IJPSR (2026), Volume 17, Issue 1 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 01 July 2025; received in revised form, 26 August 2025; accepted, 27 October 2025; published 01 January 2026

PHARMACOTHERAPEUTIC APPROACH IN *H. PYLORI* INFECTION: CURRENT INSIGHT

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Keywords:

H. Pylori infection, Pathophysiology, Diagnosis, First-line therapy, Concomitant therapy

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ABSTRACT: *Helicobacter pylori* (*H. pylori*) infection remains one of the most prevalent chronic bacterial infections globally, contributing significantly to the pathogenesis of gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer. Over the past few decades, treatment regimens have evolved significantly due to increasing antibiotic resistance, varied geographic eradication rates, and emerging evidence-based strategies. This review focuses on first-line, second-line, and rescue medications and offers a thorough summary of current pharmacotherapeutic approaches to *H. pylori* infection. Conventional triple therapy, once the gold standard, is now being replaced in many regions by bismuth quadruple therapy and concomitant regimens due to declining efficacy. The role of novel agents such as vonoprazan, rifabutin and metronidazole in enhancing eradication rates is also discussed. Furthermore, the importance of antibiotic susceptibility testing, patient compliance, and regional resistance patterns in tailoring individualized therapy is highlighted. This insight aims to support rational therapeutic decision-making and promote optimized clinical outcomes in the management of *H. pylori* infection.

INTRODUCTION: The discovery of *Helicobacter Pylori* species by Warren and Marshall not only introduce the whole new group of the bacteria to the science but also revolutionized our concept of gastroduodenal pathology and shifted global focus from pH to HP. The spiral-shaped bacteria *H. pylori* are found in the mucous layer of the human stomach. *H. pylori* can neutralise the acidity of its immediate surroundings in the stomach, but not the entire stomach, despite the fact that many bacteria cannot survive the stomach's acidic environment.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.17(1).65-74

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.17(1).65-74

Local neutralisation promotes bacterial survivability. This strategic location not only shields it from gastric acid but also from immune cells, which are typically unable to access the stomach lining despite gathering near infection sites. Furthermore, *H. pylori* actively weakens the local immune response, making it more difficult for the body to eliminate the infection [1, 2].

Worldwide, *Helicobacter pylori* infections are very common, particularly in low- and middle-income nations. According to the Centres for Disease Control and Prevention, nearly two-thirds of the global population carry this bacterium. Significant differences exist in prevalence rates between racial and ethnic groupings in the United States. According to data from 1999–2000, the infection rate was almost 64% among Mexican Americans, 52% among non-Hispanic Blacks, and 21% among

non-Hispanic Whites [3]. As a primary contributor to chronic gastritis, *H. pylori* is also linked to several serious gastrointestinal conditions in some individuals. These include peptic ulcer disease (PUD) affecting the stomach and duodenum, gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma [4, 5, 6]. Different phenotypes of habitual gastritis are convinced by complicated relations between host genetics, environmental variables, and bacterial acridity, leading to a variety of conditions associated with *H. pylori* infection [7, 8].

Giulio Bizzozero discovered *Helicobacter pylori* (*H. pylori*) as a helical bacterium in canine tummies in 1892 [9]. In 1983, Barry Marshall and Robin Warren gave them the name *Campylobacter pyloridis* because of their helical origins that act Campylobacter [10]. Goodwin *et al.* named it "*Helicobacter pylori*" in 1989 due to its spiral shape and wide presence in the stomach's pyloric region [11]. Over half of all people on the earth are infected with *H. pylori*, a small, spiral, S- shaped Gram-negative bacteria that's 0.5–1 µm wide, 2–4 µm long [12].

The United States' National Institute of Health declared in 1994 that as *H. pylori* may be the primary cause of peptic ulcer complaints, treatment should be sought. In 2005, Marshall and Warren received the Nobel Prize for their research on the physiology of *H. pylori* and how it contributes to gastritis and peptic ulcer disease [2].

As people age, *H. pylori* infections become more common. Socially and economically deprived societies develop at a faster rate [13]. Since, *H. pylori* can persist in the stomach and create chronic inflammation, it can reject both acid and the susceptible system [14]. Some exploration has linked *H. pylori* infection to the malabsorption of vital micronutrients, which may ultimately affect malnutrition in some populations [15].

