

ISSN (E): 2320-3862 ISSN (P): 2394-0530 Impact Factor (RJIF): 5.94 www.plantsjournal.com

JMPS 2025; 13(5): 208-221 © 2025 JMPS

Received: 18-07-2025 Accepted: 20-08-2025

#### Aditya Singh

IIMT College of Pharmacy, Greater Noida, Uttar Pradesh,

#### Preeti Kumari

HIMT College of Pharmacy, Greater Noida, Uttar Pradesh,

#### Nisha Gupta

HMT College of Pharmacy, Greater Noida, Uttar Pradesh.

#### Dr. Nakul Gupta

HMT College of Pharmacy, Greater Noida, Uttar Pradesh,

known in recent years due to their diverse gastroprotective properties, which include anti-inflammatory, antioxidant, anti-secretory, mucosal protective, and anti-H. pylori properties. By modifying important molecular pathways like NF-κB, MAPK, and prostaglandin signaling, a number of medicinal plants, such as Glycyrrhiza glabra, Curcuma longa, Aloe vera, Zingiber officinale, and Camellia sinensis, demonstrate effectiveness in preventing ulcers and promoting mucosal healing. Helicobacter pylori infection, NSAID use, and imbalances between mucosal defense and aggressive gastric factors continue to be significant global health challenges, particularly peptic and gastric ulcers. The need for safer and

more sustainable alternatives is highlighted by the fact that traditional pharmacological therapy, such as proton pump inhibitors and antibiotic regimens, is frequently constrained by drug resistance, recurrence, and side effects. Herbal remedies have become more well-known in recent years due to their diverse gastroprotective properties, which include anti-inflammatory, antioxidant, anti-secretory, mucosal protective, and anti-H. pylori properties. By modifying important molecular pathways like NF-κB, MAPK, and prostaglandin signaling, a number of medicinal plants, such as Glycyrrhiza glabra, Curcuma longa, Aloe vera, Zingiber officinale, and Camellia sinensis, demonstrate effectiveness in preventing

Herbal plants in gastroprotection: Advancements and

Due to Helicobacter pylori infection, NSAID use, and imbalances between mucosal defense and

aggressive gastric factors, gastrointestinal disorders especially peptic and gastric ulcers remain major global health concerns. The need for safer and more sustainable alternatives is highlighted by the fact that traditional pharmacological therapy, such as proton pump inhibitors and antibiotic regimens, is frequently

constrained by drug resistance, recurrence, and side effects. Herbal remedies have become more well-

Aditya Singh, Preeti Kumari, Nisha Gupta and Nakul Gupta

Keywords: Helicobacter pylori, Glycyrrhiza glabra, Curcuma longa, aloe vera, herbal medicine, gastric ulcer, peptic ulcer, gastroprotective action, and standardization

#### 1. Introduction

ulcers and promoting mucosal healing.

Abstract

Damage to the inside lining of the gastrointestinal system is known as a gastric ulcer. It is one type of Peptic Ulcer Disease (PUD). Excessive acid secretion damages the mucus membrane lining of the stomach, leading to an ulcer. An imbalance between defensive and aggressive factors is the etiology of gastric ulcers. The majority of stomach ulcers are brought on by Helicobacter pylori (H. pylori) infections, and long-term usage of medications like aspirin, ibuprofen, etc, is also linked to it. The frequency of symptoms is linked to stomach ulcers and may vary depending on how severe the peptic ulcer is. The most prevalent sign of it is a painful burning sensation in the chest area. Peptic ulcer disease has a very low yearly incidence, 0.10 to 0.19% only. The incidence of peptic ulcer disease has decreased, according to the current study. The mortality rate is almost one in every one of the impacted cases. Historically, a wide variety of medicinal plants have been utilized in India to treat a wide range of illnesses, either alone or in combination as polyherbal preparations. These have been used for so many years and have been highly successful in treating a variety of illnesses. Natural medications were favoured due to their lower toxicity and lack of several adverse effects that were frequently seen with many manufactured medications. It is necessary to concentrate on developing new plant-oriented medications as alternatives to current ones because many of the synthetic medications that are now on the market are linked to several negative effects. It is believed that natural plants serve as the fundamental models for creating novel compounds. Many studies are currently concentrating on using natural plants to cure PUD [1].

