wjpmr, 2025, 11(7), 50-59

SJIF Impact Factor: 6.842

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

POTASSIUM COMPETITIVE ACID BLOCKER (VONOPRAZAN) & PROBIOTICS: NEWER TREATMENT ALTERNATIVES REVOLUTIONIZING PEPTIC ULCER THERAPY

Tapan Kumar Mahato* and Komal Sharma

Faculty of Pharmacy, Bhupal Nobles' Institute of Pharmaceutical Sciences, Bhupal Nobles' University, Udaipur, Rajasthan, India.

***Corresponding Author: Tapan Kumar Mahato**

Faculty of Pharmacy, Bhupal Nobles' Institute of Pharmaceutical Sciences, Bhupal Nobles' University, Udaipur, Rajasthan, India.

Article Received on 30/04/2025 **Article Revised on 20/05/2025** **Article Accepted on 10/06/2025**

ABSTRACT

Pathogenic microorganisms cause diseases, such as peptic ulcer disease. Peptic ulcers manifest in two types: gastric and duodenal ulcers, both of which are marked by symptoms such as abdominal pain, bloating, or bleeding. This bacterium produces a significant amount of urease enzyme, which breaks down urea into ammonia and carbon dioxide, neutralizing stomach acid and creating a localized alkaline environment that protects the pathogen from stomach's acidity. Peptic ulcers are mainly caused by *Helicobacter pylori* infection and the use of non-steroidal anti-inflammatory drugs (NSAIDs). For many years, the disease has been managed using a First-line regimen (Triple therapy) or second-line (Quadruple therapy) comprising proton pump inhibitors, H_2 receptor antagonists, antibiotics and bismuth compounds. Proton pump inhibitors are used in the short-term to cause adverse effects such as headache, nausea and diarrhoea, and in the long-term, achlorhydria, mineral deficiencies such as Ca^{2+}, Mg^{2+}, Fe^{2+}, Vit B_{12}, bone fractures and gut microbiota disruption. This article focuses on the use of Vonoprazan and probiotics. Vonoprazan, a potassium-competitive acid blocker that provides better results than proton pump inhibitors with less or no adverse effects, and probiotics helps in restoring gastric microbial flora by reducing *H. pylori* load.

KEYWORDS: Vonoprazan, Potassium competitive acid blocker, Peptic ulcer disease, *Helicobacter pylori*, Clinical trials of Vonoprazan, Clinical trials of Voquezna, treatment methods of peptic ulcer disease, probiotics.

INTRODUCTION

I. Peptic ulcer disease: Causes, Pathogenesis and Clinical aspects

Peptic Ulcer Disease (PUD) involves erosion of the stomach or duodenal lining, resulting in ulcer development. The two main causes are *Helicobacter pylori* infection and NSAID use, which together account for ≥90% of cases.

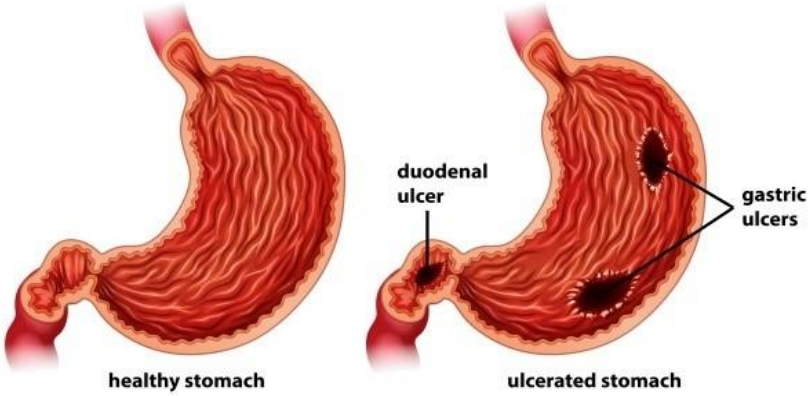

Fig. 1: Gastric and Duodenal ulcers (Courtesy: www.best-remedies.com)

1. Causes & Risk factors

Helicobacter pylori infection is the leading cause of peptic ulcers, which accounts for 70–90% of duodenal ulcers and 50–70% of gastric ulcers. The virulence factors CagA and VacA compromise mucosal defense, leading to chronic inflammation and increased acid production.[1] Another significant cause is the use of NSAIDs, which account for 25–30% of peptic ulcer disease cases. This is due to COX-1 inhibition, which reduces prostaglandins and weakens mucosal protection.[2] Additional causes include Zollinger-Ellison syndrome (gastrinoma), stress ulcers in critically ill patients, smoking, alcohol consumption, and genetic predispositions.

2. Pathophysiology

An imbalance between aggressive and protective factors results in peptic ulcers. The factors are listed in table below.