Helicobacter pylori (*H. pylori*) is a helical-shaped, gram-negative bacterium that is further current in developing countries and may infect up to 50 individuals worldwide [16, 17, 18]. The most common cause of gastric carcinoma, stomach cancer, peptic ulcer, and habitual or atrophic gastritis is *H. pylori* [19]. Nevertheless, compared to grown-ups, children and adolescents have these issues less frequently [20]. *H. pylori* infections are generally contracted in early childhood and don't go down without remedy [21]. Chinese researchers conducted a Phase 3 clinical trial in children that proved an oral *H. pylori* vaccine made from recombinant proteins was both safe and effective in preventing infections, potentially helping to lower *H. pylori* rates in communities [22]. Class 1 carcinogen *Helicobacter pylori* is connected with a threat of gastric mucosa-associated lymphoid towel (MALT) tubercles and gastric cancer [23, 24]. *Helicobacter pylori* infection is implicated in approximately 89% of gastric carcinomas and is associated with 5.5% of the worldwide cancer burden [25, 26]. It's the only type of bacteria that scientists have confirmed can cause cancer [27].

Pathophysiology: *Helicobacter pylori (H. pylori*) may colonise the human stomach mucosa for an extended period of time, thanks to its arsenal of virulence factors that allow it to evade the host immune response. These components include urease, which neutralises stomach acid, adhesins, which enhance bacterial attachment to gastric epithelial cells, high-temperature requirement A (HtrA) serine protease, which compromises epithelial integrity, and the exotoxins CagA and VacA **Fig. 1** [28, 29].

CagA (cytotoxin-associated gene A), a well-studied oncoprotein, enters gastric epithelial cells through a type IV secretion pathway. CagA alters signalling pathways within the host cell, promoting cellular proliferation, inflammation, and carcinogenesis [30]. VacA (vacuolating cytotoxin A) exacerbates tissue damage by inducing vacuolation, immune suppression, and mitochondrial dysfunction [31]. The presence of CagA and VacA is linked to more serious clinical outcomes, such as peptic ulcer disease and stomach cancer [32].

Recent research suggests that *H. pylori* infection causes epigenetic changes, specifically downregulation of DNA repair proteins such as PMS2 and ERCC1, particularly during the progression to dyspepsia [33]. Furthermore, proteins implicated in base excision and mismatch repair MLH1, MGMT, and MRE11 are epigenetically reduced in infected people [34].

Impaired DNA repair raises the risk of mutations and genomic instability, both of which are linked to stomach cancer. Furthermore, *H. pylori* has been demonstrated to cause hypermethylation of CpG islands in tumour suppressor gene promoter regions as well as modify microRNA production, which contributes to gene expression dysregulation [35].

Two pathways are hypothesised to explain *H. pylori*-induced carcinogenesis. One is linked to greater levels of reactive oxygen species (ROS) and higher rates of stomach epithelial cell mutation.

According to the "peri-genetic pathway," cytokines like IL-6 and TNF-α can affect cellular behaviour, such as adhesion and migration, without necessitating genetic alterations in tumour suppressor genes [36, 37]. These alterations cause cellular transformation, tissue invasion, and, eventually, cancer.

