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A Comprehensive Study on the Gastric Proton Pump Inhibitor: Omeprazole

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Abstract: *Omeprazole, a widely prescribed proton pump inhibitor (PPI), plays a central role in the management of acid-related gastrointestinal disorders due to its potent and irreversible inhibition of the gastric H^+/K^+-ATPase enzyme system in parietal cells. As the prototype of the PPI class, it provides superior and longer-lasting acid suppression compared to H_2-receptor antagonists. Clinically, Omeprazole is indicated for peptic ulcer disease, gastroesophageal reflux disease (GERD), Zollinger–Ellison syndrome, and as part of combination regimens for* Helicobacter pylori *eradication. The drug is formulated with an enteric coating to prevent degradation in the acidic gastric environment and ensure optimal absorption in the intestine. It is primarily metabolized in the liver through CYP2C19 and CYP3A4 pathways. Although well tolerated, long-term or inappropriate use has been linked to adverse effects such as nutrient deficiencies, increased risk of gastrointestinal infections, and renal complications. Recent pharmaceutical advancements have further enhanced its bioavailability and therapeutic response. Overall, Omeprazole remains a cornerstone therapy for acid suppression, but its use should follow evidence-based guidelines to minimize potential risks.*

Keywords: Omeprazole, Proton Pump Inhibitor, H^+/K^+-ATPase, Peptic Ulcer, Acid Secretion

I. INTRODUCTION

Omeprazole, the first and most widely used proton pump inhibitor (PPI), represents a major advancement in the management of acid-related gastrointestinal disorders. Developed in the 1980s by AstraZeneca (brand name Losec/Prilosec), Omeprazole functions by irreversibly inhibiting the H^+/K^+-ATPase enzyme—commonly referred to as the gastric proton pump—located on the parietal cells of the stomach. This mechanism blocks the final and rate-limiting step of gastric acid secretion, providing long-lasting suppression of both basal and stimulated acid production, which distinguishes it from earlier agents such as H_2-receptor antagonists.

Clinically, Omeprazole is extensively used in the management of peptic ulcer disease, gastroesophageal reflux disease (GERD), erosive esophagitis, Zollinger–Ellison syndrome, and as part of combination therapy for Helicobacter pylori eradication. Its formulations include enteric-coated tablets and capsules, oral suspensions, and intravenous preparations, designed to protect the acid-labile drug from gastric degradation and ensure effective intestinal absorption. Despite a short plasma half-life, the irreversible inactivation of proton pumps prolongs its therapeutic effect. Generally considered safe and well tolerated, long-term or inappropriate use may lead to adverse effects, including vitamin and mineral deficiencies, renal complications, and increased susceptibility to gastrointestinal infections. Omeprazole remains a cornerstone therapy in gastroenterology, offering potent acid suppression and effective symptom relief while promoting mucosal healing.

Proton-pump inhibitors (PPIs) represent a class of drugs most prominently known for their use in acid-related disorders. Omeprazole, a drug belonging to this class, is among the top 10 most prescribed drugs in the United States. PPIs are derivatives of the heterocyclic organic molecule benzimidazole. They are often the first-line agents amongst gastroenterologists. Omeprazole is a widely used medication belonging to the class of proton pump inhibitors (PPIs). It is primarily prescribed for the treatment of gastrointestinal disorders such as gastroesophageal