Table 1: Aggressive & protective factors responsible for peptic ulcer disease.

Aggressive factors	Protective factors
H. pylori, NSAIDs, acid	Mucus, bicarbonate, blood flow
Smoking, stress	Prostaglandins (PGE_2)

Mechanism

Four key factors explain the mechanism through which *H. pylori* cause ulcers. First, the urease activity of bacteria involves the production of the urease enzyme, which transforms urea into ammonia, causing damage to the mucosal lining. Second, VacA toxin triggers apoptosis in epithelial cells. Third, CagA disrupts tight junctions leading to inflammation. Finally, an increase in gastrin level results in hyperacidity.[3]

3. Clinical features

Peptic ulcers are marked by a burning sensation in the epigastric region, that worsens at night and is alleviated by eating in patients with duodenal ulcers. Other symptoms include nausea, bloating, and weight loss with serious signs such as bleeding and perforation. Complications occur in 20% of cases, leading to gastrointestinal bleeding, which manifests as hematemesis, melena, and anaemia. Perforation, which occurs in approximately 2–10% of cases, causes sudden intense pain and peritonitis. Gastric Outlet Obstruction is another complication, affecting 5% of cases, and resulting in vomiting and weight loss.[4]

4. Diagnosis

Peptic ulcers can be identified through non-invasive methods such as the urea breath test, the stool antigen test and serology (not reliable). Invasive procedures include endoscopy to obtain a biopsy specimen for histological examination and rapid urease test.[5]

II. Treatment methods for peptic ulcers[6,7]

1. Acid-suppressing drugs

Table 2: Acid suppression strategies for peptic ulcer disease management.

S. No.	Drug	Mode of action	Example with dose	Side effects
A	Proton pump inhibitors (PPIs)	Inhibiting the H^+/K^+-ATPase enzyme in parietal cells results in the reduction of strong acid production.	Omeprazole (20–40 mg/day), Esomeprazole (20–40 mg/day), Pantoprazole (40 mg/day) for a duration of 4–8 weeks (ulcer healing).	Long-term use results in hypochlorhydria, nutrient deficiencies (B12, Mg^{2+}, Ca^{2+}), bone fractures, gut dysbiosis.
B	H_2-receptor antagonists	Block histamine H_2 receptors results in reducing acid secretion.	Ranitidine (150 mg 2x/day), Famotidine (20–40 mg/day).	It is less effective than PPIs and is utilized for mild conditions or ongoing treatment.

2. *H. pylori* eradication therapy

Table 3: Combatting peptic ulcers: Modern *H. pylori* eradication strategies.

S. No.	Method	Duration	Drugs used	Efficacy
A	First-line regimen (Triple therapy)	10–14 days	PPI (e.g., Omeprazole 20 mg 2x/day) + Clarithromycin (500 mg 2x/day) + Amoxicillin (1 g 2x/day) or Metronidazole (500 mg 2x/day)	~70–85% (declining due to antibiotic resistance).
B	Second-line (Quadruple	Used when Triple	PPI (2x/day) + Bismuth	~90%.

	therapy)	therapy fails or high resistance.	subsalicylate (524 mg 4x/day) + Tetracycline (500 mg 4x/day) + Metronidazole (500 mg 3x/day)	
C	Newer alternatives	Potassium-Competitive Acid Blocker	Vonoprazan + Amoxicillin	
		For resistant strains	Rifabutin-based regimens	
D	Mucosal protective agents	Forms a gel-like coating over ulcers.	Sucralfate: 1 g 4x/day (before meals).	Diarrhea, abortion risk (avoid in pregnancy).
		Antibacterial (H. pylori), anti-inflammatory, and mucosal coating	Bismuth subsalicylate (Pepto-Bismol).	
		Prevents NSAID-induced ulcers.	Prostaglandin Analog (Misoprostol): 200 µg 4x/day.	
E	Adjuvant & alternative therapies	Antacids (Short-term relief)	Aluminum hydroxide	Neutralizes acid but causes constipation
			Magnesium hydroxide	Faster but may cause diarrhea
		Herbal/Natural Adjuncts	Liquorice (Stimulates mucus production)	
			Aloe vera (Anti-inflammatory)	
F	Probiotics	Reduce H. pylori load.	Lactobacillus spp.	

III. Proton Pump Inhibitors (PPIs)

Proton Pump Inhibitors (PPIs) irreversibly block the H^+/K^+-ATPase enzyme (proton pump) in gastric parietal cells, thereby suppressing gastric acid secretion. They require activation in acidic environments (pH < 4).

Mode of action: PPI covalently binds to cysteine residues on the proton pump and inhibit both basal and stimulated acid secretion for 18–24 h.

Chemistry of PPI: PPIs share a benzimidazole core substituted with pyridine and sulfinyl groups. Examples of PPIs with IUPAC names, brand names, generic names and their standard dose are given in Table 4.