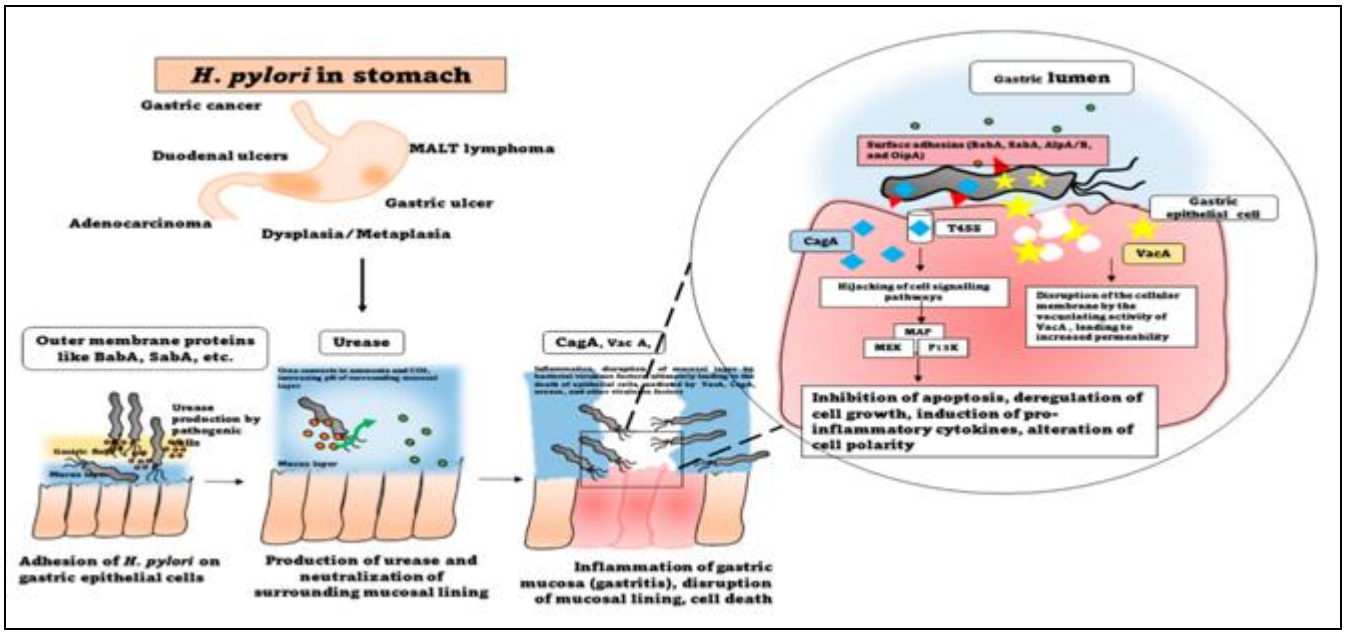

FIG. 1: PATHOPHYSIOLOGY OF *H. PYLORI* INFECTION

Sign & Symptoms: The majority of persons infected with *H. pylori* never experiences any symptoms. Whys many people do not exhibit symptoms is unknown. However, some individuals might have higher innate resilience to the negative effects of *H. pylori*. When *H. pylori* infection symptoms do manifest, they are usually associated with gastritis or a peptic ulcer and can include [38]:

- Discomfort or scorching sensation in your abdomen
- Stomachache that could worsen if you do not have food in your stomach
- Emesis
- Appetite decline
- Frequently burping
- Bloating
- Inadvertent weight reduction

Diagnosis: There are a number of tests and procedures used to determine whether you have *Helicobacter pylori* (*H. pylori*) infection. To find *H. pylori*, testing is necessary. After therapy, Retesting is essential to ensure that *H. pylori* has been eliminated. Tests can be performed with an upper endoscopy examination, a breath test, and a stool sample.

Stool Examinations:

Stool Antigen Examination: The most used stool test for identifying *H. pylori* is this one. The test searches the faces for proteins, or antigens, linked to *H. pylori* infection.

Stool PCR Examination: The stool polymerase chain reaction (PCR) test can be used to identify an *H. pylori* infection in a laboratory setting. The test can also identify changes that could render *H. pylori* resistant to antibiotic therapy. This test is not available at all medical facilities and is more costly than a stool antigen test.

Test of Breath: In order to participate in a breath test (also known as a urea breath test), you must swallow a tablet, drink, or pudding containing tagged carbon molecules. The solution will react with the stomach bacteria and release carbon if you have an *H. pylori* infection. When you exhale, the carbon is released since your body has absorbed it. The amount of carbon released is measured by blowing into a bag. Carbon molecules are detected by a specialized apparatus. Both adults and children over the age of six who are able to participate in the test may use it.

Test of Scope: A scope test, also referred to as an upper endoscopy exam, may be performed by a medical professional. This test may be carried out by your physician to look into symptoms that could be brought on by illnesses like gastritis or peptic ulcers that could be brought on by *H. pylori*. During this test, you will be given medication to help you relax. An endoscope, a long, flexible tube with a tiny camera within, will be introduced by your healthcare provider during the examination. Following that, the tube travels through your stomach, oesophagus and duodenum, the first portion of your intestine.

