International Journal of Medical and Pharmaceutical Sciences
Open access peer-reviewed Journal
Volume 2, Issue 8, Page 685-693.
https://doi.org/10.5281/zenodo.22016547

Review Article

Beyond Proton Pump Inhibitors: Tegoprazan and the Emergence of Potassium-Competitive Acid Blockade

Pavithra Biju Bijumon[1], Angitha Binu[1], Grace N. Raju*[2], Shaiju S. Dharan[3]

[1]Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Thiruvananthapuram.
[2]Assistant Professor, Department of Pharmacy Practice, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom,
[3]Principal / HOD, Department of Pharmacy Practice, Ezhuthachan College of Pharmaceutical Sciences, Marayamuttom, Thiruvananthapuram

The pharmacological suppression of gastric acid secretion remains central to the management of acid-related gastrointestinal disorders, including gastroesophageal reflux disease (GERD), peptic ulcer disease, and Helicobacter pylori infection. Proton pump inhibitors (PPIs) have long served as the mainstay of therapy due to their ability to irreversibly inhibit the gastric H^+/K^+-ATPase enzyme. However, their delayed onset of action, dependence on meal stimulated pump activation, interindividual variability in metabolism, and incomplete control of nocturnal acid secretion have highlighted the need for alternative therapeutic strategies. Potassium-competitive acid blockers (P-CABs) have emerged as a novel class of acid-suppressive agents that reversibly inhibit the proton pump by competing with potassium ions at its luminal binding site. This mechanism enables rapid, potent, and sustained acid suppression independent of acid activation. Several P-CABs, including vonoprazan, tegoprazan, fexuprazan, and revaprazan, have demonstrated promising pharmacological and clinical profiles. This review provides a comprehensive analysis of the evolution of acid suppression therapy, examines the mechanistic and pharmacological advantages of P-CABs, and presents a detailed comparison of available agents, with particular emphasis on tegoprazan. The clinical applications, safety considerations, and future directions of P-CAB therapy are also discussed, highlighting their potential to redefine the standard of care in acid-related disorders.

Keywords: Potassium-competitive acid blockers; Tegoprazan; Vonoprazan; Proton pump inhibitors; Gastric acid suppression.

INTRODUCTION

Acid-related gastrointestinal disorders represent a major global health concern, affecting a substantial proportion of the population and contributing significantly to morbidity, healthcare utilization, and economic burden. Among these conditions, gastroesophageal reflux disease (GERD), peptic ulcer disease, and Helicobacter pylori infection are particularly prevalent and often require long-term pharmacological management [1,2]. Gastric acid plays a central role in the pathogenesis of these disorders by contributing to mucosal injury, impairing healing, and influencing bacterial colonization.

The development of proton pump inhibitors marked a major milestone in the management of acid-related diseases. By irreversibly inhibiting the H^+/K^+-ATPase enzyme, PPIs effectively suppress gastric acid secretion and promote mucosal healing [3]. Their widespread adoption has significantly improved clinical outcomes and quality of life for patients. However, despite their effectiveness, PPIs are not without limitations. Clinical experience has revealed that a considerable proportion of patients continue to experience persistent symptoms despite PPI therapy, particularly in GERD [4]. Additionally, issues related

to delayed onset of action, variability in response, and incomplete acid suppression have prompted the search for alternative therapeutic approaches. In this context, potassium-competitive acid blockers have emerged as a promising new class of acid-suppressive agents. Unlike PPIs, P-CABs inhibit gastric acid secretion through a reversible, potassium-competitive mechanism that does not require acid activation. This allows for rapid and sustained acid suppression, addressing many of the limitations associated with PPIs. Among the P-CABs currently under investigation, tegoprazan has attracted considerable attention due to its favorable pharmacological profile and growing clinical evidence. This review aims to provide a comprehensive overview of the emergence of P-CABs, with a focus on their mechanistic advantages, clinical applications, and potential to transform the management of acid-related disorders.