Table 4: Generic name, IUPAC name, brand name and dose of some proton pump inhibitor drugs used for peptic ulcer treatment.

S. No.	Generic name	IUPAC name	Brand name	Standard oral dose
1	Omeprazole	5-methoxy-2-[(4-methoxy-3,5-dimethylpyridin-2-yl) methylsulfinyl]-1H-benzimidazole	Omez (Dr. Reddy's)	20–40 mg once/day for 4-8 weeks.
2	Esomeprazole	(S)-5-methoxy-2-[(4-methoxy-3,5-dimethylpyridin-2-yl)methylsulfinyl]-1H-benzimidazole	Nexpro (Torrent)	20–40 mg once/day for 4-6 weeks.
3	Lansoprazole	2-([3-methyl-4-(2,2,2-trifluoroethoxy) pyridin-2-yl]methylsulfinyl)-1H-benzimidazole	Lanzol (Zydus cadila)	15–30 mg one/day for 4-6 weeks.
4	Pantoprazole	5-(difluoromethoxy)-2-[(3,4-dimethoxypyridin-2-yl)methylsulfinyl]-1H-benzimidazole	Pantocid (Sun pharma)	40 mg once daily (before breakfast) for 4–8 weeks.
5	Rabeprazole	2-([4-(3-methoxypropoxy)-3-methylpyridin-2-yl]methylsulfinyl)-1H-benzimidazole	Rablet (Sun pharma)	20 mg once daily (before breakfast) for 4–8 weeks.

Structural Commonality: All contains a pyridine ring, sulfinyl bridge and benzimidazole group.

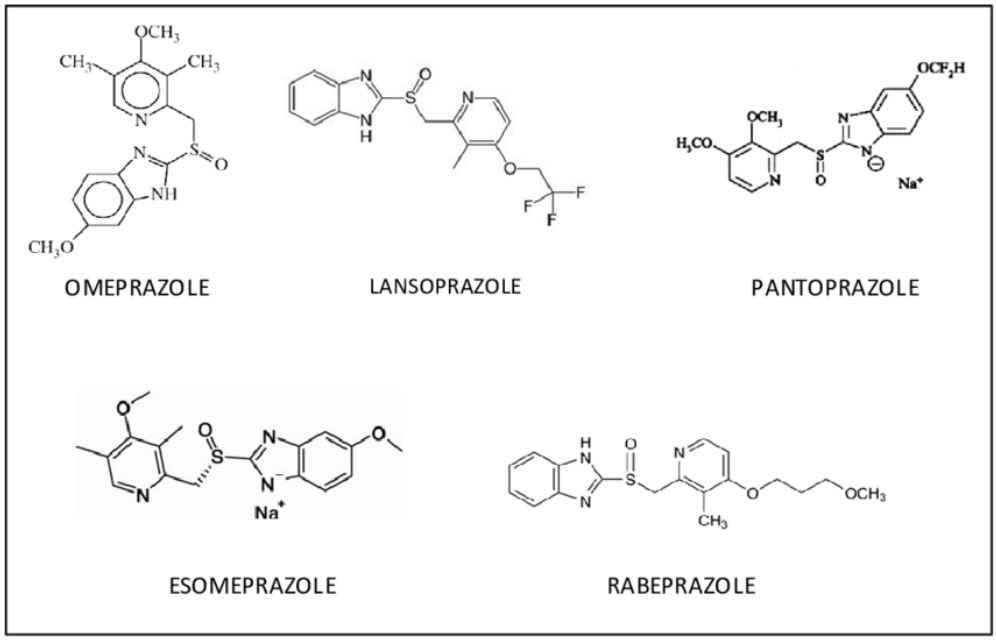

Fig. 2: Structure of different Proton pump inhibitors (Courtesy: www.mungfali.com)

Clinical indications: Gastroesophageal reflux disease (GERD), Peptic ulcer disease (*H. pylori* eradication combination), Zollinger-Ellison syndrome, Stress ulcer prophylaxis (ICU patients)

Adverse effects: In Short-term, headache, nausea, diarrhea, and long-term, achlorhydria, mineral deficiencies such as Ca^{2+}, Mg^{2+}, Fe^{2+}, Vit B_{12}, bone fractures (reduced calcium absorption), and difficile infection (gut microbiota disruption).[8,9,10,11,12]

Long-term risks: Achlorhydria & Mineral deficiencies

PPIs are highly effective but require cautious long-term use owing to achlorhydria-related complications and nutrient deficiencies.

Achlorhydria: Mechanism by which it occurs is chronic acid suppression that raises gastric pH >4, resulting in impaired protein digestion (pepsin activation requires acid) and, microbial killing (increased bacterial overgrowth).[13]

Mineral deficiencies

Table 5: Mineral deficiencies due to long term proton pump inhibitor use.