This equipment allows your healthcare provider to see any problems with your upper digestive tract. Your healthcare provider may also take tissue samples (biopsies). We look for the presence of *H. pylori* in these samples. *H. pylori* infection is typically detected by this test when it is linked to other digestive problems, making it more intrusive than a breath or stool test.

This test can be used by medical professionals to look for additional digestive disorders and to do extra testing. Additionally, if the initial round of medications tried failed to eradicate the infection, they might use this test to pinpoint the precise antibiotic that would be most effective in treating *H. pylori* infection. This test may be repeated after *H. pylori* treatment, depending on the results of the initial endoscopy or if symptoms persist.

Test-related Factors: Antibiotics have the potential to compromise test accuracy. Retesting is often done only, if at all possible, after four weeks without taking antibiotics. The accuracy of these tests may also be impacted by acid-suppressive medications like bismuth subsalicylate (Pepto-Bismol) and proton pump inhibitors (PPIs).

The accuracy of these tests may potentially be impacted by drugs called histamine (H-2) blockers, which lower stomach acid. You may need to cease taking your drugs for up to two weeks before to the test, depending on what kind of medication you use [39, 40, 55].

Eradication Regimens [41-50, 55]:

Proton Pump Inhibitors (PPIs): PPIs play essential parts of practically all *H. pylori* eradication programs. They work by blocking the proton pump, or H/K ATPase enzyme, in the parietal cells of the stomach, which results in:

1. A significant and long-lasting decrease in the secretion of gastric acid.
2. Raising the stomach pH (for the best antibiotic effectiveness, aim for a pH > 6).

Improve the stability and effectiveness of antibiotics, particularly those that are acid-labile, such as clarithromycin and amoxicillin. Stop bacterial growth, which forces *H. pylori* into a more replicative stage and increases its susceptibility to drugs. Begin prior to or during the course of antibiotics, which is typically 10–14 days. Excessive acid suppression may alter the gastric flora, even though short-term use in *H. pylori* therapy is typically safe. PPIs used in treatment of *H. Pylori* infection are given in **Table 1.**

TABLE 1: COMMONLY USED PPIS IN H. PYLORI TREATMENT

PPI	Typical Dose	Features
Omeprazole	20–40 mg BID	First-generation PPI, widely available
Esomeprazole	20–40 mg BID	S-isomer of omeprazole; more predictable action
Lansoprazole	30 mg BID	Rapid onset of action
Pantoprazole	40 mg BID	Lower potential for drug interactions
Rabeprazole	20 mg BID	High potency, less affected by CYP2C19 polymorphism
Dex lansoprazole	30–60 mg daily	Dual delayed release; less commonly used

[BID (twice daily) dosing is recommended during eradication therapy for better acid suppression]

Antibiotics:

Amoxicillin: Amoxicillin demonstrates high efficacy against *H. pylori* infections due to its low minimal inhibitory concentration ranging from ≤0.01 to 0.1 mg/L. Both laboratory studies and clinical applications show that Helicobacter pylori exhibits significant sensitivity to amoxicillin treatment. Amoxicillin, like other penicillin's, is used by inhibiting bacterial cell wall formation, resulting in cell death. At the stomach mucosa, amoxicillin has both systemic and topical effects. During oral therapy, amoxicillin is absorbed into the stomach juice and mucosa, but its efficacy in eliminating *H. pylori* is less than 20%. When administered alone, more than 2gm per day of amoxicillin does not raise the rate of *H pylori* eradication. However, the amount of amoxicillin in the gastric juice and its effectiveness in eradication both dramatically rise when omeprazole is added. It is speculated that this eradication enhancement is caused by omeprazole decreasing gastric secretions, increasing the intragastric concentration of amoxicillin to more than the minimal inhibitory concentration (MIC) of *H. pylori* and increasing stomach pH to reduce amoxicillin's minimum inhibitory concentration.

Clarithromycin: A macrolide antibiotic called clarithromycin is essential to first-line *H. pylori* eradication treatments. Bacteriostatic in nature, it prevents bacteria from synthesising proteins. A new family of macrolide antibiotics, clarithromycin is well absorbed from the gut and acid-stable. Clarithromycin offers an extended half-life of three to four hours compared to erythromycin, providing longer-lasting therapeutic effects. While both antibiotics share similar mechanisms of antibacterial action, clarithromycin demonstrates significantly superior potency specifically against *H. pylori* infections. Additionally, it is converted into a hydroxylated molecule in the liver, which also works well against *H. pylori*. Clarithromycin stands out as the most effective single-agent therapy for *H. pylori*, achieving eradication rates between 40% and 60%. The greatest eradication rate is achieved with frequent and high doses of clarithromycin. Regretfully, similar to metronidazole, clarithromycin taken as monotherapy may result in resistance. However, treatment adherence can be compromised due to the medication's tendency to produce an unpleasant metallic taste, which may lead patients to discontinue therapy prematurely.