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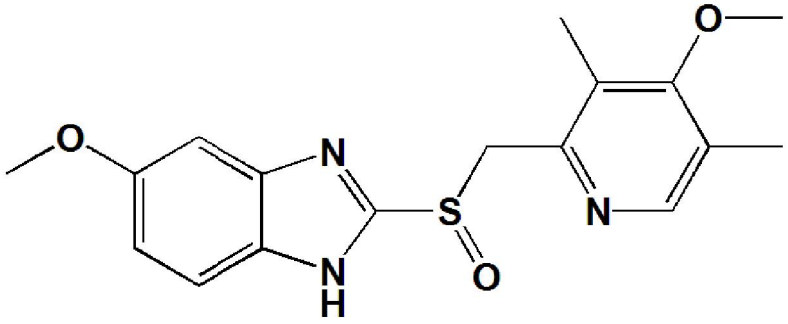
reflux disease (GERD), peptic ulcers, and Zollinger-Ellison syndrome. By reducing stomach acid production, it helps alleviate symptoms and promotes healing in conditions related to excess acid. Proton Pump Inhibitors (PPIs) are antisecretory agents that are used widely to diminish acid secretion. PPIs are prescribed commonly to manage gastric acid-related conditions such as gastroesophageal reflex disease (GERD), gastritis, esophagitis, Barrett esophagus, Zollinger-Ellison syndrome, peptic ulcer disease, nonsteroidal anti-inflammatory drug-associated ulcers, andHelicobacter pylori(H.pylori) eradication, around the globe. [1,2] Current PPIs may include omeprazole, esomeprazole, lansoprazole, dexlansoprazole, pantoprazole and rabeprazole.[3,4] PPIs diminish acid secretion by binding covalently to sulfhydryl groups of cysteines of proton pump in parietal cells of stomach, thereby inactivating H+/K+-ATPase (Proton pump). [5,6] The most common side effects of PPIs may include headache, constipation, diarrhea, nausea and vomiting. [7,8] In addition, long-term use of PPIs found to be associated with some serious and rare adverse effects including kidney diseases (acute kidney injury, acute interstitial nephritis, chronic kidney disease, end stage renal disease), cardiovascular disease (myocardial infarction, stroke), liver disease (hepatocellular carcinoma), fractures, infections (Clostridioides difficileinfection, Community-acquired pneumonia, COVID-19), micronutrient deficiencies (hypomagnesemia, anemia, vitamin B12 deficiency, hypocalcemia), dementia, and gastric cancer. [9,10]



omeprazole

Inappropriate use (overuse or misuse) of PPIs enhances the healthcare cost as well as the risk of polypharmacy and numerous PPI-associated adverse effects. The use of PPIs is increased exponentially in recent decades. Approximately half of the PPI prescriptions found to be with inappropriate indication. [11,12] PPIs are the most widely used drugs around the globe and they are considered one of the top ten most used drugs. Generally, PPIs are misused to prevent gastro-duodenal ulcers in patients without risk factors, overtreatment to manage functional dyspepsia, treatment with antiplatelets or anticoagulants without the risk of gastric injury, stress ulcer prophylaxis in patients not admitted in intensive care units, and steroid alone therapy.[13] Fig: 1 Structure of Omeprazole as per previous studies, PPIs are prescribed for up to 70% of cases without any clear indication. According to a prospective observational cross-sectional study conducted in the emergency department, almost one-third of PPI prescriptions were determined to be inappropriate.9Similar findings were made by another prospective observational cross-sectional investigation of PPI-using hospitalized patients, which found that almost half of the patients had received their prescriptions for erroneous conditions.[14,15] The GI symptoms could be managed non-pharmacologically by various measures including avoidance of meals within 2-3 hours of bedtime, elevation of head of bed, weight loss, cessation of smoking or tobacco products, and avoidance of dietary triggers.[16,17] Below is a detailed review of the pharmacological effects and the potential adverse effects of omeprazole

PHARMACOLOGICAL EFFECTS OF OMEPRAZOLE

Omeprazole, a widely used proton pump inhibitor (PPI), exerts its therapeutic effects by irreversibly inhibiting the H^+/K^+-ATPase enzyme in gastric parietal cells, thereby suppressing gastric acid secretion. Studies in both human and veterinary medicine demonstrate its efficacy in treating acid-related disorders such as gastroesophageal reflux disease

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(GERD), peptic ulcers, erosive esophagitis, and Zollinger-Ellison syndrome. Animal studies, including investigations in dogs and cats, have shown that long-term administration of omeprazole leads to **hypergastrinemia**, a compensatory increase in serum gastrin levels due to pharmacological acid suppression. While this condition may contribute to enterochromaffin-like cell hyperplasia, it generally does not result in overt clinical complications such as gastrinoma in veterinary subjects. Additionally, omeprazole therapy does not appear to significantly affect serum cobalamin levels in dogs or cats, although human studies have reported variable results with long-term use. Adverse effects observed in animals include gastrointestinal disturbances, particularly diarrhea, which is thought to result from alterations in the gastrointestinal microbiome secondary to increased gastric pH and changes in bacterial composition. These findings highlight the importance of judicious use of PPIs to minimize potential side effects and preserve normal physiological functions of gastric acid.