#### 1.1 Symptoms

While large ulcers may result in significant bleeding, small ulcers may not exhibit any symptoms at all. Loss of appetite, a feeling of fullness, mild nausea, upper abdominal pain,

**Corresponding Author:** Aditya Singh IIMT College of Pharmacy, Greater Noida, Uttar Pradesh, Journal of Medicinal Plants Studies https://www.plantsjournal.com

discomfort, and insomnia, brought up by upper abdominal pain, bloody dark feces, chest pain, exhaustion, and weight loss are typical indications and symptoms of peptic ulcers [3].

#### 1.2 Background of gastrointestinal disorders

The term "gastrointestinal" (GI) disorders refers to a broad category of illnesses that affect the digestive tract and its associated organs, including the stomach, oesophagus, small and large intestines, liver, pancreas, and gallbladder [50]. These conditions are frequently divided into two categories: functional disorders of gut-brain interactions (symptoms based on syndromes without consistent anatomical defects) and organic diseases (such as cirrhosis, peptic ulcer disease, inflammatory bowel disease, and GI malignancies) [2]. The symptoms-based criteria (ROME IV) used to identify and classify functional gastrointestinal disorders (FGIDs), now commonly referred to as disease of gut-brain interaction (DGBI), have been evaluated and used in international epidemiology research since 2020 [4, 2]. According to extensive multicentre and international surveys. DGBIs are still quite common throughout the world and are linked to significant declines in the quality of life and higher healthcare use [53, 2]. More than 40% of those polled fulfilled the criteria for at least one FGID or DGBI, according to epidemiological data from the Rome Foundation global epidemiology study (Released in 2021), underscoring the significant public health burden of these conditions [5], many gastrointestinal illnesses have a multifactorial pathophysiologic structure nowadays, with a focus on interacting anomalies in gut microbiota, immunological and mucosal function, visceral sensation, gastrointestinal motility, and bidirectional communication [6]. A major factor in symptoms, including nausea, vomiting, early satiety, constipation, and diarrhoea in both functional and pathological disorders of motility (e.g., delayed stomach emptying, altered small-bowel or colonic transit) [7]. Abdominal pain and bloating in DGBIs, such as irritable bowel syndrome and functional dyspepsia, have frequently been linked to visceral hypersensitivity, an elevated feeling of pain or discomfort from everyday gut stimulation [8]. previous gut infections are linked to long-term functional problems, low-grade mucosal immune activation, and impaired epithelial barrier function, which is a known contributor that can prolong symptoms [9]. Dysbiosis, or changes in the gut microbiota, has been linked to both upper and lower gastrointestinal illnesses and is now thought to affect immunological signalling, motility, and the gut-brain axis [7, 10]. The management of DGBIs relies heavily on biopsychosocial techniques because the microbiota-gut-brain axis offers a mechanistic foundation for understanding how psychological stressors and central nervous system processes modify GI function and symptom perception [6, 11]. Modern diagnostic techniques combine specific investigations (blood tests, imaging, endoscopy, and biopsies) with a thorough clinical history and Rome-based symptoms criteria to rule out organic disease before classifying a problem as largely functional because symptoms might overlap between conditions [2]. As a result, management strategies are multimodal: DGBIs are treated with dietary interventions, microbiome-directed therapies (where evidence supports), symptom-directed pharmacotherapy, and psychological treatments that address gut-brain interactions, whereas organic disease-directed medical or surgical therapies [6,12].

## 1.3 Prevalence and impact of gastrointestinal disorders 1.3.1 Definition and extent

Functional disorders (such as gut-brain interaction disorders like irritable bowel syndrome, or IBS), common chronic

conditions (such as gastro-oesophageal reflux disease, or GERD), inflammatory disorders (such as inflammatory bowel disease, or IBD), peptic ulcer disease, hepatopancreatobiliary diseases, and GI cancers are all included under the general term "gastrointestinal (GI) disorders." Although the pathogenesis, severity, and prognosis of these disorders vary greatly, they all share a significant public health characteristic: a high population prevalence that has a significant impact on quality of life, healthcare utilization, and financial burden [13,53].