Tetracycline: Broad-spectrum bacteriostatic antibiotics called tetracyclines bind to the 30S ribosomal subunit and stop bacteria from making proteins. These medications are mainly used together in multi-drug treatment protocols designed to eliminate *H. pylori* infections, particularly in salvage (rescue) therapy and bismuth-based quadruple therapy, which are used when normal therapies have failed. Because tetracycline resistance in *H. pylori* is still uncommon worldwide, it's a great option when levofloxacin or clarithromycin resistance is predicted. Similar to amoxicillin, this drug works well against *H. pylori* when applied topically and is stable at low pH. It can reach concentrations in the mucosa and gastric juice that are substantially greater than the established minimum inhibitory concentration (MIC). Tetracycline cannot completely treat an *H. pylori* infection when used alone, however there have been no reports of *H. pylori* resistance. This regimen permanently discolours developing teeth, hence pregnant women and children should not follow it.

Metronidazole: Among the nitroimidazole, metronidazole is substantially used to treat parasitic and anaerobic infections. It has become a common treatment for *H. pylori* infection throughout the past ten years. Although more than 70% of *H. pylori* isolates are responsive to metronidazole in Western nations, where it is rarely used, *H. pylori* eradication due to single-medication administration is rare. Indeed, in developing countries where metronidazole usage is more prevalent, studies have demonstrated that over 80% of *H. pylori* strains exhibit resistance to metronidazole.

Bismuth Salt: Essential elements of *H. pylori* eradication treatments are bismuth salts, primarily bismuth subsalicylate or bismuth sub citrate. In addition to having antibacterial and anti-inflammatory qualities, they shield mucosal membranes. When two antibiotics are administered together, the mean eradication rate increases significantly, reaching over 80%. Bismuth salt is used in first-line or rescue therapy. Particularly helpful in regions with high levels of metronidazole or clarithromycin resistance. Given the rise in

antibiotic resistance, bismuth salts are an essential and successful part of *H. pylori* eradication treatment. Their unique, multi-targeted mechanism makes them highly valuable, and they significantly improve eradication rates, even in difficult-to-treat cases. Bismuth one of the gold standards recommended by international guidelines like Maastricht VI and ACG 2022.

Current Recommended Regimens [41-50, 54, 56]:
PPI based Triple Therapy:

1. First-line in areas with <15%clarithromycin resistance.

Drugs: PPI (e.g., omeprazole) + Clarithromycin + Amoxicillin.

Dose: PPI (e.g., omeprazole)- 20–40 mg BID

Clarithromycin- 500 mg BID

Amoxicillin- 1 g BID

Duration: 10–14 days

2. Used mainly in penicillin-allergic patients (amoxicillin cannot be used).

Drugs: PPI (e.g., omeprazole) + Clarithromycin + Metronidazole

Dose: PPI (e.g., omeprazole)- 20–40 mg BID

Clarithromycin- 500 mg BID

Metronidazole- 500 mg BID

Duration: 10–14 days

Bismuth Quadruple Therapy: Bismuth salts (mainly bismuth subsalicylate or bismuth subcitrate) are key components of eradication regimens for *H. pylori*. First-line or rescue therapy. Bismuth does not induce bacterial resistance**.** Active against *H. pylori* and other GI pathogens. Promotes healing of gastric epithelium. Increases cure rates even with antibiotic resistance.

Drugs: PPI (e.g., omeprazole) + Bismuth subsalicylate /subcitrate + Tetracycline + Metronidazole

Dose: PPI (e.g., omeprazole)- 20–40 mg BID

Bismuth subsalicylate /subcitrate- 120–300 mg QID

Tetracycline- 500 mg QID

Metronidazole- 250–500 mg TID–QID

Duration: 10–14 days

Concomitant Therapy: Concomitant therapy is a non-bismuth-based, four-drug regimen used for the eradication of *H. pylori*, especially in regions where clarithromycin resistance is moderate to high. The probability of therapy failure owing to resistance is decreased by using multiple antibiotics with distinct targets.

