Science and Clinical Pharmacy Research Journal Vol: 2, No 4, 2026, Page: 1-14

Pharmacotherapy of Gastroesophageal Reflux Disease: A Descriptive Literature Review of Mechanism of Action and Clinical Rationale

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Abstrak: Penelitian ini bertujuan untuk menganalisis dan mensintesis pendekatan farmakoterapi terhadap Penyakit Refluks Gastroesofageal (GERD) dengan menelaah mekanisme aksi, landasan klinis, dan paradigma pengobatan yang berkembang. Proses penelusuran literatur mengikuti pedoman *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) melalui basis data internasional seperti PubMed, ScienceDirect, dan SpringerLink. Data dianalisis secara tematik untuk mengidentifikasi fokus farmakoterapi GERD. Hasil kajian menunjukkan bahwa *Inhibitor Pompa Proton* (IPP) tetap menjadi terapi utama karena efektivitasnya dalam menekan asam lambung dan mempercepat penyembuhan mukosa, namun munculnya kasus refraktori terhadap IPP mendorong pengembangan *Penghambat Asam Kompetitif Kalium* (PCAB) yang menawarkan onset lebih cepat, kontrol asam lebih kuat, dan stabilitas farmakodinamik yang lebih baik. Selain itu, integrasi agen prokinetik, pelindung mukosa, serta terapi herbal menunjukkan tren menuju pendekatan multimodal yang menargetkan motilitas, integritas mukosa, dan jalur inflamasi. Studi ini menegaskan pergeseran paradigma dari terapi tunggal berbasis penekanan asam menuju manajemen GERD yang personal, berbasis mekanisme, dan holistik, serta menyoroti pentingnya validasi klinis jangka panjang yang terstandarisasi.

Kata kunci: Penyakit Refluks Gastroesofageal, Inhibitor Pompa Proton, Penghambat Asam Kompetitif Kalium

DOI: https://doi.org/10.47134/scpr.v2i4.5339
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Received: 27-11-2025
Accepted: 27-12-2025
Published: 27-01-2026

Abstract: *This study aims to analyze and synthesize pharmacotherapy approaches to Gastroesophageal Reflux Disease (GERD) by examining the mechanisms of action, clinical basis, and evolving treatment paradigms. The literature search process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines through international databases such as PubMed, ScienceDirect, and SpringerLink. Data were analyzed thematically to identify the focus of GERD pharmacotherapy. The results of the study show that Proton Pump Inhibitors (PPIs) remain the primary therapy due to their effectiveness in suppressing gastric acid and accelerating mucosal healing. However, the emergence of refractory cases to PPIs has encouraged the development of Potassium Competitive Acid Blockers (PCABs), which offer faster onset, stronger acid control, and better pharmacodynamic stability. Furthermore, the integration of prokinetic agents, mucosal protectants, and herbal therapies indicates a trend toward a multimodal approach targeting motility, mucosal integrity, and inflammatory pathways. This study confirms a paradigm shift from single acid-suppression-based therapy to personalized, mechanism-based, and holistic GERD management, highlighting the importance of standardized long-term clinical validation.*

Keywords: *Gastroesophageal Reflux Disease, Proton Pump Inhibitor, Potassium Competitive Acid Blocker*

Introduction

Gastroesophageal reflux disease (GERD) is a chronic and increasingly prevalent condition worldwide, characterized by the reflux of gastric contents into the esophagus, resulting in symptoms such as heartburn and regurgitation (Savarino et al, 2021). The global burden of GERD continues to rise, with estimates suggesting a prevalence of 20–30% in Western countries and an increasing trend in Asia due to lifestyle and dietary changes (Zheng & Tao, 2025). This growing prevalence underscores the urgent need for effective and rational pharmacotherapy strategies to optimize symptom control and minimize long-term complications.

Over the past few decades, proton pump inhibitors (PPIs) have been the cornerstone of GERD management, significantly improving symptom control and mucosal healing (Chapelle et al, 2020) (Hossa & Małecka Wojciesko, 2025). However, despite their efficacy, approximately 20–40% of patients experience incomplete response to PPIs, a phenomenon referred to as PPI-refractory GERD (Rettura et al, 2021). This clinical challenge highlights the necessity of exploring alternative pharmacological strategies and developing personalized treatment regimens.