Evolution of Acid Suppression Therapy:

The pharmacological management of gastric acid secretion has undergone significant evolution over the past century. Early therapeutic approaches relied primarily on antacids, which neutralized gastric acid and provided symptomatic relief. However, their short duration of action and inability to prevent acid production limited their effectiveness [5]. The introduction of histamine H_2-receptor antagonists in the latter half of the 20th century represented the first major breakthrough in acid suppression therapy. These agents reduced acid secretion by blocking histamine-mediated stimulation of parietal cells. While effective in many cases, H_2-receptor antagonists were associated with the development of tolerance over time, leading to reduced efficacy during prolonged use [6]. The advent of PPIs revolutionized the treatment of acid-related disorders by directly targeting the final step in acid secretion. By irreversibly inhibiting the proton pump, PPIs provided more potent and sustained acid suppression compared to previous therapies [3]. As a result, they became the standard of care for a wide range of conditions. Despite their success, the limitations of PPIs have become increasingly apparent, particularly in patients requiring rapid symptom relief or those with refractory disease. These challenges have driven the development of novel agents such as P-CABs, which offer a different mechanism of action and improved pharmacological characteristics.

Limitations Of Proton Pump Inhibitors:

Although PPIs are highly effective under optimal conditions, their pharmacological properties impose several limitations that can affect clinical outcomes. One of the most significant drawbacks is their delayed onset of action. PPIs are prodrugs that require activation in the acidic environment of the parietal cell canaliculus. This process depends on the presence of actively secreting proton pumps, which are typically stimulated by food intake [7]. As a result, PPIs must be administered prior to meals to achieve maximal efficacy, and several doses are required before sufficient inhibition of proton pumps is achieved. This leads to a delay in symptom relief, which can be problematic in acute conditions. Another important limitation is interindividual variability in response. PPIs are metabolized primarily by cytochrome P450 enzymes, particularly CYP2C19. Genetic polymorphisms in these enzymes can lead to significant differences in drug metabolism, resulting in variability in plasma drug levels and therapeutic outcomes [8]. Furthermore, PPIs may not provide adequate control of nocturnal acid secretion, leading to the phenomenon of nocturnal acid breakthrough. This can compromise mucosal healing and contribute to persistent symptoms in some patients [9]. The irreversible nature of proton pump inhibition also limits the flexibility of dosing and may delay recovery of acid secretion after discontinuation. Collectively, these limitations highlight the need for alternative therapies with more predictable and rapid pharmacological effects.

Mechanism and Advantages of Potassium-Competitive Acid Blockers:

Potassium-competitive acid blockers represent a novel class of acid-suppressive agents that act directly on the gastric proton pump through reversible competition with potassium ions. The H^+/K^+-ATPase enzyme requires potassium ions to function, and P-CABs inhibit acid secretion by binding to the potassium-binding site on the luminal surface of the enzyme [10]. This mechanism offers several advantages over PPIs. First, P-CABs do not require activation in an acidic environment, allowing them to

exert their effect immediately after absorption. This results in a rapid onset of action and early symptom relief [11]. Second, P-CABs can inhibit both active and inactive proton pumps, leading to more comprehensive acid suppression from the first dose. In contrast, PPIs can only inhibit pumps that are active at the time of drug exposure. Third, the reversible nature of P-CAB binding allows for a pharmacodynamic profile that is closely related to plasma drug concentrations. This results in a more predictable and consistent therapeutic response. Finally, P-CABs have been shown to maintain intragastric pH above therapeutic thresholds for extended periods, including during nighttime, which is critical for mucosal healing and symptom control [12]. These advantages suggest that P-CABs may overcome many of the limitations associated with PPIs and provide improved clinical outcomes.

Tegoprazan

↓

Oral administration

↓

Rapid absorption into systemic circulation

↓

Accumulation in gastric parietal cells

↓

Direct, reversible inhibition of H^+/K^+-ATPase (proton pump)

(Potassium-competitive binding)

↓

Blocks final step of gastric acid secretion

↓

Marked reduction in gastric acid output

↓

Increased intragastric pH

↓

Relief and healing of acid-related disorders

(e.g., GERD, peptic ulcer disease)

Fig:1- Mechanism of Tagoprazan

OVERVIEW OF AVAILABLE P-CABS

1. Vonoprazan

Vonoprazan is the first P-CAB to be widely adopted in clinical practice. It has demonstrated potent and sustained acid suppression and has been shown to be superior to PPIs in certain clinical settings, particularly in Helicobacter pylori eradication [13].