PPI + Clarithromycin + Amoxicillin + Metronidazole (all 4 drugs together).

Higher eradication rates compared to triple therapy.

Useful when resistance patterns are unclear.

Drugs: PPI (e.g., omeprazole) + Clarithromycin + Amoxicillin + Metronidazole

Dose: PPI (e.g., omeprazole)- 20–40 mg BID

Clarithromycin- 500 mg BID

Amoxicillin- 1 g BID

Metronidazole- 500 mg BID

Duration: 10–14 days

Sequential Therapy: Sequential therapy is a treatment approach for *H. pylori* infection that uses two distinct phases of medication without bismuth compounds.

This method is designed to improve the success rate of eliminating *H. pylori* bacteria, especially in areas where the bacteria have developed resistance to clarithromycin (an antibiotic commonly used in *H. pylori* treatment).

It separates antibiotics into two steps:

First 5 Days: PPI + Amoxicillin.

Next 5 Days: PPI + Clarithromycin + Metronidazole.

Designed to overcome clarithromycin resistance partially.

Amoxicillin (First Phase): Disrupts bacterial cell walls, which prevents resistance to clarithromycin in the second phase.

Clarithromycin + Metronidazole (Second Phase): Dual action reduces risk of treatment failure, even if *H. pylori* is resistant to one of the two.

TABLE 2: STANDARD SEQUENTIAL REGIMEN

Days	Drugs Used	Dose
Day 1–5	PPI + Amoxicillin	PPI 20-40 mg BID , Amoxicillin 1 g BID
Day 6–10	PPI + Clarithromycin + Metronidazole (or Tinidazole)	PPI 20-40 mg BID, Clarithromycin 500 mg BID, Metronidazole 500 mg BID

Levofloxacin Based Triple Therapy: Levofloxacin-based triple therapy is a fluoroquinolone-containing regimen used primarily as Second-line (rescue) therapy after failure of first-line treatment, or First-line therapy in regions with low fluoroquinolone resistance. It substitutes clarithromycin or metronidazole with levofloxacin. After triple or bismuth quadruple therapy fails, levofloxacin-based triple therapy will be given.

Drugs: PPI (e.g., omeprazole) + Amoxicillin + Levofloxacin

Dose: PPI (e.g., omeprazole)- 20–40 mg BID

Amoxicillin- 1 g BID

Levofloxacin- 500 mg once daily (or BID)

Duration: 10–14 days

Rifabutin based Therapy (Rescue): Rifabutin-based triple therapy is a salvage (rescue) regimen used when two or more prior *H. pylori* eradication attempts have failed. Rifabutin-based triple therapy is an effective treatment plan for eliminating *H. pylori*, particularly inpatients with multiple prior treatment failures or antibiotic-resistant strains. While highly effective, it must be used cautiously due to potential hematologic toxicity and cost considerations.

Drugs: PPI (e.g., omeprazole) + Amoxicillin + Rifabutin

Dose: PPI (e.g., omeprazole)- 20–40 mg BID

Amoxicillin- 1 g BID

Rifabutin- 150 mg once or twice daily

Duration: 10–14 days

Novel Acid Suppressors: Vonoprazan-Based Therapy: Vonoprazan-based therapy is now considered the standard first-line eradication treatment for *H. pylori* in Japan, because of its high eradication rates and excellent acid suppression. It is also recommended in cases where clarithromycin resistance is present, typically in combination with amoxicillin ± metronidazole, to overcome reduced clarithromycin efficacy. Patients who have failed PPI-based therapy or are known rapid metabolizers of PPIs may particularly benefit from vonoprazan, as it offers more consistent acid suppression regardless of CYP2C19 genotype**.** Additionally, vonoprazan can be effectively used as a rescue option after previous treatment failures due to its improved pharmacokinetic profile. However, its use in patients with penicillin allergy is generally not recommended unless customized regimens are considered, as most vonoprazan-based therapies rely on amoxicillin as a core component.

