



**PLANT-DERIVED ANTIMICROBIAL AND ANTIULCER AGENTS AS
EMERGING THERAPEUTIC STRATEGIES AGAINST
ANTIMICROBIAL RESISTANCE AND PEPTIC ULCER DISEASE**

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ABSTRACT

Antimicrobial resistance (AMR) has emerged as a global health emergency, diminishing the effectiveness of conventional antibiotics and posing major challenges to the management of infections such as *Helicobacter pylori*-associated peptic ulcer disease (PUD). Rising resistance to clarithromycin, metronidazole, levofloxacin, and other frontline agents has significantly reduced eradication success, prompting the need for safer, multimodal therapeutic approaches. Medicinal plants represent a rich source of structurally diverse and pharmacologically active compounds, alkaloids, flavonoids, terpenoids, tannins, coumarins, phenolics, and sulfur derivatives, that exert broad-spectrum antimicrobial, antioxidant, anti-inflammatory, and gastroprotective effects. Evidence from phytochemical, spectroscopic (UV/Vis, FTIR), chromatographic (TLC, HPTLC), and biological evaluations demonstrates strong antibacterial and antiulcer activities in plants such as *Aegle marmelos*, *Terminalia chebula*, *Allium sativum*, *Phyllanthus niruri*, *Solanum nigrum*, and *Azadirachta indica*. These herbs act through multiple mechanisms, including membrane disruption, urease inhibition, anti-adhesion effects, efflux pump suppression, free-radical scavenging, mucin enhancement, and mild acid-neutralizing properties. Such multi-target actions reduce the likelihood of resistance development and offer dual benefits against microbial infection and mucosal injury. Emerging therapies, including potassium-competitive acid blockers (P-CABs) like vonoprazan and probiotic strains such as *Lactobacillus casei Shirota*, provide additional advantages through deeper acid suppression and microbiota modulation. Taken together, current evidence supports an integrative, resistance-conscious approach that combines

standardized herbal formulations with modern therapeutic advancements. These plant-derived strategies hold significant promise as sustainable, accessible, and safer alternatives for combating AMR and improving the management of PUD.

KEYWORDS: Antimicrobial resistance (AMR), *Helicobacter pylori*, Peptic ulcer disease (PUD), Plant-derived antimicrobials, Antiulcer phytochemicals, Medicinal herbs.

INTRODUCTION

Global health burden of antimicrobial resistance (AMR): Antimicrobial resistance (AMR) has become one of the most alarming public-health challenges of the 21st century, driven by excessive antibiotic use, self-medication, poor stewardship, and widespread misuse in humans and animals. According to the World Health Organization and recent global estimates, AMR contributed to 4.71 million deaths in 2021, with 1.14 million directly attributable to resistant infections, disproportionately affecting low-income regions [1,2]. Increasing resistance in pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Helicobacter pylori* has substantially reduced the effectiveness of standard antibiotic regimens. This escalating resistance crisis underscores the urgent need for safer, multi-target, plant-derived therapeutic alternatives capable of overcoming limitations of current drug therapy [3]. Mechanisms of Antimicrobial Resistance (AMR) is shown in Figure 1.