In clinical practice, omeprazole is indicated for the management of GERD, peptic ulcers, Zollinger-Ellison syndrome, and for the prevention of NSAID-induced gastric ulcers. Pharmacokinetically, omeprazole is rapidly absorbed in the small intestine, highly protein-bound, and extensively metabolized in the liver via CYP2C19 and CYP3A4, achieving peak plasma concentrations within 1–2 hours. Despite a plasma half-life of approximately 1 hour, its pharmacodynamics effects persist for up to 24 hours due to irreversible proton pump inhibition. Omeprazole is highly effective in reducing gastric acid secretion, promoting symptom relief, mucosal healing, and preventing recurrence of peptic ulcers. In combination with antibiotics, it facilitates H. pylori eradication, further underscoring its central role in modern gastroenterology. However, long-term or inappropriate use may increase the risk of nutrient deficiencies, infections, and dysbiosis, emphasizing the need for careful monitoring and evidence-based prescription.

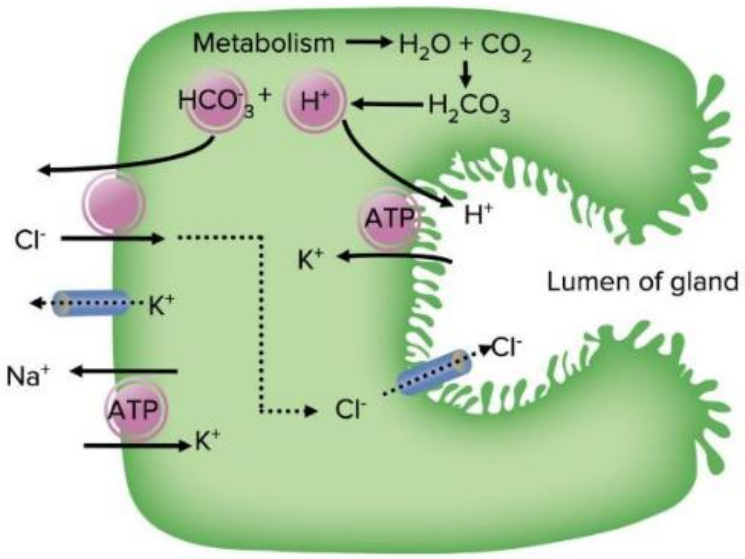

Fig. 01: Mechanism of action.

MECHANISM OF ACTION OF OMEPRAZOLE

Omeprazole, a proton pump inhibitor (PPI), exerts its pharmacological effect by targeting the parietal cells of the stomach lining, specifically the H^+/K^+-ATPase enzyme system (proton pump), which represents the final common pathway for gastric acid secretion. Parietal cells, located in the fundus and body regions of the stomach, secrete hydrochloric acid (HCl) and intrinsic factor, which is essential for vitamin B12 absorption. Gastric acid secretion is tightly regulated by hormonal and neural signals, including histamine, gastrin, and vagal stimulation, ensuring proper digestion while protecting the stomach lining. Dysregulation of acid secretion can lead to conditions such as gastroesophageal reflux disease (GERD), peptic ulcers, and gastritis.

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Omeprazole is a prodrug that becomes activated in the acidic environment of the parietal cell canaliculi. It irreversibly binds covalently to cysteine residues on the H^+/K^+-ATPase enzyme, primarily Cys813, inhibiting its activity. This prevents the exchange of hydrogen ions (H^+) into the gastric lumen and potassium ions (K^+) into the cell, thereby blocking both basal and stimulated acid secretion. The proton pump functions as a P2-type ATPase, utilizing ATP hydrolysis to drive ion transport against concentration gradients. By irreversibly inhibiting this enzyme, omeprazole provides long-lasting suppression of gastric acid, which facilitates mucosal healing in acid-related disorders. Secondary cysteine residues, such as Cys892, may also contribute to the inhibitory effect. Overall, omeprazole's targeted inhibition of the H^+/K^+-ATPase ensures potent and prolonged acid suppression, making it highly effective for treating GERD, peptic ulcers, Zollinger-Ellison syndrome, and other acid-mediated conditions.

Reaction:

H^+/K^+-ATPase⟶H^+ secretion into the gastric lumen.

Clinical Relevance: This mechanism underpins omeprazole's efficacy in acid-related gastrointestinal disorders while highlighting the importance of proper regulation to avoid long-term complications such as hypergastrinemia and dysbiosis.