### 1.3.2 Epidemiology: Trends and estimates of prevalence

Functional gastrointestinal illnesses and symptom-based ailments are still quite common worldwide, according to recent comprehensive syntheses. Rome criterion pooled estimates for IBS show a global prevalence in the single digits to low teens (pooled estimates vary by survey method and diagnostic criteria: for example, ~9% using Rome III in international analyses; Rome IV figures are generally lower but noticeable) <sup>[54]</sup>. According to GERD symptom-based prevalence meta-analyses, the prevalence is estimated to be between 10 and 14 percent worldwide, with significant geographical heterogeneity and a general upward trend in incident and prevalent cases over the past few decades. These figures show both increased awareness and diagnosis, as well as actual increases in illness incidence in many areas <sup>[14, 15]</sup>.

### 1.3.3 Burden: Medical expenses, morbidity, and mortality

Beyond prevalence, GI problems have significant effects on the health system. GI diseases and related cancers cause hundreds of thousands of deaths worldwide each year and cost billions of dollars in healthcare expenses [13]. Recent national and international analyses quantify millions of clinical encounters, significant hospital admissions, and large direct medical expenditures annually. Additionally, the system-level burden is increased by the prevalence of GI cancers in specific areas and the frequency of diagnostic procedures (such as endoscopies) [14].

### 1.3.4 Influence on productivity and life quality

Numerous gastrointestinal illnesses, particularly functional disorders such as IBS and chronic GERD, are linked to substantial declines in health-related quality of life, elevated psychiatric comorbidity (depression, anxiety), and decreased productivity at work (presenteeism and absenteeism) [53]. The persistent symptoms of functional disorders and the chronic, relapsing character of illnesses like IBD cause long-term disability that goes much beyond the acute expenditures of medical therapy [54].

### 1.3.5 Causes of temporal and geographic variation

Methodological variations (case definitions, survey techniques), demographic changes (ageing populations), lifestyle and environmental exposures (dietary westernisation, obesity, antibiotic exposure, urbanisation), and enhanced diagnostic capabilities are some of the factors contributing to variation in prevalence over time and between nations [15]. Rising incidence of diseases like GERD and IBD that have historically been more prevalent in high-income environments are frequently reported in low- and middle-income nations, indicating significant roles for shifting environmental risk profiles and healthcare access [14].

## **1.3.6** Implications for research and the health system Priorities include:

a) Strengthening primary-care recognition and evidence-

based management to reduce avoidable hospital utilisation.

- b) Expanding access to diagnostic endoscopy and targeted therapies when appropriate
- c) Investing in preventive strategies focused on modifiable risk factors (diet, obesity, antibiotic stewardship.
- d) Funding multidisciplinary research into pathophysiology (microbiome, gut-brain axis), long-term outcomes, and cost-effective delivery models [13].
- e) Harmonising case definitions and surveillance methods to improve comparability across studies due to the high prevalence and significant cumulative burden. Recent national and international burden evaluations that measure both health loss and cost support these aims [15].

#### 1.3.7 Future directions and gaps

There are still several important gaps, including the under-representation of low- and middle-income nations in high-quality epidemiologic studies, the uneven application of standardised diagnostic criteria (symptom vs. endoscopy-confirmed definitions; Rome III vs. IV), the scarcity of real-world cost-of-illness data in many areas, and the lack of knowledge regarding the impact of early-life and environmental exposures on lifetime risk <sup>[54]</sup>. Coordinated worldwide surveillance, registries (especially for GI malignancies and IBD), and longitudinal cohort studies combining clinical, environmental, and genomic data will be necessary to close these gaps <sup>[13]</sup>.

# 2. Limitations of conventional treatments in gastric disease

## 2.1 Three pillars support conventional management of gastric disease

Endoscopic ± surgical interventions for complications (bleeding, perforation, strictures, malignancy), pharmacologic acid suppression (primarily proton pump inhibitors, or PPIs) for acid-related injury and symptom control, and elimination of *Helicobacter pylori* when present [16]. Although the morbidity and mortality rates from peptic ulcer disease and its associated consequences have significantly decreased as a result of these therapies, their efficacy in numerous contexts is compromised by significant and widely acknowledged limitations [17].