S. No.	Mineral	Requirement	Problems arise
1	Calcium	Requires acidic pH for solubilization.	PPI use decreases Ca^{2+} absorption which gives rise to osteoporosis.
2	Magnesium	--	Hypomagnesemia due to impaired intestinal absorption.
3	Iron & B_{12}	--	Acid-dependent uptake compromised.

Regular monitoring (Mg^{2+} and Ca^{2+} levels) is recommended for chronic users.[14]

IV. Vonoprazan (A potassium-competitive acid blocker or P-CAB)

Vonoprazan is a potassium-competitive acid blocker (P-CAB), its IUPAC 1-[5-(2-fluorophenyl)-1-[(pyridin-3-yl)sulfonyl]-1H-pyrrol-3-yl]-N-methylmethanamine and its structure is given below.

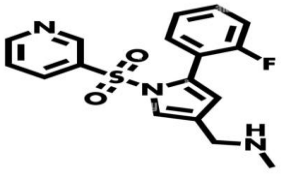

Fig. 3: Structure of vonoprazan (Courtesy: www.alamy.com)

In Japan, it is often paired with amoxicillin in a dual-therapy approach to treat *Helicobacter pylori* infections. This combination reflects a growing trend towards more efficient and user-friendly eradication treatments.

Fig. 4: Vono-20 (Vonoprazan tablets 20 mg), Manufactured by Dr Reddy's Laboratories Ltd. (Courtesy: www.pharmeasy.in)

Vonoprazan is better than PPIs: it delivers quicker, more potent, and longer-lasting acid suppression than conventional proton pump inhibitors (PPIs) such as omeprazole or lansoprazole.

Mode of action of vonoprazan: It competitively obstructs the K+ site of gastric H+/K+-ATPase, also known as the proton pump, resulting in a rapid reduction in acid production. Unlike proton pump inhibitors (PPIs), PCABs do not require activation in acidic environments and remain effective regardless of food consumption.[15,16]

Dual therapy in japan

Table 6: PPI + Amoxicillin: Japan's efficient dual therapy for peptic ulcer disease.

S. No.	Drugs	Dose	Duration	Eradication rate
1	Vonoprazan	20 mg twice daily	7 days	~85-90%,
2	Amoxicillin	750 mg twice daily		

Research indicates that dual therapy achieves eradication rates of approximately 85-90%, which surpasses those of PPI-based triple therapy (PPI + amoxicillin + clarithromycin/metronidazole). This dual therapy approach is particularly beneficial in areas with high resistance to clarithromycin.[17,18]

US Status: In 2022, vonoprazan, marketed as voquezna, received approval in the United States for treating GERD and eradicating *H. pylori*, although it has not yet become a common choice for dual therapy. Presently, US guidelines continue to endorse triple or quadruple therapy based on PPIs, such as a combination of PPI, amoxicillin, clarithromycin, and either metronidazole or bismuth.[19,20]

Fig. 5: Voquezna (vonoprazan) (Courtesy: www.goodrx.com)

Advantages of Vonoprazan + Amoxicillin dual therapy: The regimen is simpler, involving only two drugs compared to the traditional three or four drugs. This leads to better adherence, as there are fewer side effects, such as gastrointestinal issues associated with clarithromycin.[21]

Possible limitations: Although resistance to amoxicillin can diminish its effectiveness, the resistance levels remain low in many areas. It is not yet a standard treatment outside Japan; however, research is being conducted in other countries.[22]

V. Clinical trials of Vonoprazan (Potassium-competitive acid blocker - P-CAB) in Japan vs. the US Clinical trials & approvals in Japan

Table 7: Efficiency and safety: Key findings from vonoprazan trials in Japan.

S. No.	Program	Year	Design	Results	Reference
A	*H. pylori* eradication	Trial (2015)	Phase 3 RCT comparing	Eradication rate: 84.5% (Vonoprazan) vs. 69.3%	23

	(Dual therapy)		Vonoprazan (20 mg bid) + amoxicillin (750 mg bid) × 7 days vs. PPI-based triple therapy.	(PPI) in clarithromycin-resistant strains.	
B	GERD & erosive esophagitis	Trial (2015)	Vonoprazan (20 mg/day) vs. lansoprazole (30 mg/day)	Healing rate at Week 4: 96% (Vonoprazan) vs. 91% (PPI). Faster symptom relief (Day 1 vs. Day 3 with PPI).	24

FDA Approvals & Key Trials in US

Table 8: FDA approvals and pivotal clinical trials of Vonoprazan in U.S.