2. Tegoprazan

Tegoprazan is a newer P-CAB that has gained attention due to its rapid onset of action, favorable pharmacokinetics, and strong clinical efficacy. It has been evaluated in multiple clinical trials and has shown promising results in GERD and peptic ulcer disease [14].

3. Fexuprazan

Fexuprazan is another emerging P-CAB with potent acid-suppressive effects. Early clinical studies have demonstrated its efficacy in GERD treatment, with a safety profile comparable to existing therapies [15].

4. Revaprazan

Revaprazan is one of the earlier P-CABs developed but has shown less potent acid suppression compared to newer agents. Its clinical use remains limited [16].

Pharmacodynamics:

Tegoprazan produces a rapid increase in intragastric pH and maintains pH above 4 for extended periods. This sustained acid suppression is essential for symptom relief and mucosal healing [17].

Pharmacokinetics:

Tegoprazan is rapidly absorbed, exhibits high bioavailability, and is not significantly affected by food intake. It undergoes hepatic metabolism and is primarily eliminated via fecal excretion [18].

Clinical Efficacy in Erosive Esophagitis and Gerd:

In patients with erosive esophagitis linked to GERD, Tegoprazan has shown strong effectiveness that is at least as good as, and in some cases better than, standard proton pump inhibitor therapy. Large randomized studies have found that taking tegoprazan OD, usually 50 mg leads to high rateof healing for the damaged lining in patients with confirmed erosive esophagitis. This confirms tegoprazan is just as effectives PPIs for healing erosive esophagitis. [31,32] Also, the safety and side effects were similar between the two treatments, showing tegoprazan is a good alternative to PPIs. Meta-analyses of clinical trials further support tegoprazan's effectiveness. These reviews show healing rates are similar or slightly better than with standard PPI therapy. A review that included data from many trials found no big differences in healing rates at 4 and 8 weeks between tegoprazan and PPIs. The risk of problems was also similar, there was no significant increase in serious side effects with tegoprazan. [33,34] Recent data from Phase 3 clinical trials suggest tegoprazan may be better than lansoprazole in treating GERD, including erosive esophagitis. These large studies showed tegoprazan had significantly better results in healing the esophagus at both 2-8 weeks compared to lansoprazole, even in more severe cases. This implies that tegoprazan's quick action andlong-lasting acid control lead to better healing outcomes than non-inferiority, though these results are still pending full peer review. Safety and side effects were similar between the two treatments. [35,36] Regarding GERD symptoms like heartburn and regurgitation, tegoprazan provides fast and meaningful relief in both erosive and non-erosive reflux disease. In trials where tegoprazan was compared to esomeprazole or used in as-needed doses, patients on tegoprazan reported resolving heartburn and regurgitation faster than those on traditional PPIs, with many symptoms gone within 30 minutes and lasting for 24 hours. This benefit was seen even in patients who didn’t respond well to usual acid suppressants, showing tegoprazan's quick action in reducing symptoms. Keeping the healing and symptom control long-term is another key part of treating GERD. In studies where patients with healed erosive esophagitis were followed for up to 24 weeks, tegoprazan kept the healing stable and was at least as good as, and sometimes better than, lansoprazole, nomatter the initial severity of the esophagitis. The strong safety profile and stable levels of gastrin suggest that tegoprazan is suitable not only for healing but also for long-term management of GERD. [37,38]

Role in Helicobacter Pylori Eradication:

Tegoprazan is a new type of medicine called a potassium-competitive acid blocker (P-CAB). It is becoming more important in treating infections caused by the bacteria-Helicobacter pylori because it stops stomach acid more quickly, strongly and for a longer time than older medicines called protonpump inhibitors (PPIs). [39,37] Keeping stomach acid low is important because it helps maintain a high pHlevel in the stomach. This high pH helps antibiotics like clarithromycin and amoxicillin work better against the bacteria. In clinical studies, tegoprazan combined with amoxicillin and clarithromycin (called triple therapy) has shown results that are just as good as lansoprazole-based treatments when used as the first choicefor treating *H. pylori*. [40-41] A big study in South Korea found that both 50 mg and 100 mg doses of tegoprazan had high successrates (around 85-86%) that met the standards for being just as effective as lansoprazole-based treatments. The safety of tegoprazan was also similar to other treatments, with no serious sideeffects, making it a good first choice in standard triple therapy. One review of six studies found that tegoprazan-based treatments were better than PPI-based treatments, with higher success rates and similar side effects. [42,43] These findings suggest that tegoprazan could be better than PPIs in practical situations. In addition to standard triple therapy, tegoprazan has been shown to work well in more intensive treatment methods like concomitant therapy (a quadruple treatment without bismuth) and longer treatment times. For example, a 10-day treatment with tegoprazan, amoxicillin, clarithromycin, and metronidazole hadvery high success rates (>90%) even in people who had antibiotic resistance. This shows that tegoprazan's ability to reduce stomach acid can help make multidrug treatments more effective against resistant strains, which is especially important because resistance to clarithromycin is increasing worldwide. Evidence also suggests that making the treatment longer, from 7 days to 14 days, can improve success rates in areas where antibiotic resistance is high.[44]

Real-world data show that a 14-day plan with tegoprazan has higher success rates and is still safe, showing how important the length of treatment is for the best results. Studies also indicate that tegoprazan might make resistant *H. pylori* more sensitive to standard antibiotics. Lab tests show that it can increase the effectiveness of clarithromycin, fluoroquinolones, metronidazole, and amoxicillin against resistant strains, suggesting it may help antibiotics work betterin some cases. However, not all studies show that tegoprazan is much better than PPIs in every situation. Some real-world and past studies have found similar success rates between tegoprazan and PPI-based treatments, suggesting the benefits may depend on factors like where the treatment is given, which antibiotics are used, and how long the treatment lasts. Still, tegoprazan has a similar safety profile and better acid control than PPIs, making it a good alternative in both regular and more advanced treatment plans. [45,46,47]

Gastric Ulcer Healing and Other Gi Indications:

In treating gastric ulcers, tegoprazan has proven to be very effective and well accepted in direct comparisons with other treatments in clinical trials. A large study involving many hospitals compared tegoprazan (50 mg or 100 mg, OD) with lansoprazole (30 mg OD), which is a commonly used acid reducer. Patients had confirmed gastric ulcers seen by endoscopy, After 4 and 8 weeks of treatment, the rates of ulcer healing were similar across all groups, with over 90% of patients showing healing in both the tegoprazan and lansoprazole groups. [48,49] When looking at the results of patients who followed the treatment plan closely, the healing rates at 4 weeks were also similar, showing that both doses of tegoprazan worked as well as lansoprazole in healing ulcers. Importantly, the number of side effects from treatment was similar between the two groups, and there was no greater increase in stomach acid levels with tegoprazan, showing it is safe. These results support-tegoprazn as an effective and safe option to replace proton pump inhibitors for healing gastric ulcers. Besides common stomach ulcers, tegoprazan also shows promise in treating other stomach-related issues, like ulcers that form during certain medical procedures. [50,51] For instance, in patients who had a procedure called endoscopic submucosal dissection to treat stomach cancer, a study found that tegoprazan given at 50 mg led to similar healing rates for the ulcers formed after the procedure, compared with esomeprazole at 40 mg, after 8 weeks. Although the healing rate at 4 weeks was slightly higher with tegoprazan, the overall healing and safety were the same between the groups. Real-world and experimental evidence also suggests that tegoprazan may help with other stomach-related conditions beyond ulcers and acid reflux. A recent study on healthy adults showed that tegoprazan does not significantly slow down how quickly the stomach empties food or cause discomfort after eating, which could be beneficial for people with functional stomach issues or post-meal distress. The study noted that tegoprazan's strong acid reduction started on the first day of treatment and did not cause delays in stomach movement, which is different from some other acid reducers, and this might make it better for overall stomach tolerance. [52,53,54]