The emergence of potassium-competitive acid blockers (PCABs) represents a promising evolution in acid suppression therapy. Unlike PPIs, PCABs inhibit gastric H^+/K^+-ATPase reversibly and competitively, offering faster onset and more stable acid suppression (Ahmed et al, 2025) (Kim, 2025). Their potential for on-demand therapy and effectiveness in PPI-refractory cases has positioned them as an important therapeutic innovation (D'Souza et al, 2024).

Beyond acid suppression, the pathophysiology of GERD involves multifactorial mechanisms, including impaired esophageal motility, transient lower esophageal sphincter relaxation, and mucosal hypersensitivity (Cha & Lee, 2025) (Yadlapati et al, 2022). These insights have driven the use of adjunctive therapies such as prokinetics and neuromodulators to address non-acid reflux and functional symptoms (Bucan et al, 2025) (Savarino et al, 2021). Consequently, GERD management has transitioned from a one-size-fits-all approach to a phenotype-based, individualized strategy.

Another dimension gaining attention is mucosal protection. Agents such as alginates and sucralfate provide a physical barrier against gastric acid exposure, reducing esophageal irritation (Komolafe et al, 2025) (Rettura et al, 2021). Their adjunctive use in refractory GERD or in patients intolerant to high-dose acid suppressants enhances therapeutic outcomes while minimizing drug-related adverse effects.

Concerns about the long-term safety of PPIs, particularly in pediatric and elderly populations, further emphasize the need for rational pharmacotherapy. Reports have linked chronic PPI use to nutrient malabsorption, increased infection risk, and kidney dysfunction (Cohen et al, 2015) (Cuzzolin et al, 2023) (Kröner et al, 2021). These findings necessitate ongoing evaluation of benefit-risk profiles and reinforce the value of emerging alternatives like PCABs and natural compounds.

Recent studies have explored the integration of natural and complementary therapies into GERD management. Natural products with anti-inflammatory and antioxidant

properties, such as flavonoids and polyphenols, have shown potential in modulating reflux symptoms and mucosal healing (Chen et al, 2022) (Komolafe et al, 2025). These findings open new avenues for holistic and patient-centered management.

Moreover, recent advancements in understanding the gut–brain axis have revealed its significant influence on GERD pathophysiology. Stress, sleep disturbances, and psychological factors can exacerbate reflux symptoms, suggesting that neuromodulators and behavioral interventions may complement pharmacotherapy (Cha & Lee, 2025) (Yadlapati et al, 2022). This aligns with the growing emphasis on multidimensional, biopsychosocial approaches in chronic gastrointestinal disorders.

Despite these advancements, significant gaps remain in optimizing GERD pharmacotherapy. Clinical heterogeneity among patients, variability in drug response, and incomplete understanding of molecular mechanisms pose barriers to universal treatment success (Zheng & Tao, 2025). Consequently, a deeper exploration of the interplay between drug mechanisms, clinical outcomes, and patient characteristics is imperative.

In addition, the rational selection of pharmacotherapy must consider pharmacokinetic interactions, patient comorbidities, and adherence patterns. Personalized treatment algorithms integrating pharmacogenomic data may further refine therapeutic precision in GERD management (Savarino et al, 2021).

From a clinical standpoint, the rational use of pharmacotherapy in GERD is not merely about symptom relief but also about optimizing long-term safety and quality of life (Bucan et al, 2025). This calls for a multidisciplinary approach encompassing pharmacological, dietary, and lifestyle modifications.

The urgency of this topic is amplified by the persistent global rise in GERD prevalence and the economic burden associated with chronic medication use and complications. Understanding the pharmacological rationale and evolving therapeutic mechanisms is essential for clinicians, researchers, and policymakers alike (Hossa & Małecka Wojciesko, 2025).

Theoretically, this article contributes to the scientific understanding of GERD pharmacotherapy by synthesizing recent developments in drug mechanisms and clinical applications. Practically, it provides clinicians with an evidence-based framework for rational and individualized therapeutic decision-making.