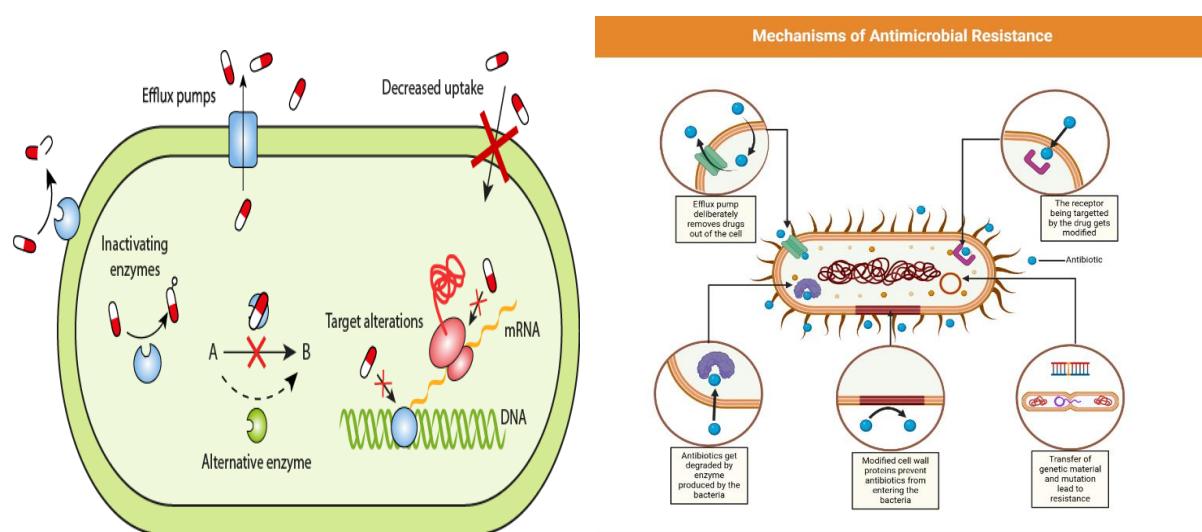


Figure 1. Mechanisms of Antimicrobial Resistance (AMR). A conceptual diagram showing key AMR mechanisms including mutation accumulation, biofilm formation, efflux pump overexpression, enzymatic antibiotic degradation, and horizontal gene transfer. [1, 2, 16]

Figure 1 illustrates the major mechanisms through which bacteria develop antimicrobial resistance. These include enzymatic degradation of antibiotics (e.g., β -lactamases), modification of drug targets, reduced membrane permeability, and active efflux pump systems that expel drugs from bacterial cells. Horizontal gene transfer via plasmids, transposons, and bacteriophages accelerates the spread of resistance traits within and across species. Biofilm formation further enhances survival by creating a protective barrier that limits antibiotic penetration. Together, these multi-layered mechanisms reduce antibiotic efficacy, complicate infection control, and highlight the need for plant-derived, multi-target therapies capable of bypassing or inhibiting resistance pathways.

Peptic ulcer disease and *H. pylori* as AMR-linked threats: Peptic ulcer disease (PUD) remains a major gastrointestinal disorder globally, primarily driven by *H. pylori* infection, NSAID overuse, oxidative stress, and hyperacidity [4]. Rising resistance to clarithromycin, metronidazole, and levofloxacin has significantly reduced eradication success, with rates dropping below 70% in many regions [5]. Conventional triple therapy and PPI-based regimens have lost effectiveness due to antibiotic resistance and inadequate acid suppression [6]. These failures have shifted scientific focus toward plant-based antimicrobials, which offer anti-*H. pylori*, antioxidant, acid-neutralizing, and mucosal-protective properties essential for dual infection and ulcer management [7,8].

Medicinal plants as promising antimicrobial alternatives: Medicinal plants provide a chemically diverse reservoir of bioactive metabolites such as alkaloids, flavonoids, terpenoids, tannins, glycosides, and phenolic acids [9]. These phytochemicals act through multi-site mechanisms, reducing the likelihood of bacterial resistance [3]. Studies consistently validate the antimicrobial effects of *Azadirachta indica*, *Allium sativum*, *Terminalia chebula*, *Phyllanthus niruri*, *Aegle marmelos*, *Solanum nigrum*, *Aloe barbadensis*, and others [4,10,5]. In addition to antibacterial activity, many herbs exhibit urease-inhibitory, anti-adhesion, anti-biofilm, antioxidant, and anti-inflammatory effects, addressing multiple pathways of MDR infection and mucosal injury [10,3].

4. Herbal antimicrobial and anti-*H. pylori* insights from recent studies

4.1 Broad-spectrum antibacterial activity of medicinal plants against MDR pathogens: Mahato and Sharma (2018) reviewed extensive antibacterial evidence for medicinal plants, emphasizing their relevance in combating multidrug-resistant pathogens. The article highlights that plant-derived compounds such as alkaloids, flavonoids, tannins, phenolics,

resins, and essential oils exhibit broad-spectrum activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, and MRSA. Numerous studies summarized in the review show that ethanolic and methanolic extracts often produce strong inhibition zones, outperforming aqueous extracts. The authors emphasize the low toxicity, cost-effectiveness, and multi-target mechanisms of herbal antimicrobials, supporting their promise as alternatives for AMR-related infections [9].

