *H. pylori* infection [66]

Cinnamon

It is demonstrated that extracts of cinnamon helps in fighting against *H. pylori* by inhibiting bacterial urease enzyme inside stomach [70].

Curcumin

Curcumin, an active constituent of *Curcuma longa* (turmeric) has a great therapeutic potential against *H. pylori* associated gastroduodenal diseases and also was very effective in eradicating *H. pylori* from infected mouse stomach [71].

Garlic (*Allium sativum)*

Garlic contains thiosulfonates, terpenoids, steroids and other phenols which may be responsible for its medicinal value. It is reported that *H. pylori* is susceptible to 40 ug/ml of garlic extract [72].

Green tea

Green tea one of the popular beverages worldwide has shown its antibiotic activity against *H. pylori in vitro* and *in vivo*. Antioxidant catechin present in green tea has shown excellent antibacterial activity against *H. pylori*. Epigallocatechin gallate showed strongest activity with MIC = 8 ug/ml for 50% of the tested strain. Effect of green tea is dose dependent [73].

Ginger *(Zingiber officinale)*

Gingerols are group of structurally related polyphenolic compounds isolated from ginger are found to be active constituent and inhibits the growth of CagA+ strains. MIC range of 0.78 to 12.5ug/ml was significantly active against CagA+ strains of *H. pylori* [74].

Liquorice (*Glycyrrhiza glabra)*

Liquorice has been used in traditional ways in many countries for the management of *H. pylori.* The rhizomes and roots of *G. glabra* contain antimicrobial, antioxidant, antiadhesive, anticancer and anti-ulcer activities. Gutgard is an extract from *G. glabra.* This could reduce *H. pylori* gastric colonization significantly [69].

Nutmeg *(Myristica fragrans)*

Through various investigations it has been proved that *M. fragrans* seeds have very strong anti *H. pylori* activity *in vitro.* Dihydroguaiaretic acid which is isolated from aril of seed also showed a strong anti *H. pylori* activity. The major action of these seeds is suppression of acidity and volume of gastric secretion. An herbal formulation containing *M. fragrans* have remarkably inhibited gastric ulcer and hypersecretion in rats [75].

Honey

Manuka honey has shown bacteriostatic properties on *H. pylori* at a 50 mL/l concentration. According to Osato *et al.*, osmotic effect was shown to be the important reason for killing *H. pylori* [76].

Propolis

A mixture which is collected by honey bees from different plant sources to maintain the structural stability of the hive. Propolis is considered as natural antibiotic because of its high content of phenolic compounds. According to one of the reports 30% ethanolic extracts of propolis have inhibited the growth of several *H. pylori* clinical isolates *in vitro* through agar dilution, disc diffusion, agar-well diffusion methods [76].

Essential oil

Thyme oil and Eucalyptus oil

A study carried out by Esmaeili *et al.* for determining *anti-H. pylori* activity using essential oils of *T. valgaris* and *E. globulus* with *H. pylori* ATCC 700392, *T. valgaris* showed better inhibitory activity [77].

Mastic gum

Mastic gum derived from *Pistacia lentiscus* tree, has anticancer, antimicrobial activity [78] α-terpineol and (E)-methyl isoeugenol are the components present in Mastic gum contribute to anti-*H. pylori* activity as per the research conducted by Miyamoto *et al.*[79].

Carrot seed oil

(*Daucus carota*) researchers have proved among 16 different essential oil considered for anti-*H. pylori*activity, carrot seed oil exhibited better result followed by cinnamon bark oil [78, 79].

CONCLUSION

Gastric ulcer and cancers are the most prevalent gastrointestinal disorder, resulting from oxidative stress, *Helicobacter pylori* infection, up-regulation of proton potassium ATPase (PPA) activity,

down-regulation of gastric mucosal defense, etc. Further, the biotic and abiotic environment influences the efficacy with which *H. pylori* colonizes surfaces. The presence of microorganisms such as *S. epidermidis* and other general intestinal microflora can facilitate the colonization and persistency of *H. pylori* in the environment. The mechanism involved in these interactions remains unknown but we speculate that they are complex and it will be interesting to characterize the molecules involved in this interaction (80, 81). Currently, there is no human vaccine available against this pathogen. Acquisition of resistance to antibiotics would represent a major therapeutic problem. Thus it is very important to test for antibiotic resistance in food-borne and clinical isolates of *H. pylori* and to reconsider critically the use of antibiotics. A better understanding of these processes will have a significant impact on the research concerning the spread of infectious microorganisms in general and on food safety. With respect to above facts, the authors emphasize the role of phytochemicals as they offer better contribution to antiulcer/anti-*H. pylori* activity. Thus, suggesting the possible usage of bioactive which may find better application in ulcer management and ulcer therapy. The current review embarks, *H. pylori* as an organism which is much intelligent to be understood.

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CONFLICT OF INTERESTS

All authors declare no conflict of interest

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