## 2.2 Treatment failure and increasing antibiotic resistance in *H. pylori* eradication therapy

As worldwide antibiotic resistance rises, the traditional paradigm of short-course multi-drug antibiotic regimens coupled with acid suppression is being challenged (clarithromycin, metronidazole, levofloxacin). With normal triple and some quadruple regimens, resistance rates have resulted in decreased eradication rates, increasing the likelihood of treatment failures and necessitating salvage therapy [18]. When local susceptibility data are ignored, empirical regimens frequently fail due to geographic diversity in resistance patterns. Although access to trustworthy culture or molecular susceptibility testing is still restricted, clinicians in many areas increasingly mandate the use of either susceptibility-guided medication or more recent regimens (such as bismuth quadruple therapy or customised regimens)

Practical implications include increased antibiotic exposure and recurring medical visits, which prolong resistance cycles, and the danger of recurrent ulcers and stomach cancer in vulnerable patients if *H. pylori* is not eradicated <sup>[18]</sup>.

# 2.3 Acid suppression (PPI) limitations include misuse, negative side effects, and insufficient symptom control

PPIs have several drawbacks and are not always effective in curing diseases, although they are quite effective at suppressing acid and promoting mucosal repair. A sizable subgroup of patients (referred to as PPI-refractory GERD or functional heartburn) continues to experience symptoms even after taking PPIs as prescribed by guidelines [20]. This is frequently due to non-acid reflux, hypersensitivity, motility issues, or non-oesophageal causes rather than the PPI's incapacity to lower acid. Furthermore, chronic renal disease, gastrointestinal infections (including C. difficile), vitamin deficiencies, bone fracture risk, and other potential negative effects have been linked to long-term PPI exposure, raising concerns about extended, inappropriate use [21]. Last but not least, improper long-term prescriptions and a lack of deprescribing are frequent, leading to preventable safety and financial problems [22].

# 2.4 Endoscopic and surgical interventions: Efficacy but variable durability and resource limits

Acute bleeding control has been enhanced, and the necessity for emergency surgery has decreased thanks to endoscopic procedures (heat coagulation, clips, injection, and more recent haemostatic powders and devices) [16]. However, rebleeding still happens, particularly when the reason (e.g., malignant ulcer) cannot be determined, when underlying coagulopathy or antithrombotic medication cannot be reversed, or when stigmata of recent haemorrhage are evident [17]. The availability of sophisticated modalities and operator expertise is also critical to the success of endoscopic therapy; in low-resource environments or after hours, delays or inadequate procedures may exacerbate results. Although surgery has a greater morbidity and mortality rate and is less preferred by many patients, it is nevertheless a life-saving option for refractory conditions [23].

## 2.5. Diagnostic heterogeneity and misclassification reduce treatment effectiveness

Numerous symptoms related to the stomach are non-specific and can be found in structural, inflammatory, and functional problems. Some patients treated empirically never have aciddriven

*H. pylori*-driven disease, while others with alarm features or non-acid mechanisms may be undertreated or mismanaged <sup>[20]</sup> Symptom-based treatment, such as empirical PPI trials and empirical *H. pylori* test-and-treat, can be effective but runs the risk of misclassification. The application of guidelines and evaluation of the efficacy of treatments are complicated by the variation in diagnostic criteria (symptom-based vs. endoscopy-confirmed disease) in research and practice <sup>[16]</sup>.

#### 2.6 Equity and system-level constraints

Health-system barriers, such as restricted access to endoscopy and susceptibility testing, inconsistent application of regimens based on guidelines, fluctuating availability and cost of newer agents (e.g., potassium-competitive acid blockers like *vonoprazan*), and inadequate antimicrobial stewardship, reduce the impact of even effective therapies [19]. Low- and middle-income nations are disproportionately affected by these disparities, since a combination of limited resources and evolving epidemiology (such as an increase in IBD/GERD) leads to growing disparities in results [24].

## 2.7 Research and clinical implications: What traditional methods overlook

- a) Antibiotic resistance and the need for susceptibilityguided or novel anti-*H. pylori* strategies
- b) Non-acid, functional, and biopsychosocial factors contributing to chronic symptoms
- c) Long-term safety and rational deprescribing of acid suppression
- d) Structural health-system limitations to providing individualised care are all issues that conventional therapies reduce morbidity but frequently ignore [18].

Surveillance of local resistance patterns, increased accessibility to diagnostic testing (pH-impedance, culture, or molecular testing), the development and fair distribution of novel treatments (including P-CABs like *vonoprazan* when appropriate), and health-system interventions to guarantee guideline-concordant care and antimicrobial stewardship are all necessary to close these gaps [24].