4.2 Therapeutic importance of *Aegle marmelos* in managing AMR and peptic ulcer disease:

Mahato and Sharma (2021) highlighted that *Aegle marmelos* Linn. (Bael) possesses broad-spectrum antibacterial and antiulcer activity, making it a promising herbal agent in the era of antimicrobial resistance. The abstract emphasizes that *A. marmelos* exhibits diverse pharmacological effects, including antioxidant, anti-inflammatory, antihistaminic, hepatoprotective, and immune-modulatory actions. Its antibacterial potential extends to pathogens responsible for gastrointestinal infections, while its antiulcer activity is linked to mucosal protection, acidity reduction, and improved healing. The review further notes that WHO recommends the use of herbal antimicrobials to reduce AMR, strengthening the therapeutic relevance of *A. marmelos* in PUD and *H. pylori* management [15].

4.3 Herbal antimicrobials as dual-acting therapeutics for AMR and Peptic ulcer disease:

Mahato (2021) highlighted that antimicrobial resistance (AMR) continues to rise globally, making peptic ulcer disease increasingly difficult to manage with conventional quadruple therapy. The review documented 20 medicinal plants possessing both antibacterial and antiulcer activities, offering dual benefits against *H. pylori* infection and gastric mucosal damage. Herbs such as *Acacia arabica*, *Aegle marmelos*, *Allium sativum*, *Azadirachta indica*, *Phyllanthus niruri*, *Solanum nigrum*, and *Terminalia chebula* showed strong evidence of antimicrobial, gastroprotective, and healing effects. The paper emphasized WHO's recommendation to shift toward herbal antimicrobials to reduce AMR and improve treatment safety [7]. Table 1 represents some major medicinal plants with antimicrobial and antiulcer properties.

Table 1. Some major medicinal plants with antimicrobial and antiulcer properties.

Plant Name	Key Bioactive Compounds	Antimicrobial Actions	Antiulcer / Gastroprotective Actions	Ref. No.

<i>Terminalia chebula</i>	Ellagitannins, gallic acid, flavonoids	Anti- <i>H. pylori</i> , anti-biofilm	Antioxidant, mucosal healing, acid-neutralizing	9,4,10,8,3
<i>Allium sativum</i>	Allicin, sulfur compounds	Strong antibacterial including <i>H. pylori</i>	Anti-inflammatory, epithelial protection	9,4,3
<i>Aegle marmelos</i>	Tannins, coumarins, flavonoids, alkaloids	Active against GI pathogens and MDR strains	Reduces acidity, ulcer index, oxidative stress	7,11,3
<i>Phyllanthus niruri</i>	Phyllanthin, flavonoids	Anti- <i>H. pylori</i> , urease inhibition	Antioxidant, gastroprotective	9,10
<i>Solanum nigrum</i>	Alkaloids, glycosides	Potent urease inhibitor	Anti-inflammatory, mucosal restoration	10
<i>Aloe barbadensis</i>	Anthraquinones, polysaccharides	Moderate antibacterial	Gastroprotective, antioxidant, mild antacid	8,11,3
<i>Azadirachta indica</i>	Nimbidin, limonoids	Strong antibacterial including <i>H. pylori</i>	Anti-inflammatory, ulcer healing	9,4

4.4 Dual antimicrobial and antiulcer potential of *Aegle marmelos* in AMR and PUD

management: Mahato (2020) extensively reviewed the antibacterial and antiulcer potential of *Aegle marmelos*, highlighting its wide spectrum of activity against Gram-positive and Gram-negative pathogens, including *E. coli*, *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, and MDR strains. Ethanolic and methanolic extracts consistently demonstrated the strongest antimicrobial efficacy, attributed to phytochemicals such as flavonoids, tannins, alkaloids, saponins, and coumarins. The review also documented significant antiulcer activity in multiple animal models, with reductions in gastric acidity, ulcer index, oxidative stress, and gastric lesions. These findings validate *A. marmelos* as a promising dual-acting herbal agent for AMR-related infections and peptic ulcer management [8]. Key Antiulcer Mechanisms of Medicinal Plants is shown in Figure 2.