S. No.	Program	Year	Design	Results	Reference
A	Phalcon-EE Trial (GERD, 2022)	2022	Phase III RCT (vonoprazan 20 mg vs. lansoprazole 30 mg)	Week 8 healing rate: 93% (vonoprazan) vs. 85% (PPI). Superior in severe esophagitis (LA Classification Grade C/D).	[25]
B	Phalcon-HP trial (*H. pylori*, 2023)	2023	Vonoprazan triple therapy (VAC: vonoprazan + amoxicillin + clarithromycin)	Eradication rate: 84.7% (VAC) vs. 78.7% (PPI triple therapy)	[26]

Key Differences: Japan vs. U.S.

Table 9: Key differences in clinical trials of Vonoprazan: Japan Vs the U.S.

S. No.	Parameter	Japan (approved 2015)	US (Approved 2022-23)
1	GERD indication	Healing & maintenance	Healing only (not maintenance)
2	*H. pylori* therapy	Dual (Vonoprazan + Amoxicillin)	Triple (VAC regimen)
3	Ulcer indication	Approved	Not approved
4	Dosing	20 mg once/bid	20 mg once daily (GERD)

Ongoing research in US and Japan[27, 28]

Table 10: Ongoing research on Vonoprazan in Japan and United states.

Country	Phase	Purpose
U.S.	Phase 3 trial	NSAID-induced ulcers
Japan	Post-marketing surveillance	For long-term safety

VI. *Helicobacter pylori*: Morphological and Functional characteristics

Helicobacter pylori is a Gram-negative, microaerophilic bacterium with a distinctive helical morphology (0.5–1.0 µm wide; 2–4 µm long), optimized for gastric colonization. Its spiral shape and 4–6 sheathed unipolar flagella enable corkscrew motility through viscous stomach mucus, while protective flagellar sheathing enhances acid resistance. Gram-negative cell walls contain lipopolysaccharides (LPS) and adhesins, which are critical for mucosal attachment and immune evasion. These structural adaptations facilitate persistent stomach colonization, which drives the pathogenesis of gastritis, peptic ulcers, and gastric cancer.

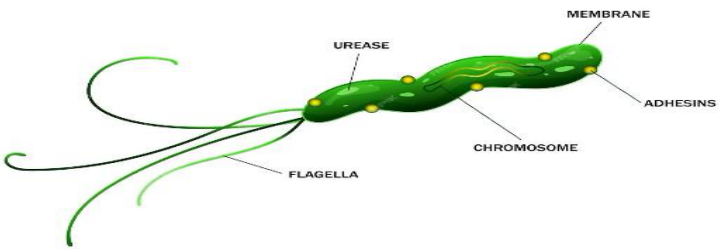

Fig. 6: Morphology of *Helicobacter pylori* (Courtesy:www.freepik.com)

This bacterium produces abundant *urease*, a critical enzyme that hydrolyze urea to ammonia and carbon dioxide. This biochemical reaction serves two vital functions: (1) it neutralizes gastric acid in the immediate vicinity and (2) it generates a localized alkaline microenvironment that shields the pathogen from stomach acidity. In addition, *H. pylori* exhibits robust biofilm-forming capabilities. Embedding within this extracellular polymeric matrix, enhances protection against host immune responses and antimicrobial agents while facilitating persistent colonization of the gastric mucosa.

Characteristic microscopic features of *Helicobacter pylori*

Microscopic identification of *Helicobacter pylori* utilizes multiple staining techniques: Gram staining reveals faint staining, curved gram-negative bacilli, while specialized silver stains (Warthin-Starry or Giemsa) provide enhanced visualization of the organisms in gastric tissue biopsies. Phase-contrast microscopy of fresh cultures demonstrated the characteristic corkscrew motility of the bacterium, which is attributable to its polar flagella. These combined methods allow for reliable morphological confirmation of *H. pylori* in both clinical specimens and laboratory cultures.[29,30]

Virulence amplifiers: Critical factors enhancing *H. pylori* pathogenicity

1. Mechanisms of microbial pathogenicity: Essential bacterial virulence factors

Table 11: Survival strategies: *H.pylori's* key virulence factors.

S. No.	Factors	How it effects
i	Urease enzyme	*H. pylori* secretes the urease enzyme, which breaks down urea to form ammonia (NH_3) and CO_2. This reaction neutralizes stomach acid, creating a localized pH buffer that enables the bacteria to survive in the acidic environment (pH ~1.5–4).
ii	Flagella	The flagella of *H. pylori* facilitate its movement, allowing it to swim through the gastric mucusa and reach the less acidic epithelial surface, where the pH ranges from approximately 5 to 7.
iii	Adhesion proteins	Facilitates adherence to gastric epithelial cells, hindering their removal. Examples include BabA, SabA, and HopQ, which attach to host receptors such as Lewis antigens.
iv	Toxins	After being delivered into host cells via the Type IV secretion system (T4SS), such as CagA (Cytotoxin-associated gene A), it disrupts cell signaling, leading to inflammation, cell death, and an increased risk of cancer. VacA (Vacuolating cytotoxin) creates pores in host cells, resulting in nutrient loss and suppression of the immune system.
v	Biofilm formation	The biofilm protects *H. pylori* from antibiotics and immune responses.