Therefore, the primary objective of this article is to provide a descriptive literature review on the pharmacotherapeutic mechanisms and clinical rationality in the management of GERD. It aims to bridge existing knowledge gaps, evaluate recent therapeutic trends, and propose directions for optimized, patient-centered care in GERD management.

Methodology

This study employed a qualitative research design with a descriptive approach through an extensive library-based literature review. The qualitative descriptive methodology was chosen for its capacity to provide a detailed, systematic, and contextual understanding of pharmacotherapeutic mechanisms and clinical rationality in gastroesophageal reflux disease (GERD) management. This approach aligns with the article's objective to synthesize

and interpret findings from diverse scholarly works rather than to test hypotheses quantitatively (Bingham, 2023) (Pratt, 2025). The descriptive orientation enables the exploration of pharmacological patterns, therapeutic innovations, and rational treatment frameworks based on interpretive analysis of academic sources (Abraham & P, 2024) (Doyle et al, 2019).

Data Sources and Literature Selection

Data for this study were obtained from academic books, peer-reviewed journal articles, systematic reviews, and official health organization reports related to GERD pharmacotherapy. The principal sources include high-impact scientific databases and published articles discussing proton pump inhibitors (PPIs), potassium-competitive acid blockers (PCABs), mucosal protective agents, and complementary approaches in GERD management (Bucan et al, 2025) (Hossa & Małecka Wojciesko, 2025) (Savarino et al, 2021).

Inclusion criteria encompassed peer-reviewed publications published between 2015 and 2025, written in English, and explicitly addressing pharmacotherapeutic mechanisms, clinical rationale, therapeutic effectiveness, safety profiles, or evolving treatment paradigms in GERD. Studies examining both conventional and complementary pharmacological interventions, including PPIs, PCABs, prokinetics, mucosal protectants, and herbal or natural products, were included provided they demonstrated clear relevance to GERD management. Exclusion criteria included non-peer-reviewed documents, opinion-based articles without empirical or conceptual grounding, studies focusing exclusively on surgical or lifestyle interventions without pharmacological discussion, publications lacking explicit relevance to GERD, articles with significant methodological limitations, and studies published prior to 2015. This selective process ensured that the included literature met standards of scientific rigor, topical relevance, and conceptual alignment with the study objectives (Bandaranayake, 2024) (Granikov et al, 2020) (Jimenez et al, 2024).

Data Collection Technique

The data collection process followed the library research technique, which involves identifying, organizing, and analyzing information from credible and academically verified sources. Searches were conducted using structured keywords such as “GERD pharmacotherapy,” “PPI mechanism,” “PCAB efficacy,” and “acid suppression therapy.” The process adhered to the systematic review principles of transparency and replicability (Togia & Malliari, 2017). Each source was screened for relevance, scientific rigor, and methodological clarity before inclusion, ensuring data validity and trustworthiness (Bingham, 2023) (Pratt, 2025).

Data Analysis Procedure

Data analysis proceeded through four major phases: (1) identification of themes, (2) data reduction, (3) categorization of concepts, and (4) inductive synthesis. Thematic analysis was applied to extract central ideas such as pharmacological mechanisms, therapeutic outcomes, and clinical implications of GERD treatment modalities (Belotto, 2018) (Vila-Henninger et al, 2022). The iterative process of reading, coding, and reinterpreting the data followed the cyclical model proposed in contemporary qualitative research (Bingham, 2023) (Kalpokaite & Radivojevic, 2018). Data were continuously compared to reveal conceptual patterns and relationships between therapeutic strategies.

Validity and Reliability

To maintain the credibility and dependability of the findings, several validation techniques were implemented. Triangulation of sources was conducted by comparing interpretations from multiple articles addressing similar therapeutic domains (Hossa & Małecka Wojciesko, 2025) (Savarino et al, 2021) (Zheng & Tao, 2025). Conceptual peer review was also applied, where interpretations were cross-checked with recent pharmacological reviews to minimize researcher bias and enhance consistency (Abraham & P, 2024) (Fife & Gossner, 2024). Documentation of analytical decisions was maintained throughout the research to ensure auditability and transparency (Belotto, 2018) (Bingham, 2023).