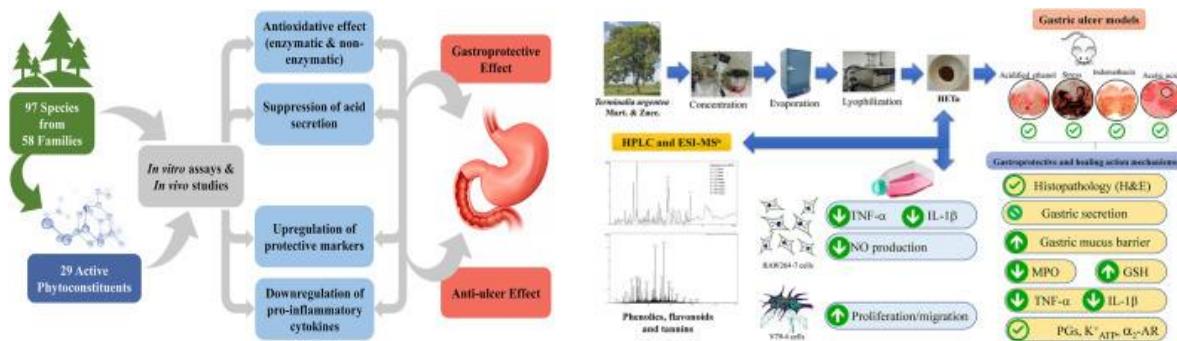


Figure 2. Key Antiulcer Mechanisms of Medicinal Plants. Diagram representing antioxidant action, mucosal protection, prostaglandin enhancement, acidity reduction, and epithelial healing mediated by plant-derived compounds. [7, 8, 20]

Figure 2 summarizes the key antiulcer mechanisms of medicinal plants. Phytochemicals such as flavonoids, tannins, phenolics, alkaloids, and coumarins enhance mucosal protection by increasing mucus secretion, strengthening epithelial integrity, and promoting prostaglandin-mediated cyto-protection. Their antioxidant properties neutralize reactive oxygen species, reducing oxidative stress and tissue injury. Many herbs also inhibit gastric acid secretion, buffer excess acidity, and suppress inflammatory mediators that contribute to ulcer formation. Some plant metabolites exhibit anti-*H. pylori* activity through urease inhibition, membrane disruption, or anti-adhesion effects. These combined actions demonstrate the multi-target therapeutic potential of herbal remedies in managing peptic ulcer disease.

4.5 Antimicrobial efficacy of ethnomedicinal plants against *E. coli* and *H. pylori*: Recent work by Mahato and Sharma (2024) demonstrated the strong antibacterial potential of several ethnomedicinal plants against *Escherichia coli* and *Helicobacter pylori*, two major pathogens associated with gastrointestinal infections and ulcer formation. Their study revealed that *Eclipta prostrata*, *Azadirachta indica*, and *Allium sativum* exhibited potent inhibition of *E. coli*, while garlic and neem showed the highest activity against *H. pylori*, supported by low MIC values. The authors attributed these effects to phytochemicals such as allicin, nimbidin, wedelolactone, and flavonoids, which act via membrane disruption, oxidative stress, and enzyme inhibition, reducing resistance risks [4].

4.6 Comprehensive herbal strategies against *H. pylori* and antimicrobial resistance: Mahato and Sharma (2025) highlighted that *Helicobacter pylori* infection remains the leading cause of peptic ulcer disease, yet increasing antimicrobial resistance has severely reduced the success of standard therapies such as triple and quadruple regimens. The article provides

extensive evidence of 117 medicinal plants demonstrating anti-*H. pylori* activity, including potent herbs like *Acacia arabica*, *Allium sativum*, *Aegle marmelos*, *Curcuma longa*, *Phyllanthus niruri*, and *Terminalia chebula*. Multiple mechanisms were identified, urease inhibition, anti-adhesion effects, biofilm disruption, anti-inflammatory pathways, and antioxidant protection, making herbal drugs promising tools to combat *H. pylori*-induced ulcers and AMR challenges [14]. *Helicobacter pylori* Pathogenesis in Peptic Ulcer Disease is shown in Figure 3.