2. Host factors

Table 12: Human-pathogens interactions in *H. pylori* disease.

S. No.	Host factors	How it effects
i	Gastric pH	Low stomach acid (hypochlorhydria) promotes bacterial overgrowth.
ii	Mucus layer	*H. pylori* secretes mucinases to penetrate the mucus barrier results in due to mucus degradation.
iii	Genetic susceptibility	Blood group O is at higher risk due to increased adhesion (Lewis antigen expression).

3. Environmental & Dietary factors

Table 13: Role of diet and environment in *H. pylori* Transmission and Persistence.

S. No.	Environmental & dietary factors	How it effects
i	Poor sanitation & crowding	Fecal-oral/oral-oral transmission
ii	High-salt diet	Increases CagA expression causes higher inflammation and cancer risk.
iii	Smoking & alcohol	Smoking leads to a decrease in gastric blood flow, which weakens the mucosal defence. Alcohol interferes with the mucus barrier.
iv	Chronic stress & acid secretion	Prolonged stress impacts gut movement and acid production, creating a conducive environment for *H. pylori*.

4. Medical Factors

Table 14: Clinical determinants of *H. pylori* infection and outcomes.

S. No.	Medical factors	How it effects
i	Proton pump inhibitors (PPIs)	Lowering stomach acid levels aids in the survival of *H. pylori*. Prolonged use of PPIs leads to increased persistence of colonization.
ii	Antibiotic resistance	Antibiotic Resistance due to mutations in 23S rRNA (clarithromycin) or rdxA gene (metronidazole).

5. Microbial Interactions: *H. pylori* modifies the gut microbiome, thereby decreasing the competition for nutrients.

Therapeutic implications based on the factors promoting the growth and virulence of *Helicobacter pylori*: Focus on inhibiting the urease enzyme with compounds such as acetohydroxamic acid, enhancing gut health with probiotics such as Lactobacillus, and avoiding prolonged use of PPIs unless absolutely essential.[31,32]

X. Probiotics[33,34]

Probiotics are living microorganisms that, when administered in sufficient quantities, offer health advantages to the host. Often referred to as "good" or "beneficial" bacteria, they assist in maintaining a healthy microbial balance in the gut and other areas of the body.

Microbes in yakult drink

Yakult is a popular probiotic fermented milk beverage containing a specific strain of beneficial bacteria. The key microbial and nutritional details are as follows:

Table 15: Key microbial and nutritional profile of Yakult probiotic fermented milk beverages.

S. No.	Microbial strain/Nutritional content	Details	
1	Primary probiotic strain	Lactobacillus casei strain Shirota (LcS), Discovered by: Dr. Minoru Shirota (1930, Japan).	
		Survives in stomach acid and bile that's why reaches intestines alive which improves gut microbiota balance and enhances immunity and digestion.	
2	Other microbial components	*Lactobacillus casei Shirota* ferments skimmed milk + sugar (lactose) that produces lactic acid, giving Yakult its tangy taste.	
		No harmful bacteria present.	
		Pasteurized to kill pathogens (but LcS is added post-pasteurization).	
3	Nutritional content (Per 65mL bottle)	**Component**	**Amount**
		Calories	50 kcal
		Sugars	11 g
		Protein	1 g
		L. casei Shirota	≥6.5 billion CFU (Colony Forming Units)
4	Health benefits of Yakult	**Function**	**How?**
		Gut health	Reduces bloating, constipation, and diarrhoea and competes with harmful bacteria (*E. coli*, *H. pylori*).
		Immunity boost	Stimulates IgA production and macrophage activity.
		Lactose digestion	Helps break down lactose (beneficial for mild lactose intolerance).
		Scientific evidence	Yakult's LcS improves IBS symptoms. Reduces *H. pylori* load when combined with antibiotics.
5	Safety & side effects	Safe for most people, but may cause gas/bloating initially.	
		High sugar content hence moderate intake for diabetics.	

Comparison of Yukult with other Probiotic drinks (Actimel & Kefir)

7(a) **7(b)** **7(c)**

Fig 7(a): Yakult Probiotic Drink (courtesy: www.amazon.in), 7(b): Actimel probiotic drink (Courtesy: www.nakup.itesco.cz) and 7(c): Kefir Fermented Probiotic Beverage, Manufactured by seven turns private limited, Mumbai (Courtesy: www.amazon.in)

Table 16: Comparative analysis of Yakult with other probiotic beverages (Actimel & Kefir).