Methodological Rigor and Relevance

This methodological framework guarantees that the descriptive qualitative approach captures the complex, multifaceted nature of GERD pharmacotherapy. By synthesizing theoretical and empirical findings through literature analysis, the study provides a comprehensive understanding of current therapeutic trends, clinical rationality, and future directions in GERD management (Ahmed et al, 2025) (Bucan et al, 2025) (Savarino et al, 2021). The combination of rigorous data analysis, selective inclusion of credible literature, and methodological transparency ensures that the conclusions drawn are both valid and practically relevant for healthcare professionals, researchers, and policymakers.

Result and Discussion

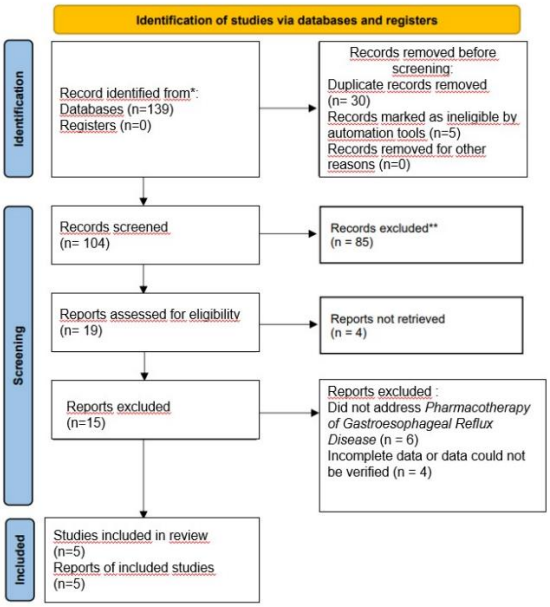

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)

The literature selection process for this study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A total of 139 records were identified from six databases (PubMed, ScienceDirect, SpringerLink, Scopus, ResearchGate, and Google Scholar). After removing 30 duplicate records and 5 that were marked as ineligible by the automated system, 104 articles remained for screening based on

titles and abstracts. Of these, 85 were excluded for being irrelevant to the focus of pharmacist patient education.

To ensure rigor and relevance, the literature selection followed specific inclusion and exclusion criteria. The inclusion criteria were as follows: (1) studies published between 2015 and 2025) ((2) written in English) ((3) peer-reviewed journal articles) ((4) studies focusing on pharmacist-led or pharmacist-involved patient education or counseling interventions) ((5) research reporting measurable outcomes related to knowledge, behavior change, or clinical improvement) (and (6) studies with accessible full-text versions. The exclusion criteria included: (a) review articles, commentaries, or conference abstracts) ((b) studies not addressing the pharmacist's educational or counseling role) (and (c) articles with incomplete or unverifiable data.

Of the 19 articles assessed for full-text eligibility, 4 were excluded due to limited access. The remaining 15 full-text articles were further evaluated, and 10 were excluded—6 for not addressing pharmacist educational interventions and 4 for having incomplete or unverifiable data. Ultimately, 5 studies met all eligibility criteria and were included in this systematic review as the primary sources.

The findings of this literature-based study reveal that pharmacotherapy for Gastroesophageal Reflux Disease (GERD) has evolved substantially in the past decade, emphasizing acid suppression, mucosal protection, and individualized therapy strategies. Syntheses from 2020 and 2025 highlights a continuous shift from traditional proton pump inhibitors (PPIs) toward newer classes such as potassium-competitive acid blockers (PCABs), prokinetics, and herbal-based interventions, each contributing uniquely to symptom control and mucosal healing.

1. Mechanisms of Action and Therapeutic Evolution

The analysis indicates that PPIs remain the gold standard in GERD pharmacotherapy due to their high efficacy in suppressing gastric acid secretion through H^+/K^+-ATPase inhibition in parietal cells (Hossa & Małecka Wojciesko, 2025) (Katz et al, 2021). However, 20–40% of patients experience PPI-refractory GERD, leading to the exploration of alternative acid-suppressive therapies such as PCABs ((Ahmed et al, 2025) (Hossa & Małecka Wojciesko, 2025). PCABs, including vonoprazan, act through competitive and reversible potassium binding, resulting in a faster onset of action and more consistent pH control than PPIs (K et al, 2022).