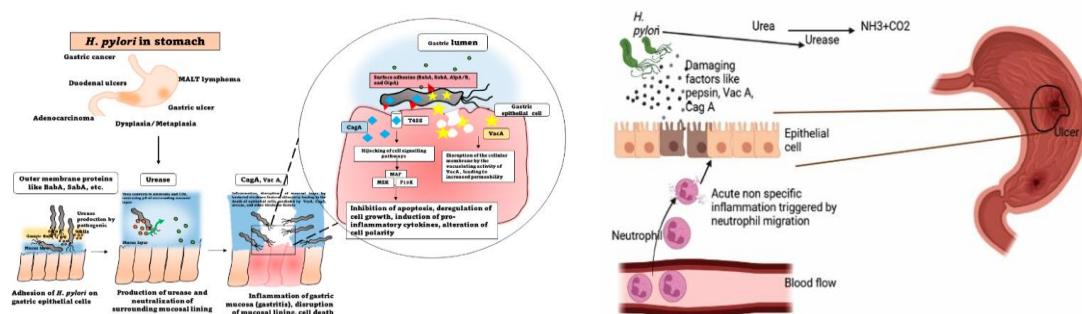


Figure 3. *Helicobacter pylori* Pathogenesis in Peptic Ulcer Disease. Mechanistic illustration of *H. pylori*-induced gastric injury showing adhesion, urease activity, ammonia production, mucosal inflammation, and epithelial damage leading to ulceration. [17, 18, 19]

Figure 3 depicts the pathogenesis of *Helicobacter pylori* within the gastric mucosa. The bacterium survives acidic conditions using urease, which converts urea into ammonia, neutralizing stomach acid. Adhesins enable attachment to epithelial cells, while virulence factors such as CagA and VacA trigger inflammation, cellular damage, and disruption of mucosal defenses. Chronic infection leads to oxidative stress, cytokine release, epithelial erosion, and ultimately gastric ulcer formation. Persistent colonization, combined with rising antibiotic resistance, contributes to therapeutic failures. Understanding these pathogenic mechanisms supports the development of plant-based antimicrobials that inhibit urease, reduce adhesion, and protect gastric tissues.

4.7 Multifunctional plant-derived antimicrobials against MDR pathogens and *H. pylori*: Mahato, Ojha, and Patel (2025) provided a comprehensive overview of plant-derived antimicrobials as emerging solutions to combat multidrug-resistant (MDR) pathogens. The review highlighted that phytochemicals, including alkaloids, flavonoids, terpenoids, tannins, and phenolic acids, exert multifaceted antimicrobial mechanisms such as membrane disruption, efflux pump inhibition, quorum-sensing suppression, enzyme inhibition, and

biofilm degradation. Spectroscopic (UV/Vis, FTIR) and chromatographic (HPTLC, HPLC) analyses support the presence of potent metabolites in plants like *Terminalia chebula*, *Allium sativum*, and *Aloe barbadensis*. The article also emphasized synergistic interactions between plant extracts and antibiotics, alongside gastroprotective and urease-inhibitory actions beneficial for managing resistant *H. pylori* infections [3].

4.8 Acid-neutralizing capacity of herbal drugs in ulcer management: Mahato and Sharma (2025) reported that several antibacterial and antiulcer herbal drugs possess measurable acid-neutralizing capacity (ANC), supporting their role as natural antacid alternatives. Their quantitative analysis showed that *Acacia arabica* (0.54 mEq/g) and *Terminalia chebula* (0.46 mEq/g) exhibited the highest ANC among the tested botanicals, followed by *Aloe barbadensis* and *Aegle marmelos*. These herbs demonstrated the ability to buffer gastric acid and may reduce reliance on synthetic antacids linked to rebound acidity and nutrient malabsorption. The study highlights the therapeutic potential of herbal drugs in acidity and ulcer management through mild but safer long-term gastric buffering [11].