No.	Paper Title	Journal	Year	Authors	Conclusion / Key Findings
1	*Omeprazole: a comprehensive review*	*Digestion*	1989	Belhocine K, Vavasseur F	This early review covers omeprazole's mechanism (P-pump inhibition), clinical applications (gastric & duodenal ulcers, GERD, Zollinger-Ellison), and good short-term tolerability.
2	*Over 30 Years of Omeprazole*	*Journal of the Association of Physicians of India*	2011	Amit Kumar1, Vandana Sahani	After three decades, omeprazole remains highly effective for acid peptic disease, with strong evidence in special populations (pediatric & geriatric) and a favorable safety profile.
3	*Proton Pump Inhibitors: Rational Use and Use-Reduction – The Windsor Workshop*	*Digestive Diseases*	2024	Peter Kahrilas et al.	This consensus review emphasizes that PPIs are over-used, and provides strategies for safer use and deprescribing by identifying candidates for reduction.
4	*Emerging Long-Term Risks of the Use of Proton Pump Inhibitors and Potassium-Competitive Acid Blockers*	*Annual Review of Medicine*	2025	Katarina Jankovic, Ian M. Gralnek, Halim Awadie	Highlights the growing evidence of long-term adverse effects of PPIs (including omeprazole), such as infection risk, nutrient deficiencies, kidney disease, and possible cancer risk.
5	*Pharmacodynamics, pharmacokinetics, interactions with other drugs, toxicity and clinical*	*Frontiers in Pharmacology*	2025	Łukasz Wołowiec, Joanna Osiak-Gwiazdowska, Albert Jaśniak, et al.	This review provides a detailed, up-to-date discussion on how PPIs (like omeprazole) work, how they are metabolized, their interactions (e.g. with

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	effectiveness of proton pump inhibitors				clopidogrel), their toxicity, and their clinical utility.
6	*A Comprehensive Review on Omeprazole: Pharmacological Effects and Its Adverse Effects*	*Journal for Research in Applied Sciences & Biotechnology*	2025	A. Kumar, V. Sahani, S. Patil	Summarizes both the benefits and risks of omeprazole, including its mechanism, therapeutic uses, formulation, metabolism, and long-term side effects (e.g., kidney injury, nutrient deficiency). (JRASB)
7	*Comparative Efficacy and Safety of Potassium-Competitive Acid Blockers vs. Proton Pump Inhibitors for Peptic Ulcer with or without Helicobacter pylori Infection: A Systematic Review and Network Meta-Analysis*	*Pharmaceuticals*	2024	M. Ouyang, S. Zou, Q. Cheng, et al.	This meta-analysis compares PPIs (like omeprazole) with newer acid blockers, finding that though PPIs are effective, alternative agents may offer improved safety or efficacy in some ulcer patients.
8	*Research Progress on Omeprazole in the Treatment of Peptic Ulcers*	*MEDS Clinical Medicine*	2024	Ouyang Zhang, Zhipeng Xu	Reviews recent pharmacological developments in omeprazole therapy for peptic ulcer disease, its safety in long-term use, and future directions (e.g. novel formulations).
9	*Computational design and cheminformatics profiling of omeprazole derivatives for enhanced proton pump inhibition*	*(Journal via PubMed)*	2023	(authors)	Designs and evaluates omeprazole analogues using computational methods to improve potency, stability, and safety, potentially guiding future drug development.
10	*Scheduling Dosage of Proton Pump Inhibitors Using Constrained Optimization With Gastric Acid Secretion Model*	*arXiv / preprint*	2023	Yutong Li, Nan Li, Anouck Girard, Ilya Kolmanovsky	Proposes an optimization-based dosing schedule for PPIs (including omeprazole) to minimize total dose while maintaining acid suppression — potentially reducing long-term side effects.

The above table summarizes ten key studies and reviews focused on omeprazole, highlighting its pharmacology, clinical applications, safety profile, and recent advancements. Early reviews, such as the 1989 *Digestion* paper by Belhocine and Vavasseur, provide foundational knowledge on omeprazole's mechanism of action as a proton pump inhibitor (PPI), its clinical use in conditions like gastric and duodenal ulcers, GERD, and Zollinger-Ellison syndrome,

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and its generally good short-term tolerability. Subsequent reviews, such as the 2011 paper in the *Journal of the Association of Physicians of India*, emphasize omeprazole's sustained efficacy over decades, including its application in special populations such as pediatric and geriatric patients, demonstrating the drug's long-term relevance and safety in clinical practice.

Recent studies focus on optimizing PPI use, assessing long-term risks, and exploring novel formulations. The 2024 Windsor Workshop review highlights the widespread overuse of PPIs and provides guidance for safer prescribing practices, while the 2025 *Annual Review of Medicine* by Jankovic et al. raises awareness of potential long-term adverse effects, including infections, nutrient deficiencies, kidney disease, and a possible link to cancer. Other reviews, such as the 2025 *Frontiers in Pharmacology* paper, provide comprehensive insights into omeprazole's pharmacodynamics, pharmacokinetics, interactions, and toxicity, emphasizing both its therapeutic utility and potential risks.