In addition to acid suppression, prokinetic agents (e.g., itopride, mosapride) have been shown to enhance gastric motility and reduce esophageal exposure to refluxed contents, particularly in patients with delayed gastric emptying (Hossa & Małecka Wojciesko, 2025) (Jung et al, 2021). This combination of acid control and motility enhancement has demonstrated synergistic benefits, as summarized in Table 1 below.

Table 1. Mechanisms and Clinical Rationale of Major GERD Pharmacotherapies

Therapeutic Class	Primary Mechanism	Clinical Rationale	Key Sources
PPIs	Irreversible inhibition of H^+/K^+-ATPase	First-line) (effective for acid suppression and mucosal healing	(Hossa & Małecka Wojciesko, 2025) (Katz et al, 2021)
PCABs (e.g., Vonoprazan)	Reversible K^+ inhibition of acid pump	Rapid, potent, alternative for PPI non-responders	(Ahmed et al, 2025) (K et al, 2022)
Prokinetics	Enhances GI motility and gastric emptying	Adjunctive in PPI-refractory GERD	(Jung et al, 2021)
Mucosal Protectants	Creates protective barrier) (reduces acid exposure	Add-on in refractory or sensitive cases	(K et al, 2022)
Herbal/Natural Products	Antioxidant, anti-inflammatory, mucosal protection	Complementary) (beneficial in mild to moderate GERD	(Komolafe et al, 2025) (Zheng & Tao, 2025)

2. Clinical Rationale and Effectiveness

Clinical findings reinforce the efficacy of PPIs as first-line therapy, particularly for healing erosive esophagitis and alleviating typical symptoms like heartburn and regurgitation (Velagala et al, 2022). However, PPIs do not address underlying pathophysiological factors such as transient lower esophageal sphincter relaxation (TLESR) or visceral hypersensitivity, which explains partial symptom persistence in some patients (Ahmed et al, 2025) (Katz et al, 2021). The introduction of PCABs addresses this limitation by providing rapid acid suppression and flexible dosing schedules, making them suitable for both maintenance and on-demand therapy (Hossa & Małecka Wojciesko, 2025).

Combination therapy, particularly PPI plus prokinetic agents, has been supported by meta-analytical evidence as more effective than PPI monotherapy in reducing reflux episodes and improving symptom control (Jung et al, 2021). Nevertheless, some trials note limited improvement in quality-of-life scores, indicating that pharmacological benefits may not always translate into subjective patient satisfaction (Velagala et al, 2022).

3. Emerging Role of Natural and Herbal Therapies

Recent studies have highlighted the growing interest in herbal formulations and natural products as alternative or complementary therapies for GERD. Compounds such as quercetin, genistein, and flavonoids found in traditional formulations like Sini Zuojin Decoction and Hewei Jiangni Granule demonstrate anti-inflammatory and antioxidant properties, modulating the NF-κB and MAPK pathways and protecting esophageal mucosa from acid-induced damage (Chen et al, 2022) (Cheng et al, 2022) (Li et al, 2020) (Park et al, 2021).

Moreover, Komolafe et al. (2025) and Zheng & Tao (2025) emphasized the potential of herbal treatments in regulating the microbiota-gut-brain axis, which contributes to stress-related reflux mechanisms. While preclinical and early clinical studies show promise, limitations persist regarding standardization of herbal dosage, long-term safety, and pharmacokinetic consistency (Komolafe et al, 2025) (Li et al, 2020).

4. Comparative Analysis with Previous Research

When compared with earlier pharmacological paradigms, recent findings underscore a paradigm shift toward multi-targeted GERD management. Unlike the 2010s focus on acid suppression alone, current strategies incorporate neurogenic, motility, and inflammatory pathways (K et al, 2022) (Zheng & Tao, 2025). While PPIs remain the backbone of GERD treatment, PCABs have redefined pharmacodynamics with faster symptom relief and fewer drug-drug interactions. Herbal agents further expand therapeutic possibilities, particularly for patients resistant to synthetic acid suppressants or concerned about long-term adverse events (Komolafe et al, 2025) (Park et al, 2021).