# 3. Herbal medicine as an alternative therapy 3.1 Justification and extent

Herbal remedies are utilised as supplementary or alternative therapy for stomach issues all over the world. These include single-plant extracts, multi-herb formulations (such as traditional Chinese medicine, Ayurvedic, and other ethnomedicinal preparations), and isolated phytochemicals [25]. Cultural acceptability, perceived safety, and multi-target pharmacology which includes anti-inflammatory, mucoprotective, anti-secretory, antibacterial, pro-motility, and antioxidant effects are what make them appealing. Herbal treatments are appealing as prospective non-antibiotic agents against Helicobacter pylori and as supplements to traditional care (to improve symptom control or lessen adverse effects) due to their multi-mechanistic action [26].

#### 3.2 Clinical efficacy evidence

According to randomised trials and meta-analyses, some herbal preparations (like peppermint oil and some multi-herb formulations) can lower global symptom scores and abdominal pain when compared to a placebo for Functional Gastrointestinal Disorders (FGIDs), IBS, and dyspepsia [78]. In short-term trials, the effect sizes of these herbal preparations are comparable to those of some conventional agents. The preparation and trial methods have an impact on the quality of the evidence [26].

# 3.3 Non-Erosive Reflux Disease (NERD) and Gastro-Oesophageal Reflux Disease (GERD)

Certain Chinese herbal formulas (such as *Banxia houpu, Banxia xiexin*, and related formulas) have been shown to alleviate symptoms in individuals with refractory symptoms when used as monotherapy or as adjuncts to PPIs in systematic reviews and Randomised Controlled Trials (RCTs), most of which are from East Asia [21]. Conclusions are encouraging but not conclusive due to heterogeneity and methodological limitations [80].

Peptic ulcer disease and mucosal protection: Preclinical and clinical research have shown that several plants, including liquorice, aloe, and flavonoid-rich extracts, have anti-ulcer and mucoprotective properties. Some small clinical trials indicate that using these plants as an adjuvant can reduce symptoms and speed healing, but there are still few high-quality, large RCTs available [28, 25].

#### 3.4 Action mechanisms

Herbal agents work through a variety of complementary mechanisms, including direct antimicrobial activity (disruption of membranes, inhibition of urease or adhesion), cytoprotection (mucus secretion, prostaglandin modulation), anti-inflammatory and antioxidant pathways (inhibition of NF- $\kappa B$ , reduction of cytokine release), modification of gastric acid secretion and motility, and positive effects on the gut microbiome <sup>[28]</sup>. In theory, these multi-target effects may be more effective than single-target medications for addressing intricate, multifactorial causes of stomach disease <sup>[25]</sup>.

# 3.5 Quality, safety, and interactions between herbs and drugs

Herbal remedies are not risk-free. Adulteration, varying phytochemical content, contamination, hepatotoxicity with specific herbs, and clinically significant herb-drug interactions (St. John's wort-type interactions affecting PPI or antibiotic metabolism; *glycyrrhizin/licorice* with corticosteroids or antihypertensives, for example) are among the concerns <sup>[29]</sup>. Safety evaluations and pharmacovigilance are crucial before widespread recommendations are made because many trials fail to disclose adverse events and product standardization <sup>[25]</sup>.

Limitations of the available data:

Small sample sizes, brief follow-up, diverse formulations and dosages, uneven quality control of herbal remedies, trial geographic clustering (many from East Asia), and inconsistent methodological rigour (blinding, randomisation, placebo control) are the main drawbacks <sup>[78]</sup>. Therefore, even while the results are encouraging, systematic reviews frequently conclude that more stringent safety monitoring and higher-quality multi-cente RCTs with standardised, quality-assured goods are needed <sup>[27]</sup>.