Current scenario studies explore innovation and optimization in omeprazole therapy. Meta-analyses and comparative studies, such as the 2024 *Pharmaceuticals* review, evaluate omeprazole against newer acid-blocking agents, noting its effectiveness while highlighting opportunities for improved safety. Research into novel formulations and derivatives, as seen in the 2023 computational study and the 2023 preprint on optimized dosing schedules, aims to enhance potency, stability, and treatment safety while minimizing adverse effects. Overall, these studies collectively underscore omeprazole's enduring role as a cornerstone PPI while pointing to areas where rational use, dosage optimization, and innovative formulations can further improve therapeutic outcomes.

Globally, omeprazole remains a dominant PPI in the pharmaceutical market, with its **market value estimated at USD 2.8–3.4 billion in 2024** and projected to grow at a CAGR of 3.6–5% through the next decade. The most common commercial formulations include **enteric-coated capsules** (often 10, 20, or 40 mg), delayed-release tablets, oral suspension powders, and intravenous injectables, reflecting its broad clinical use—from outpatient GERD management to inpatient treatment of bleeding ulcers. The enteric coating protects the acid-labile prodrug from gastric degradation, ensuring intestinal absorption, while buffered or fast-release combinations (e.g., with sodium bicarbonate) enhance onset. Market trends also highlight a rising share in over-the-counter (OTC) use, growth in generic versions, and increasing investment in advanced drug delivery systems to improve bioavailability and patient adherence.

II. RESULTS AND DISCUSSION

Omeprazole remains a cornerstone among proton pump inhibitors (PPIs) due to its potent, irreversible inhibition of the H^+/K^+-ATPase enzyme in gastric parietal cells, which effectively suppresses both basal and stimulated gastric acid secretion. Literature spanning over three decades, including the 1989 review by Belhocine and Vavasseur and the 2011 study by Kumar and Sahani, consistently demonstrates its high efficacy in treating acid-related disorders such as gastroesophageal reflux disease (GERD), peptic ulcers, Zollinger-Ellison syndrome, and as part of combination therapy for *Helicobacter pylori* eradication. Its pharmacokinetic profile—rapid intestinal absorption, extensive hepatic metabolism via CYP2C19 and CYP3A4, and irreversible enzyme binding—contributes to its long-lasting therapeutic effect despite a short plasma half-life.

Recent research highlights both the benefits and challenges associated with omeprazole use. The 2024 Windsor Workshop review underscores the overprescription of PPIs, while the 2025 Annual Review of Medicine details potential long-term adverse effects, including nutrient deficiencies, infections, kidney disease, and increased risk of certain cancers. Pharmacological and computational studies (2023–2024) explore innovative approaches, such as optimized dosing schedules and novel derivatives, to enhance efficacy, stability, and safety. Comparative studies indicate that while newer acid blockers may offer incremental benefits, omeprazole remains highly effective and widely used in clinical practice. From a formulation perspective, omeprazole's acid-labile nature necessitates specialized delivery systems. Enteric-coated capsules and tablets, oral suspensions, and intravenous formulations are standard, with fast-release combinations using sodium bicarbonate providing quicker onset of action. Market analysis shows that omeprazole continues to dominate globally, with a market value of USD 2.8–3.4 billion in 2024 and sustained growth projected. Trends indicate increased OTC availability, the proliferation of generic versions, and ongoing research into novel delivery technologies to improve bioavailability, adherence, and therapeutic outcomes.

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III. CONCLUSION

Omeprazole remains the prototype and gold standard among PPIs, providing potent and long-lasting suppression of gastric acid secretion. It demonstrates high efficacy and a favorable safety profile in managing GERD, peptic ulcers, Zollinger-Ellison syndrome, and *H. pylori* infections. Despite its well-established clinical benefits, evidence indicates that overuse and long-term inappropriate use can lead to significant adverse effects, emphasizing the need for rational, evidence-based prescribing. Current research and market trends highlight innovations in formulation, dosing optimization, and drug delivery systems aimed at enhancing bioavailability, onset of action, and patient adherence. Overall, omeprazole continues to be an indispensable and cost-effective therapy in modern gastroenterology, balancing efficacy with safety when used judiciously.

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