5. Summary of Findings

The overall analysis suggests that modern GERD pharmacotherapy is transitioning toward personalized, mechanism-based treatment. PPIs and PCABs provide effective acid suppression, whereas prokinetics and mucosal protectants serve as valuable adjuncts. Meanwhile, natural and herbal agents represent a rapidly developing complementary domain. However, consistent clinical validation, standardization, and integration of multi-target therapies remain critical for achieving durable outcomes in GERD management.

Discussion

The results of this literature review highlight how pharmacotherapy for Gastroesophageal Reflux Disease (GERD) has progressed toward greater mechanistic precision and clinical rationality. This section provides a critical interpretation of those findings by linking them with existing pharmacological and pathophysiological theories, identifying implications, limitations, and directions for future research.

Integrative Interpretation of Pharmacotherapy Mechanisms

The persistence of Proton Pump Inhibitors (PPIs) as the mainstay of GERD treatment aligns with their proven capacity to suppress acid secretion through H^+/K^+-ATPase inhibition in gastric parietal cells (Hossa & Małecka Wojciesko, 2025) (Katz et al, 2021). However, as the findings confirm, refractory GERD remains a major therapeutic challenge—affecting up to 40% of patients despite optimal PPI use. This aligns with the theoretical understanding that GERD is multifactorial, involving motility dysfunction, mucosal sensitivity, and inflammatory processes beyond acid hypersecretion (K et al, 2022) (Velagala et al, 2022).

The introduction of Potassium-Competitive Acid Blockers (PCABs), such as vonoprazan, represents a significant theoretical shift. Unlike PPIs, PCABs act via reversible K^+ competition, offering faster onset, prolonged duration, and stable pH regulation (Ahmed et al, 2025) (Hossa & Małecka Wojciesko, 2025). These pharmacokinetic improvements

support the notion of dynamic acid modulation rather than complete suppression, addressing limitations of PPIs in maintaining 24-hour gastric control. This mechanism enhances clinical rationality and reinforces the pharmacological concept of target affinity optimization, where reversible binding confers flexibility and efficacy.

Rational Clinical Application and Theoretical Correlation

Clinically, combining PPIs with prokinetic agents demonstrates a theoretically coherent approach to GERD management. Prokinetics, by enhancing gastric emptying and lower esophageal sphincter tone, address non-acidic reflux components, aligning with motility-based pathophysiological models (Jung et al, 2021). Such combination therapies exemplify multimodal pharmacotherapy, which integrates multiple mechanisms to improve symptomatic outcomes.

However, findings from multiple meta-analyses suggest that while symptom control improves, the quality-of-life index may not proportionally increase (Velagala et al, 2022). This gap reflects the complexity of GERD, in which visceral hypersensitivity and neurogenic inflammation play pivotal roles that acid-suppressive therapy alone cannot address. Thus, clinical outcomes reaffirm the theoretical framework that GERD requires mechanism-specific, phenotype-based therapy, rather than uniform acid inhibition strategies.

The Role of Herbal and Natural Therapies: Mechanistic and Conceptual Insights

Emerging research on herbal and natural products such as Sini Zuojin Decoction and Hewei Jiangni Granule offers a new theoretical frontier by targeting inflammatory, oxidative, and neurogenic pathways (Chen et al, 2022) (Cheng et al, 2022) (Li et al, 2020). These interventions act on the NF-κB and MAPK signaling cascades, mitigating mucosal inflammation and oxidative injury, which complements conventional pharmacotherapy. The bioactive compounds—quercetin, genistein, and flavonoids—modulate cytokine release and enhance mucosal integrity (Komolafe et al, 2025) (Park et al, 2021) (Zheng & Tao, 2025).

Conceptually, this reflects a shift from symptom suppression toward mucosal protection and homeostatic restoration. Herbal agents also align with the microbiota-gut-brain axis model, addressing stress-mediated reflux mechanisms that conventional drugs overlook (Zheng & Tao, 2025). Nevertheless, despite promising preclinical and early clinical evidence, a major limitation persists in dosage standardization and pharmacokinetic validation, as emphasized by Komolafe et al. (2025). Hence, the integration of herbal pharmacotherapy requires a standardized clinical evaluation framework to ensure reproducibility and safety.