## 4. Herbal plants with gastroprotective activity 4.1 The anti-inflammatory herbs

The main cause of mucosal damage and ulceration is chronic gastric inflammation, which can be caused by H. pylori, NSAIDs, bile reflux, or stress. Herbs that reduce mucosal inflammation therefore have gastroprotective effects by reducing pro-inflammatory cytokines (TNF-α, IL-1β, and IL-6), blocking NF-κB signaling, and reducing inflammatory cell infiltration. Bioactive flavonoids, terpenoids, and phenolic acids found in many medicinal plants (including standardised multi-herbal combinations) operate on these molecular targets, reducing neutrophil infiltration, myeloperoxidase activity, and improving histology scores in animal and cell models. Mechanistically, these activities both prevent further tissue damage and establish a biochemical milieu that promotes mucosal healing. These anti-inflammatory routes are compiled in recent systematic and experimental studies, which also offer preclinical and early clinical support for TCM recipes, Ayurvedic botanicals, and standardized mixes [30, 31, 32]

**Recent plants:** In recent investigations, various elements of TCM formula, ginger (gingerols/shogaols), liquorice (glycyrrhizin), turmeric (curcumin), and others have been shown to exhibit NF-κB inhibition, decreased cytokine release, and histological mucosal protection [33, 34].

#### 4.2 The antioxidant plants

Excess reactive oxygen/nitrogen species, or oxidative stress, is a major mediator of gastric mucosal injury because it

Journal of Medicinal Plants Studies https://www.plantsjournal.com

weakens mucosal defense and destroys proteins, lipids, and DNA. By

- a) Scavenging free radicals,
- b) Increasing endogenous antioxidant enzymes (SOD, catalase, and GSH), and
- c) Avoiding lipid peroxidation of gastric membranes, antioxidant herbs protect the stomach.

The phytochemical classes that are most closely linked to these activities are tannins, phenolic acids, flavonoids, and some terpenoids. In ethanol, NSAID, and stress ulcer models, multi-component extracts with strong antioxidant capacity (as determined by *in vitro* radical-scavenging assays and *in vivo* indicators) lower ulcer index and speed up mucosal healing [35, 36].

**Representative plant/evidence:** In 2021-2024, studies showed that Phy-Blica-D and numerous extracts from *Ferula spp*. Exhibit both *in vitro* antioxidant activity and *in vivo* ulcer prevention; in 2023, *Melissa officinalis* (lemon balm) showed both antioxidant and gastroprotective properties [35, 102].

### 4.3 Theanti-secretory herbs

Inhibition of histamine-driven pathways (H2 receptor modulation), downregulation or direct inhibition of gastric H<sup>+</sup>/K<sup>+</sup>-ATPase (proton pump), blockade of cholinergic (M3) or gastrin (CCK2) signaling, or indirect reduction through modulation of enterochromaffin-like cells are some of the mechanisms by which herbs with anti-secretory properties work to prevent excessive gastric acid secretion, which contributes to mucosal erosion and peptic ulceration. In animal and molecular investigations, several plant extracts and isolated phytochemicals have demonstrated decreased gastric acid output or lower expression/activity of acid-secreting receptors/enzymes. Herbal blends that decrease stomach acidity indicators and histamine-mediated signaling have also been reported in recent formulation research [34,81].

**Example:** Standardised herbal formulae have been demonstrated to lower histamine receptor expression and proton pump function in recent 2024-2025 investigations; neem and some alkaloid-rich extracts have been found to suppress  $H^+/K^+$ -ATPase activity in preclinical tests [82,34].

### 4.4 Herbs that preserve the mucosa

The physical and biochemical barriers of the stomach are strengthened by mucosal protective agents, which also improve mucosal microcirculation, promote glycoprotein layer integrity, increase Prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) synthesis, stimulate mucus and bicarbonate secretion, and improve epithelial restitution. Many herbs contain mucilage-forming chemicals, saponins, and polysaccharides that increase the thickness and viscosity of stomach mucus; others speed up reepithelialization by upregulating Growth Factors (EGF) and angiogenic or repair pathways. Because mucosal protection can lessen acid or NSAID-induced damage without the need for severe acid suppression, it has significant clinical value. Herbs and decoctions that boost mucosal defence factors and enhance endoscopic/histologic healing have been documented in recent studies and TCM investigations (2020-2025) [38, 39].

**Representative plants:** Include slippery elm (mucilage polysaccharides), aloe vera, liquorice (deglycyrrhizinated preparations), and several multi-herbal concoctions that increase PGE<sub>2</sub> and stomach mucus [34, 39].