Safety and Tolerability

When it comes to safety and how well people tolerate tegoprazan, it shows a good profile in all clinical studies and development phases. In early studies with healthy people taking single or multiple doses, tegoprazan was generally well accepted, with most side effects being mild and going away on their own. [26,28] There was no significant build-up of the drug with repeated use, and the acid reduction was fast and depended on the dose, showing both safety and effectiveness. Larger studies and reviews of multiple clinical trials further support that tegoprazan is well tolerated compared to proton pump inhibitors. Most reported side effects are mild stomach issues like diarrhea, nausea, or stomach pain, and headaches that usually go away without treatment. This meta-analysis data suggests no significant increase in serious side effects with tegoprazan compared to PPIs, supporting its use in long-term acid control and ongoing treatment. [52,49,48]

CONCLUSION:

In conclusion, Tegoprazan is a promising new treatment in acid-reducing therapy as a potassium-competitive acid blocker. It works differently from traditional proton pump inhibitors. Clinical studies show that tegoprazan quickly and strongly reduces stomach acid, which helps treat various acid-related

stomach problems like gastroesophageal reflux disease, erosive esophagitis, stomach ulcers, and helps get rid of the bacteria Helicobacter pylori. It also has a similar safety profile. Importantly, tests show that tegoprazan works well regardless of a person's CYP2C19 gene type, which can affect how well PPIs work, making tegoprazan more reliable across different people. For conditions like erosive esophagitis and GERD, reviews show that tegoprazan has similar healing results as PPIs after 4 to 8 weeks of treatment, with similar improvements in symptoms and side effects. This suggests it can be used instead of PPIs in everyday practice. Its fast action may be especially helpful for quick symptom relief in people with non-erosive reflux disease. In treating H. pylori, studies show that tegoprazan-based treatments may be more effective than PPI-based ones, without causing more side effects. This makes it a strong option in current treatment plans. In terms of safety, tegoprazan is generally well-tolerated. Common side effects, like mild stomach issues or headaches, are similar to those of PPIs. It also doesn't raise stomach acid levels as much as some PPIs do. This is good news, and these findings have been confirmed in combined studies. However, more long-term data is still needed. Early observations suggest that tegoprazan's way of working may reduce some risks linked to long-term acid suppression, like infections from Clostridioides difficile, but these findings need more research to confirm. Despite the positive results, there are still some things we don't know. Most studies and reviews have been done on Asian populations with short follow-up times, which may limit how broadly the results can be applied. More long-term comparisons between tegoprazan and PPIs, especially in different groups of people like those with severe stomach damage or those need in ongoing treatment, are needed to know exactly where tegoprazan fits in treatment plans. These gaps show the importance of future studies that include people from different countries and groups to fully understand the long-term benefits and safety of tegoprazan. Overall, the current evidence supports that tegoprazan is a safe and effective alternative to PPIs for many acid-related stomach problems. It offers quick action, predictable acid control, and similar safety and effectiveness as PPIs. This makes it a valuable option in gastroenterology, especially for people who don't respond well to PPIs or need fast symptom relief. However, more research is needed to confirm long-term results and to define tegoprazan's role in different patient groups and situations.

REFERENCES

1. Habbal M, Scaffidi MA, Rumman A, Khan R, Ramaj M, Al-Mazroui A, et al. Tegoprazan vs. proton pump inhibitors for erosive esophagitis: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2025.
2. Hussaini H, Kebede TM, Afework TS, et al. Comparative efficacy and safety of tegoprazan versus proton pump inhibitors for erosive esophagitis: a systematic review and meta-analysis. Cureus. 2025.
3. Nayyer MA, Rasool H, Murtaza H, et al. Tegoprazan vs proton pump inhibitors for erosive esophagitis: systematic review. Eur J Gastroenterol Hepatol. 2025.
4. Dong P, Lin L, Sun K, et al. Accuracy of the diagnosis of GERD by P-CAB treatment. BMC Gastroenterol. 2025.
5. Lim HS, Yoon Hj, Jung HK, et al. Effects of tegoprazan on gastric emptying and postprandial symptoms in humans. Dig Dis Sci. 2025.
6. Kim HS, Choi YK, et al. Acid-suppressive effect of tegoprazan: phase 1 comparative study. Transl Clin Pharmacol. 2025.
7. Randomised clinical trial: tegoprazan vs lansoprazole in gastric ulcer treatment. PubMed. 2025.
8. Tegoprazan-containing vs PPI-containing therapy for H. pylori eradication. JGH Open. 2025.
9. Tegoprazan inhibits gastric H+/K+-ATPase: preclinical evidence. ScienceDirect. 2018.
10. Tegoprazan reversibly binds H+/K+-ATPase, offering rapid acid suppression. PMC Meta-analysis. 2025.
11. Tegoprazan-based triple therapy for H. pylori eradication. PMC. 2026.
12. Tegoprazan's comparative eradication rates vs vonoprazan. Gut and Liver. 2025.
13. P-CAB vs PPI acid suppression review. Frontiers Medicine. 2025.
14. Effects on serum gastrin: P-CAB vs PPI. JNMG Journal. 2025.
15. Shin CM, Choi SC, Cho JW, Kim SY, Lee OJ, Kim DH, et al. Comparison of tegoprazan and