Drink	Probiotic strain	CFU (Colony forming unit) Count
Yukult	*Lactobacillus casei Shirota*	6.5 billion/bottle
Actimel	*L. casei* DN-114 001	10 billion/bottle
Kefir	Multiple strains (yeast + bacteria)	15–50 billion/serving

CONCLUSION

Vonoprazan, a potassium-competitive acid blocker (P-CAB), combined with amoxicillin, is a novel method for treating *Helicobacter pylori* infections. This medication offers faster, more effective, and longer-lasting acid suppression than traditional proton pump inhibitors. In addition, they have fewer adverse effects than PPIs do. It blocks the K+ site of gastric H+/K+-ATPase, also known as the proton pump, which leads to decreased acid production. Unlike proton pump inhibitors, vonoprazan does not require activation in acidic environments and remains effective regardless of food intake. Dual therapy is particularly advantageous in regions with high clarithromycin resistance. In Japan, vonoprazan received approval in 2015 after successfully completing all clinical trial phases except for post-marketing surveillance, which is currently ongoing to assess its long-term safety. Meanwhile, the US FDA approved the drug (marketed as Voquezna) in 2022-23 for use in treating gastroesophageal reflux disease and, in combination with amoxicillin and clarithromycin for peptic ulcers. Given the benefits of vonoprazan, initiating clinical trials in India could provide significant advantages for patients with peptic ulcers. However, the use of probiotic drinks containing friendly living bacteria provides significant benefits to patients with peptic ulcer. Probiotics help restore gastric microbial flora by reducing *H. pylori* load.

ACKNOWLEDGEMENT

We are extremely grateful to all the authors listed in the references below, as their work has enabled us to write this article.

Disclamer

This article was drafted with the assistance of Paperpal paraphrasing, ChatGPT AI and Deepseek AI tools.

REFERENCES

1. Malfertheiner, P., Megraud, F., O'Morain, C. A., Gisbert, J. P., Kuipers, E. J., Axon, A. T., … El-Omar, E. M. Management of *Helicobacter pylori* infection—the Maastricht V/Florence Consensus. *Gut, 2017; 66*(1): 6–30. https://doi.org/10.1136/gutjnl-2016-312288 jwatch.org+9pubmed.ncbi.nlm.nih.gov+9publires.unicatt.it+9
2. Lanas, A., & Chan, F. K. L. NSAIDs and peptic ulcers: Outcomes and mechanisms. *Gastroenterology, 2017; 152*(3): 630–636. https://doi.org/10.1053/j.gastro.2016.09.063
3. Suerbaum, S., & Michetti, P. *Helicobacter pylori* infection. *New England Journal of Medicine, 2002; 347*(15): 1175–1186. https://doi.org/10.1056/NEJMra020542
4. Kavitt, R. T., Lipowska, A. M., & Cohen, J. Diagnosis and treatment of peptic ulcer disease. *The American Journal of Medicine, 2019; 132*(3): 321–331. https://doi.org/10.1016/j.amjmed.2018.09.031
5. Chey, W. D., Leontiadis, G. I., Howden, C. W., & Moss, S. F. ACG clinical guideline: Management of peptic ulcer disease—Diagnosis. *American Journal of Gastroenterology, 2017; 112*(7): 988–1013. https://doi.org/10.1038/ajg.2017.95
6. American College of Gastroenterology. *ACG clinical guideline: Peptic ulcer disease*. *American Journal of Gastroenterology, 2022; 117*(6): 867–886. https://doi.org/10.14309/ajg.0000000000001765
7. Malfertheiner, P., Megraud, F., Leja, M., O'Morain, C. A., Atherton, J., Axon, A. T., … El-Omar, E. M. *Maastricht VI/Florence Consensus Report: Management of Helicobacter pylori infection*, 2022.