4.9 Spectroscopic identification of bioactive compounds in key antiulcer herbs: Mahato and Sharma (2024) demonstrated through UV/Vis and FTIR spectroscopic characterization that *Terminalia chebula* and *Allium sativum* contain potent bioactive compounds supporting their antiulcer and anti-*H. pylori* effects. *T. chebula* showed a λ_{max} at 278 nm, indicating polyphenols such as ellagitannins and flavonoids, while *A. sativum* exhibited a λ_{max} at 254 nm, confirming sulfur compounds like allicin. FTIR analysis identified phenolic O–H groups, aromatic C=C, glycosidic bonds in *T. chebula*, and sulfur functional groups in garlic. These phytochemicals correlate with antimicrobial, anti-inflammatory, and mucosal-protective actions crucial for PUD and AMR management [12].

4.10 Urease inhibition by medicinal plants as a strategy against *H. pylori*: Mahato and Sharma (2025) evaluated the urease inhibition potential of 20 medicinal plants as an innovative strategy to control *Helicobacter pylori*, a major etiological agent of peptic ulcer disease. Their results identified *Solanum nigrum* (IC_{50} : 1.25 $\mu\text{g}/\text{mL}$), *Terminalia chebula* (2.44 $\mu\text{g}/\text{mL}$), and *Phyllanthus niruri* (2.54 $\mu\text{g}/\text{mL}$) as the most potent inhibitors, outperforming the standard thiourea (4.22 $\mu\text{g}/\text{mL}$). These extracts exhibited strong dose-dependent inhibition due to flavonoids, tannins, and alkaloids that interfere with urease-mediated gastric survival of *H. pylori*. Several commonly used herbs like *Azadirachta indica*

and *Eclipta prostrata* showed weak activity, emphasizing phytochemical variability [10]. Urease inhibition pathway of herbal extracts is shown in Figure 4.

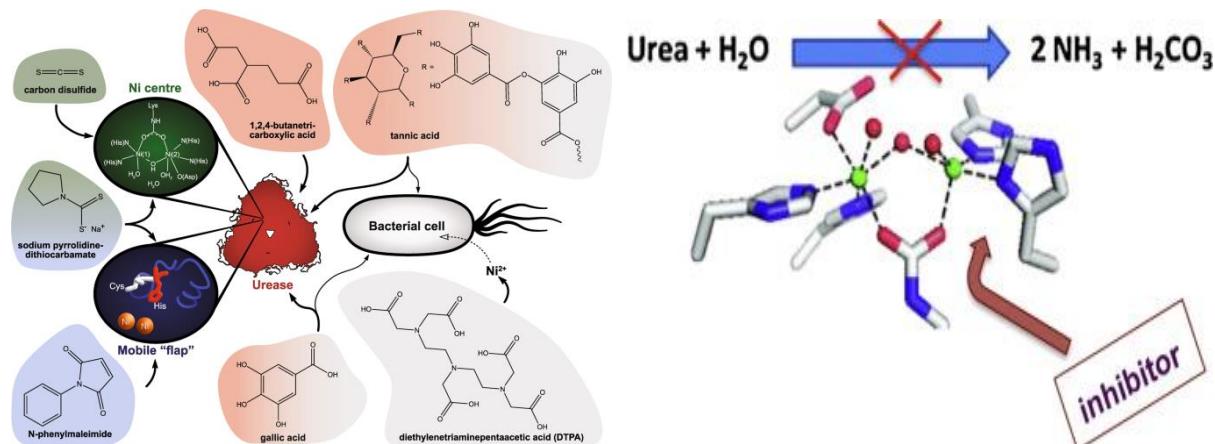


Figure 4. Urease Inhibition Pathway of Herbal Extracts. Illustration showing how herbal phytochemicals inhibit urease enzyme activity, preventing *H. pylori* survival in acidic environments. [10, 21, 22]

Figure 4 illustrates how medicinal plant extracts inhibit urease, a key enzyme that enables *H. pylori* to survive acidic gastric environments. Urease converts urea into ammonia and carbon dioxide, creating a protective alkaline cloud around the bacteria. Phytochemicals, such as flavonoids, tannins, alkaloids, and phenolics, interfere with urease activity by chelating nickel ions at the enzyme's active site or altering its structural conformation. This inhibition disrupts pH neutralization, making *H. pylori* vulnerable to gastric acid and host defenses. Urease inhibition is a critical mechanism through which herbal medicines reduce bacterial load and support ulcer healing.