lansoprazole in patients with erosive esophagitis up to 4 weeks: a multi-center, randomized, double-blind, active-comparator phase 4 trial. Neurogastroenterol Motil 2025; 37.
16. Mori H, Suzuki H. Role of acid suppression in acid-related diseases: proton pump inhibitor and potassium-competitive acid blocker. J Neurogastroenterol Motil 2019; 25:6–14.
17. Simadibrata DM, Syam AF, Lee YY. A comparison of efficacy and safety of potassium-competitive acid blocker and proton pump inhibitor in gastric acid-related diseases: a systematic review and meta-analysis. J Gastroenterol Hepatol 2022; 37:2217–2228.
18. Sawaid IO, Samson AO. Proton pump inhibitors and cancer risk: a comprehensive review of epidemiological and mechanistic evidence. J Clin Med 2024; 13:1970.
19. Moayyedi P, Eikelboom JW, Bosch J, Connolly SJ, Dyal L, Shestakovska O, et al.; COMPASS Investigators. Safety of proton pump inhibitors based on a large, multi-year, randomized trial of patients receiving rivaroxaban or aspirin. Gastroenterology 2019; 157:682–691.e2.
20. Segna D, Brusselaers N, Glaus D, Krupka N, Misselwitz B. Association between proton-pump inhibitors and the risk of gastric cancer: a systematic review with meta-analysis. Therap Adv Gastroenterol 2021; 14:17562848211051463.
21. Scarpignato C, Hunt RH. Potassium-competitive acid blockers: current clinical use and future developments. Curr Gastroenterol Rep 2024; 26:273–293.
22. Han S, Choi HY, Kim YH, Nam JY, Kim B, Song GS, et al. Randomised clinical trial: safety, tolerability, pharmacokinetics, and pharmacodynamics of single and multiple oral doses of tegoprazan (CJ-12420), a novel potassium-competitive acid blocker, in healthy male subjects. Aliment Pharmacol Ther 2019; 50:751–759.
23. Chandan S, Deliwala S, Mohan BP, Ramai D, Dhindsa B, Bapaye J, et al. Vonoprazan versus lansoprazole in erosive esophagitis - A systematic review and meta-analysis of randomized controlled trials. Indian J Gastroenterol 2023; 42:475–484.
24. Wang Y, Dai X, Zhang X. Network meta-analysis of comparing different dosages of potassium-competitive acid blocker with proton-pump inhibitor in acid-related disorders. Clin Transl Gastroenterol 2024; 15: e00776.
25. Fang Y, Lou D, Zhou J, Zhang Q, Dai Y, Ren W. Efficacy and safety of potassium-competitive acid blockers versus proton pump inhibitors in treating erosive esophagitis: a meta-analysis based on randomized controlled trials. J Clin Gastroenterol 2024; 58:841–850.
26. Zhuang Q, Chen S, Zhou X, Jia X, Zhang M, Tan N, et al. Comparative efficacy of P-CAB vs proton pump inhibitors for grade c/d esophagitis: a systematic review and network meta-analysis. Am J Gastroenterol 2024; 119:803–813.
27. Pounder R, Smith J. Drug-induced changes of plasma gastrin concentration. Gastroenterol Clin North Am 1990; 19:141–153.
28. C. Scarpignato and R. H. Hunt, “The Potential Role of Potassium- Competitive Acid Blockers in the Treatment of Gastroesophageal Re-flux Disease,” Current Opinion in Gastroenterology 35 (2019): 344–355.
29. C. Scarpignato and R. H. Hunt, “Editorial: Potassium- Competitive Acid Blockers for Acid-Related Diseases- Tegoprazan, a New Kid on the Block,” Alimentary Pharmacology & Therapeutics 50 (2019): 960–962.
30. J. G. Hwang, I. Jeon, S. A. Park, et□ al., “Pharmacodynamics and Pharmacokinetics of DWP14012 (Fexuprazan) in Healthy Subjects with Different Ethnicities,” Alimentary Pharmacology & Therapeutics 52 (2020): 164 8–1657.
31. H. Jenkins, Y. Sakurai, A. Nishimura, et□al., “Randomised Clinical Trial: Safety, Tolerability, Pharmacokinetics and Pharmacodynam-ics of Repeated Doses of TAK- 438 (Vonoprazan), a Novel Potassium- Competitive Acid Blocker, in Healthy Male Subjects,” Alimentary Pharmacology & Therapeutics 41 (2015): 636–648.
32. D. K. K im, K. H. Lee, S. J. Kim, et□al., “Effect s of Tegoprazan, a Novel Potassium- Competitive Acid Blocker, on Rat Models of Gastric Acid-Related Disease,” Journal of Pharmacology and Experimental Thera-peutics 369 (2019): 318–327.