### 4.5 Anti-Helicobacter pylori herbs

Chronic gastritis and peptic ulcer disease are primarily caused by H. pylori infection; plant-derived antimicrobials can help eradicate this infection either by themselves (in low-burden situations) or in conjunction with conventional antibiotics, particularly in light of the growing drug resistance. In order to lessen colonisation, mechanisms include urease inhibition, quorum-sensing disruption, anti-adhesion effects, direct bactericidal activity (membrane disruption, enzyme inhibition), and host immune response modification. A few small clinical trials and well-characterized preclinical studies suggest potential adjunctive benefit, but emphasize heterogeneity and the need for standardized clinical trials. Recent systematic reviews and experimental papers (2020-2024) have catalogued foods and medicinal plants (e.g., Terminalia spp., berberine-containing plants, certain tanninrich extracts, and standardised herbal blends) with in vitro and some in vivo anti- H. pylori activity [40,41].

**Examples:** In the 2020-2024 literature, berberine/protoberberine alkaloids, Terminalia species, and extracts rich in polyphenols and tannins have all demonstrated anti-*H. pylori* action [83].

#### 5. Mechanisms of action

#### 5.1 Inhibition of inflammatory mediators

Numerous plant extracts with gastroprotective properties work by inhibiting important pro-inflammatory pathways in the stomach mucosa. According to experimental research and reviews, phytochemicals (flavonoids, triterpenes, and alkaloids) limit neutrophil infiltration and mucosal damage following harmful stimuli (ethanol, NSAIDs, and HCl) by suppressing cytokines like TNF- $\alpha$ , IL-1 $\beta$ , and IL-6, inhibiting COX-2 and iNOS expression, and reducing NF- $\kappa$ B activation. This anti-inflammatory activity speeds up the healing of preexisting ulcers and lessens acute harm [42,28].

### **5.2** Scavenging of free radicals (antioxidant activity)

In several ulcer models, oxidative stress and reactive oxygen/nitrogen species (ROS/RNS) play a key role in mucosal damage. Strong radical-scavenging action (DPPH, ABTS, lipid peroxidation assays) and the restoration of endogenous antioxidant defenses (SOD, catalase, GSH) are demonstrated by a variety of plant extracts and isolated substances, maintaining mitochondrial function and epithelial integrity. Thus, antioxidant activity promotes healing processes and inhibits the development of mucosal ulcers [43, 44].

#### 5.3 Reduction of gastric acid secretion

Several medicinal herbs lower stomach acidity by either directly blocking the parietal cell H+/K+-ATPase or by altering stimulatory signals. Plant-derived compounds that decrease basal/stimulated acid output, decrease the expression of gastrin or histamine receptors, or function as reversible inhibitors of proton pump activity have been reported in preclinical studies. These compounds have an antisecretory effect that is similar to conventional agents in mechanism, albeit not always as potent, and aid in the healing of ulcers [85, 42]

### 5.4 Enhancement of mucus and mucosal defensive factors

In addition to stimulating mucin gene expression, herbal extracts frequently increase the production and thickness of gastric mucus, as well as the levels of protective prostaglandins and bicarbonate secretion. When paired with

enhanced mucosal blood flow and epithelial cell proliferation, improved mucus barrier function strengthens intrinsic defenses against ulcerogenic insults by reducing acid/pepsin back-diffusion and providing physical protection for regenerating epithelium [28, 45].

## 5.5 Direct antibacterial effects (notably against *Helicobacter pylori*)

Numerous natural compounds exhibit anti-*Helicobacter pylori* activity both *in vitro* and *in vivo* (growth suppression, urease inhibition, interference with adhesion/biofilm). These antibacterial qualities often exhibited by polyphenols, essential oils, and alkaloids offer an alternative or adjunct to traditional antibiotic regimens and, when used in combination strategies, may aid in overcoming resistance, as *H. pylori* is a major etiologic factor in peptic ulcer disease [41, 28].

#### 6. Clinical evidence

### 6.1 Clinical trials of single herbal preparations

Clinical studies evaluating single-plant preparations (such as licorice/Glycyrrhiza spp., turmeric/curcumin, and Bletilla striata polysaccharides) for stomach protection, ulcer healing, and Helicobacter pylori eradication or symptom treatment have been conducted steadily over the last five years. Standardized licorice preparations have been linked to better ulcer healing in pooled analyses, while isolated polysaccharide-rich extracts have shown promise in mucosal repair studies. Several Randomized Controlled Trials (RCTs) and small, well-conducted open-label studies report faster symptomatic improvement and higher rates of endoscopic healing or bacterial suppression compared to placebo or standard care. Findings are promising but not yet conclusive for widespread clinical adoption because individual trials usually have limited sample sizes, little follow-up, and inconsistent extract standardization [81, 46].