Drugs: Vonoprazan + Amoxicillin + Clarithromycin

Dose: Vonoprazan- 20 mg BID

Amoxicillin- 1 g BID

Clarithromycin- 500 mg BID

Duration: 7–14 days

Management of *H. pylori* Infection [53-56]: The management of Helicobacter pylori infection involves several antibiotic regimens, each tailored to the patient's local resistance patterns and individual clinical considerations. Triple therapy, which combines a stomach acid-blocking medication (PPI) with the antibiotic's amoxicillin and clarithromycin, was traditionally considered

the standard initial treatment approach. However, its eradication rate is now only around 70–80%, making it more suitable for regions with low clarithromycin resistance.

To improve outcomes in areas with moderate resistance, sequential therapy is often used. This treatment approach works in two stages: first, patients take an acid-reducing medication (PPI) along with amoxicillin, then in the second stage, they continue the acid reducer but switch to taking clarithromycin and metronidazole instead. This stepwise approach achieves eradication rates of about 85–92% by reducing the likelihood of resistance to clarithromycin. Bismuth quadruple therapy is the recommended treatment choice for patients living in areas where bacteria show strong antibiotic resistance or for those who are allergic to penicillin. This regimen combines a PPI with bismuth, tetracycline, and metronidazole, achieving eradication rates between 85% and 90% even in resistant infections.

Lastly, concomitant therapy which involves the simultaneous use of a PPI, amoxicillin, clarithromycin, and metronidazole has emerged as a flexible and highly effective option. It is particularly useful in diverse clinical scenarios, offering eradication rates of around 90%, and is effective even in settings with moderate resistance to individual antibiotics. Each regimen has specific advantages and ideal use cases, and choosing the appropriate one is essential to maximize treatment success and minimize resistance development.

TABLE 3: REGIMENS WITH USES & ERADICATION RATE

Regimens	Components	Eradication Rate	Ideal Use
Triple Therapy	PPI + Amoxicillin + Clarithromycin	~70–80%	Low resistance areas
Sequential Therapy	PPI + Amoxicillin (→) PPI + Clarithromycin + Metronidazole	~85–92%	Moderate resistance
Bismuth Quadruple	PPI + Bismuth + Tetracycline + Metronidazole	~85–90%	High resistance, penicillin allergy
Concomitant Therapy	PPI + Amoxicillin + Clarithromycin + Metronidazole	~90%	Flexible, high efficacy

Empirical Therapy vs Tailored Therapy:

TABLE 4: DIFFERENCE BETWEEN EMPIRICAL THERAPY VS TAILORED THERAPY

Feature	Empirical Therapy	Tailored Therapy
Basis of treatment	Regional data/guidelines	Individual resistance profile
Cost	Lower	Higher (diagnostics involved)
Time to start therapy	Immediate	Delayed (requires testing)
Accuracy of targeting resistance	Moderate	High
Eradication rate	~70–85% (variable)	>90% (in many studies)
Suitability	First-line, resource-limited settings	After failure or where testing is available

CONCLUSION: The pharmacotherapeutic management of *H. pylori* infection is undergoing significant transformation in response to rising antibiotic resistance and variable treatment efficacy. While traditional triple therapy may still be effective in select populations, bismuth-containing quadruple therapy and newer regimens incorporating potassium-competitive acid blockers or rifabutin offer promising alternatives. Personalized therapy guided by antibiotic susceptibility testing and regional resistance data is increasingly recognized as essential for improving eradication rates. Future strategies should also consider patient adherence, cost-effectiveness, and potential adjuvants like probiotics to enhance treatment success. Continued research and surveillance are crucial to developing innovative approaches and ensuring effective long-term control of *H. pylori*-associated diseases.

ACKNOWLEDGEMENT: The authors would like to express their sincere gratitude to School of Pharmacy, R. K. University, for their valuable support and guidance during the preparation of this review article.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' Contributions: All authors contributed equally to the study conception, design, data collection, analysis, and manuscript preparation. All authors read and approved the final manuscript.

CONFLICTS OF INTERESTS: The authors declare that they have no competing interests.

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How to cite this article:
Tilva TM and Ajudia RP: Pharmacotherapeutic approach in *H. pylori* infection: current insight. Int J Pharm Sci & Res 2026; 17(1): 65-74. doi: 10.13040/IJPSR.0975-8232.17(1).65-74.