4.11 Chromatographic profiling and standardization of key antiulcer medicinal plants:

Mahato and Sharma (2025) conducted phytochemical profiling and chromatographic analysis (TLC and HPTLC) of *Terminalia chebula*, *Allium sativum*, and *Phyllanthus niruri* to identify bioactive markers linked with antimicrobial and antiulcer effects. TLC revealed characteristic bands for tannins, flavonoids, alkaloids, and phenolic acids, while HPTLC confirmed the presence of gallic acid, ellagic acid, allicin derivatives, and phyllanthin. As shown in the chromatographic fingerprints, *T. chebula* exhibited strong phenolic intensity, correlating with its anti-*H. pylori* and mucosal-protective activity. These standardized profiles support quality control and justify the therapeutic potential of these herbs in PUD and AMR management [13].

4.12 Emerging modern therapies complementing herbal approaches in PUD management:

Mahato and Sharma (2025) emphasized that emerging alternatives such as potassium-competitive acid blockers (P-CABs) and probiotics are reshaping PUD therapy amid rising antimicrobial resistance. The article showed that Vonoprazan provides faster, stronger, and longer-lasting acid suppression than proton pump inhibitors, with clinical trials demonstrating 84–90% *H. pylori* eradication rates, especially in clarithromycin-resistant strains. Probiotics, including *Lactobacillus casei Shirota*, help reduce *H. pylori* load, restore gastric flora, and improve treatment tolerance. The combined evidence supports integrating newer acid blockers and probiotics with herbal therapies for safer, resistance-conscious management of ulcer disease [6].

4.13 Integrating standardized herbal therapies with modern approaches in PUD management:

Mahato and Sharma (2025) highlighted that peptic ulcer disease persists as a global burden due to rising antimicrobial resistance and limitations of current therapies. Their review demonstrated that numerous medicinal plants, including *Glycyrrhiza glabra*, *Moringa oleifera*, *Azadirachta indica*, and *Curcuma longa*, exhibit potent anti-*H. pylori*, anti-inflammatory, antioxidant, and acid-neutralizing properties. Advances in TLC, HPTLC, FTIR, and UV/Vis standardization have improved quality control and reproducibility of herbal therapeutics. The authors emphasized that integrating standardized herbal remedies with modern treatments enhances eradication rates, reduces PPI-related side effects, and supports WHO directives for sustainable, resistance-conscious management of PUD [5].

CONCLUSION

The growing burden of antimicrobial resistance and the declining efficacy of conventional ulcer therapies highlight the urgent need for innovative, multi-target treatment strategies. Medicinal plants provide a valuable solution by offering broad-spectrum antimicrobial, urease-inhibitory, antioxidant, and mucosal-protective activities that address both infection and gastric injury. Evidence from modern analytical and biological studies confirms the therapeutic potential of *Terminalia chebula*, *Aegle marmelos*, *Allium sativum*, *Phyllanthus niruri*, and other traditional herbs in suppressing *H. pylori*, reducing gastric acidity, and enhancing mucosal defense. Their diverse phytochemicals act synergistically through mechanisms that inherently limit resistance development. Integrating these standardized herbal therapies with emerging modalities such as potassium-competitive acid blockers and probiotics can improve treatment outcomes while reducing antibiotic dependence.

Collectively, plant-derived therapeutics offer a safe, affordable, and sustainable pathway for managing peptic ulcer disease in an era increasingly challenged by antimicrobial resistance.

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Disclaimer: This article is based on a comprehensive review of published scientific literature and drafted using AI tools for language improvement. All interpretations, analyses, and conclusions are derived from the referenced sources. The authors have made every effort to ensure the accuracy and reliability of the information presented. This work is intended solely for academic, educational, and research purposes. and should not be considered a substitute for professional medical advice, diagnosis, or treatment. The mention of specific medicinal plants or therapeutic approaches does not imply endorsement or guarantee of clinical efficacy. Readers are advised to consult qualified healthcare professionals before applying any of the discussed interventions. The authors declare no conflicts of interest.

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