Comparative Synthesis with Previous Models

Compared with prior GERD management paradigms—dominated by acid suppression alone—the present findings mark a paradigmatic evolution toward holistic, patient-centered pharmacotherapy. Previous frameworks treated GERD as a purely acid-driven disorder, whereas recent studies confirm its immunological, neurological, and microbiological dimensions (Hossa & Małecka Wojciesko, 2025) (Zheng & Tao, 2025). This aligns with modern pharmacological theory that advocates for polymechanistic

intervention, acknowledging complex system interactions in chronic gastrointestinal diseases.

Still, therapeutic diversity introduces challenges. Variations in drug response, adherence, and metabolic factors (e.g., CYP2C19 polymorphisms influencing PPI metabolism) can produce heterogeneous outcomes, complicating the universal application of these findings. Thus, personalized therapy remains a critical area for clinical refinement.

Limitations and Future Research Directions

Several limitations characterize the current literature synthesis. First, many comparative studies on PCABs and natural products rely on short-term trials, lacking longitudinal follow-up to assess relapse and safety outcomes (Cheng et al, 2022) (Li et al, 2020). Second, heterogeneity in study design and outcome measurement (e.g., symptom scales, pH monitoring duration) restricts direct meta-analytical comparison. Additionally, most herbal studies lack placebo-controlled randomization and pharmacodynamic correlation, limiting their integration into clinical guidelines.

Future research should emphasize:

1. Long-term comparative trials between PPIs, PCABs, and combined therapies.
2. Mechanistic biomarker analysis to stratify GERD phenotypes for tailored treatment.
3. Standardization of herbal formulations to ensure safety, bioavailability, and reproducibility.
4. Exploration of microbiota modulation as an adjunctive therapeutic target.

Theoretical and Clinical Implications

This study contributes significantly to GERD pharmacotherapy literature by demonstrating that mechanistic diversification—from acid control to mucosal and neural modulation—constitutes the next frontier of treatment. Theoretically, it strengthens the integration between molecular pharmacology and clinical gastroenterology, showing how mechanistic understanding directly informs rational therapeutic design. Practically, the findings advocate for personalized, multimodal therapy, potentially transforming GERD management from symptom control to long-term disease modulation.

Conclusion

This qualitative descriptive study concludes that pharmacotherapy for Gastroesophageal Reflux Disease (GERD) has undergone a significant paradigm shift from conventional acid suppression toward an integrative, mechanism-based therapeutic model. The analysis demonstrates that while Proton Pump Inhibitors (PPIs) remain the foundational therapy due to their efficacy in acid inhibition and mucosal healing, emerging Potassium Competitive Acid Blockers (PCABs) such as vonoprazan provide faster, more stable, and individualized symptom control. Furthermore, adjunctive agents including prokinetics and mucosal protectants enhance therapeutic outcomes by addressing motility and mucosal resilience. The study also highlights the growing scientific validation of herbal and natural-based formulations that target inflammatory, neurogenic, and microbiota-mediated pathways, reflecting a shift toward holistic, multi-target management. These

findings deepen the theoretical understanding of GERD as a multifactorial disorder influenced by neuroimmunological and metabolic interactions, thereby enriching pharmacological and gastroenterological discourse. Academically, the study supports the advancement of personalized, multimodal therapy frameworks, while socially and culturally, it underscores the integration of traditional medicine into evidence-based clinical practice. Nonetheless, methodological limitations such as short-term clinical trials and heterogeneity in herbal research designs warrant more standardized and longitudinal studies. Future research should explore pharmacogenomic personalization, long-term safety, and synergistic effects between modern and natural therapeutics to strengthen the scientific foundation of rational GERD pharmacotherapy. Based on the findings, it is recommended that clinicians and healthcare practitioners adopt a personalized, multimodal pharmacotherapy approach by integrating conventional acid-suppressive agents with motility and mucosal-protective therapies. Academics are encouraged to expand research through triangulated qualitative and clinical methods to better understand patient-specific factors influencing GERD outcomes. Future studies should also explore long-term safety, pharmacogenomic variations, and the standardized integration of herbal medicine to strengthen the scientific basis of rational GERD management.

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