Gut. https://doi.org/10.1136/gutjnl-2022-327745 socgastro.org.br+1pubmed.ncbi.nlm.nih.gov+1
8. Brunton, L. L., Knollmann, B. C., & Hilal-Dandan, R. (Eds.). *Goodman & Gilman's The Pharmacological Basis of Therapeutics* (14th ed.). McGraw-Hill, 2018.
9. Katzung, B. G., Masters, S. B., & Trevor, A. J. *Katzung & Trevor's Basic & Clinical Pharmacology* (12th ed.). McGraw-Hill, 2012.
10. Shin, J. M., & Kim, N. *Acid-suppressive therapy and gastric microbiota*. *World Journal of Gastroenterology, 2013; 19*(42): 7216–7234. https://doi.org/10.3748/wjg.v19.i42.7216
11. Freedberg, D. E., Kim, L. S., Yang, Y. X. The risks and benefits of long-term proton pump inhibitor use. *JAMA, 2017; 318*(7): 614–623. https://doi.org/10.1001/jama.2017.10969
12. Wishart, D. S., Feunang, Y. D., Guo, A. C., & Wilson, M. Proton pump inhibitors. In *DrugBank Online*, 2022. https://go.drugbank.com/categories/DBCAT000450
13. Chey, W. D., Leontiadis, G. I., Howden, C. W., & Moss, S. F. ACG clinical guideline: Treatment of *H. pylori* infection. *American Journal of Gastroenterology, 2017; 112*(7): 988–1013. https://doi.org/10.1038/ajg.2017.95
14. McCarthy, C. (2015). Proton-pump inhibitors and fracture risk. *BMJ, 2015; 351*: h4843. https://doi.org/10.1136/bmj.h4843
15. Hori, Y., et al. Potassium-competitive acid blockers: A new therapeutic option. *Pharmacology & Therapeutics, 2011; 132*(2): 157–169. https://doi.org/10.1016/j.pharmthera.2011.05.009
16. Jenkins, H., Sakurai, Y., Nishimura, A., & Hiramatsu, N. Vonoprazan: A new era in acid suppression therapy. *Therapeutic Advances in Gastroenterology, 2022; 15*: 1–20. https://doi.org/10.1177/17562848221100144
17. Sue, S., et al. Efficacy and safety of vonoprazan-based dual therapy for *H. pylori* eradication. *Journal of Gastroenterology, 2020; 55*(3): 249–258. https://doi.org/10.1007/s00535-019-01639-w
18. Murakami, K., et al. Vonoprazan-based triple vs dual therapy for *H. pylori*. *Gut, 2016; 65*(1): A1–A144. https://doi.org/10.1136/gutjnl-2016-312388
19. U.S. Food and Drug Administration. *Voquezna® (vonoprazan) prescribing information*, 2022. Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214674s000lbl.pdf
20. Chey, W. D., et al. ACG clinical guideline: *Helicobacter pylori* treatment. *American Journal of Gastroenterology, 2022; 117*(6): 867–886. https://doi.org/10.14309/ajg.0000000000001765
21. Suzuki, S., et al. Vonoprazan outperforms PPIs in high-resistance settings. *Helicobacter, 2019; 24*(4): e12596. https://doi.org/10.1111/hel.12596
22. Matsuzaki, J., et al. Emerging *H. pylori* resistance to amoxicillin in Japan. *Journal of Clinical Medicine, 2020; 9*(6): 1831. https://doi.org/10.3390/jcm9061831
23. Murakami, K., et al. Vonoprazan-based triple versus dual therapy for *H. pylori*. *Gut, 2016; 65*(1): A1–A144. https://doi.org/10.1136/gutjnl-2016-312388
24. Ashida, K., Sakurai, Y., Hori, T., Kudou, K., Nishimura, A., & Hiramatsu, N. Randomised clinical trial: Vonoprazan, a novel potassium-competitive acid blocker, vs. lansoprazole for the healing of erosive oesophagitis. *Alimentary Pharmacology & Therapeutics, 2016; 43*(2): 240–251. https://doi.org/10.1111/apt.13750
25. Phathom Pharmaceuticals, Inc. *Voquezna® (vonoprazan) prescribing information*. U.S. Food and Drug Administration, 2022; Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214674s000lbl.pdf
26. Chey, W. D., Leontiadis, G. I., Howden, C. W., Moss, S. F., & Crowe, S. E. ACG clinical guideline: Helicobacter pylori infection. *American Journal of Gastroenterology, 2023; 118*(5): 849–856. https://doi.org/10.14309/ajg.0000000000002251
27. Pharmaceuticals and Medical Devices Agency (PMDA). *Vonoprazan approval report*. Retrieved from https://www.pmda.go.jp/
28. U.S. Food and drug administration, 2022: [Voquezna® Approval (2022)](https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2022)
29. Center for disease control and prevention. *Helicobacter pylori (H. pylori) and peptic ulcer disease*. https://www.cdc.gov/ulcer/
30. NIH National Cancer Institute (*H. pylori* and Cancer Risk). https://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents/h-pylori-fact-sheet
31. Suerbaum, S., & Michetti, P. *Helicobacter pylori* infection. *The New England Journal of Medicine,2002; 347*(15): 1175–1186.
32. Cover, T. L., & Blaser, M. J. *Helicobacter pylori* in health and disease. *Science Translational Medicine, 2009; 1*(5): 5ra14.
33. Yakult Honsha Co., Ltd. *Yakult Science*. https://www.yakult.co.jp/english/
34. Gotteland, M., Brunser, O., & Cruchet, S. Systematic review: Are probiotics useful in controlling gastric colonization by *Helicobacter pylori*? *Alimentary Pharmacology & Therapeutics*, 2005; 23(8): 1077–1086.