33. D. M. Simadibrata, E. Lesmana, and R. Fass, "Vonoprazan Is Su-perior to Lansoprazole for Healing of Severe but Not Mild Erosive Esophagitis: A Systematic Review with Meta-Analysis of Random-ized Controlled Trials," Journal of Gastroenterolog y and Hepatology 39 (2024): 988–999.
34. H. Mizuno, N. Matsuhashi, M. Sakaguchi, et□al., "Recent Effective-ness of Proton Pump Inhibitors for Severe Reflux Esophagitis: The First Multicenter Prospective Study in Japan," Journal of Clinical Biochemis-try and Nutrition 57 (2015): 233–238.
35. M. Zhang, Y. Xiao, and M. Chen, "The Role of Vonoprazan in Pa-tients With Erosive Esophagitis," Therapeutic Advances in Gastroenter-ology 15 (2022): 17562848221122623.
36. Y. Cheng, J. Liu, X. Tan, et□al., "Direct Comparison of the Efficacy and Safety of Vonoprazan Versus Proton- Pump Inhibitors for Gastro-esophageal Reflux Disease: A Systematic Review and Meta- Analysis," Digestive Diseases and Sciences 66 (2021): 19- 28.
37. L. Laine, K. DeVault, P. Katz, et□al., "Vonoprazan Versus Lansopra-zole for Healing and Maintenance of Healing of Erosive Esophagitis: A Randomized Trial," Gastroenterology 164 (2023): 61–71.
38. B. F. Kessing, A. J. Bredenoord, P. W. Weijenborg, G. J. M. Hem-mink, C. M. Loots, and A. J. P. M. Smout, "Esophageal Acid Exposure Decreases Intraluminal Baseline Impedance Levels," American Journal of Gastroenterology 106 (2011): 2093–2097.
39. E. Yang, S. Kim, B. Kim, et□ al., "Night- Time Gastric Acid Suppres-sion by Tegoprazan Compared to Vonoprazan or Esomeprazole," British Journal of Clinical Pharmacology 88 (2022): 3288–3296.
40. S. H. Kim, K. B. Cho, H. J. Chun, et□al., "Randomised Clinical Trial: Comparison of Tegoprazan and Placebo in Non- Erosive Ref lux Dis-ease," Alimentary Pharmacology & Therapeutics 54 (2021): 402– 411.
41. C. P. Gyawali, R. Yadlapati, R. Fass, et□al., "Updates to the Modern Diagnosis of GERD: Lyon Consensus 2.0," Gut 73 (2024): 361–371.
42. N. Kim, S. W. Lee, S. I. Cho, et□ al., "The Prevalence of and Risk Factors for Erosive Oesophagitis and Non- erosive Reflux Disease: A Nationwide Multicentre Prospective Study in Korea," Alimentar y Phar-macology & Therapeutics 27 (2008): 173–185.
43. W. Moon, M. I. Park, G. M. Kim, et□al., "Normal 24- Hour Ambula-tory Esophageal pH Values in Koreans," Gut Liver 2 (2008): 8–13.
44. A. J. Wang, M. J. Liang, A. Y. Jiang, et□al., "Gastroesophageal and Laryngopharyngeal Ref lux Detected by 24- Hour Combined Impedance.
45. Johnson LF, Demeester TR. Twenty-four-hour pH monitoring of the distal esophagus. A quantitative measure of gastroesophageal reflux. Am J Gastroenterol. 1974; 62:325–332.
46. Richter JE, Bradley LA, DeMeester TR, Wu WC. Normal 24-hr ambulatory esophageal pH values. Influence of study center, pH electrode, age, and gender. Dig Dis Sci. 1992; 37:849–856.
47. Moon W, Park MI, Kim GM, et al. Normal 24-hour ambulatory esophageal pH values in Koreans. Gut and Liver. 2008; 2:8–13. doi: 10.5009/gnl.2008.2.1.8.
48. Kim GH, Huh KC, Lee YC, et al. Normal ambulatory 24-hour esophageal pH values in Koreans - a multicenter study. J Korean Med Sci. 2008; 23:954–958. doi: 10.3346/jkms.2008.23.6.954.
49. Lam HG, Breumelhof R, Roelofs JM, Van Berge Henegouwen GP, Smout AJ. What is the optimal time window in symptom analysis of 24-hour esophageal pressure and pH data? Dig Dis Sci. 1994; 39:402–409.
50. Wiener GJ, Richter JE, Copper JB, Wu WC, Castell DO. The symptom index: a clinically important parameter of ambulatory 24-hour esophageal pH monitoring. Am J Gastroenterol. 1988; 83:358–361.
51. .Breumelhof R, Smout AJ. The symptom sensitivity index: a valuable additional parameter in 24-hour esophageal pH recording. Am J Gastroenterol. 1991; 86:160–164.
52. Weusten BL, Roelofs JM, Akkermans LM, Van Berge-Henegouwen GP, Smout AJ. The symptom-association probability: an improved method for symptom analysis of 24-hour esophageal pH data. Gastroenterology. 1994; 107:1741–1745.

53. Kagawa T, Iwamuro M, Ishikawa S, et al. Vonoprazan prevents bleeding from endoscopic submucosal dissection-induced gastric ulcers. Aliment Pharmacol Ther. 2016; 44: 583-591.
54. Miwa H, Uedo N, Watari J, et al. Randomised clinical trial: efficacy and safety of vonoprazan vs. lansoprazole in patients with gastric or duodenal ulcers - results from two phase 3, non-inferiority randomised controlled trials. Aliment Pharmacol Ther. 2017; 45: 240-252.
55. Li CY, Su M, Yan YY, et al. KFP-H008 blocks gastric acid secretion through inhibiting H+-K+-ATPase. Eur J Pharmacol. 2017; 810:112–9. 10.1016/j.ejphar.2017.06.020.
56. Jung JH, Lee JH, Yoon S-J, et al. Pharmacological activities of DWP14012, a novel acid pump antagonist for the treatment of acid-related diseases, including gastroesophageal reflux disease. J Neurogastroenterol Motil. 2018;24(Suppl 1): S9–16.
57. Sunwoo J, Oh J, Moon SJ, et al. Safety, tolerability, pharmacodynamics and pharmacokinetics of DWP14012, a novel potassium-competitive acid blocker, in healthy male subjects. Aliment Pharmacol Ther. 2018;48(2):206–18.
58. McGill MR, Jaeschke H. Biomarkers of drug-induced liver injury. Adv Pharmacol. 2019; 85:221–39.

Cite: Pavithra Biju Bijumon, Angitha Binu, Grace N. Raju*, Shaiju S. Dharan, Beyond Proton Pump Inhibitors: Tegoprazan and the Emergence of Potassium-Competitive Acid Blockade, Int. J. Med. Pharm. Sci., 2026, 2 (8), 685-693. https://doi.org/10.5281/zenodo.22016547