# **6.2** Clinical trials of herbal formulations (multi-herb combinations and integrative approaches)

Multicenter studies and larger pragmatic trials have assessed integrative regimens and multi-herb formulations, particularly those based on Traditional Chinese Medicine and other ethnomedical systems. Certain combination formulae, when added to normal eradication regimens or used as adjuvants, may boost *H. pylori* eradication rates, decrease antibiotic-related side effects, and, in some situations, shorten the required antibiotic exposure, according to network meta-analyses and randomised trials. Notably, when herbal adjuncts were used in conjunction with traditional therapy, several 2020-2024 trials found improved symptom relief and greater eradication rates. Cross-study comparisons and clinical translation are made more difficult by the variety of formula composition, dose, duration, and outcome definitions [47,87].

### **6.3** Meta-analyses of clinical studies

Between 2020 and 2025, several systematic reviews and meta-analyses synthesise observational data and accessible RCTs to provide pooled estimates for safety and efficacy. For endpoints including ulcer healing, symptom scores, and decreases in inflammatory markers, these meta-analyses frequently identify moderate benefit signals for particular herbs or classes (such as licorice extracts, certain polyphenol-rich preparations, and botanicals containing polysaccharides). Although plant-derived extracts may reduce bacterial load and enhance eradication when taken as an adjuvant, meta-analyses addressing anti-Helicobacter pylori effects stress that

inconsistent outcome measurements, small-study effects, and publication bias undermine confidence in pooled effect sizes. Larger, well-powered trials with standardized preparations and objective goals (endoscopy, validated symptom ratings, and microbiological testing) are also recommended by a number of recent meta-analytic attempts [48,50].

## 6.4 Safety and efficacy considerations advancements and role

Recent pharmacovigilance studies and systematic reviews have documented the general tolerability of many traditional preparations as well as new safety signals (hepatotoxicity, herb-drug interactions, idiosyncratic reactions) that call for systematic monitoring, advancing the safety evaluation of herbal gastroprotective agents. Product standardization (quantification of active constituents), contamination/ adulteration, variable bioavailability, and interactions with antibiotics or acid-suppressants used to treat peptic illness are major problems for clinical use. More rigorous RCT designs in various regions, better extraction and standardization techniques (particularly for polysaccharides and standardized polyphenol fractions), and a greater focus on combining herbal adjuvants with antimicrobial stewardship to lower antibiotic exposure while preserving eradication efficacy are some of the advancements since 2020. As long as safety monitoring, quality control, and evidence-based dosing are followed, the evidence generally supports the use of specific, well-standardized herbal medications as adjuncts in H. pylori management and as a complementary function in gastroprotection [51, 52, 53].

# **6.5** Limitations of the current clinical evidence and research priorities

Heterogeneous intervention definitions (whole herb vs. extract; different standardization markers), subjective or inconsistent goals, incomplete reporting of randomization/blinding in certain trials, and underreporting of adverse events are some examples of contemporary problems. To advance the field, the literature suggests:

- Multicenter, sufficiently powered RCTs with preregistered protocols and CONSORT-style reporting for herbal interventions;
- The use of chemically standardised extracts with defined marker compounds and stability data;
- Objective endpoints (microbiological eradication confirmed by urea breath test or culture, endoscopic healing, validated symptom instruments);
- 4) Integrated pharmacokinetic and herb-drug interaction studies; and
- 5) Robust in normal gastroenterological therapy, these steps will make it clear which herbal agents are scalable, safe, and effective [54].

## 7. Advancements in herbal medicine research 7.1 Herbal extract standardisation

The last five years have seen a significant shift in the field from descriptions of crude extracts to botanical products that are chemically defined and repeatable. Multi-marker chromatographic fingerprints, targeted quantification of one or more bioactive marker molecules, and orthogonal quality checks (microbial limits, heavy-metal/pesticide screening, and micro- and macroscopic identification) are already commonplace in modern standardisation. In order to obtain a comprehensive chemical signature that enhances batch-to-batch consistency and facilitates bioactivity correlation

studies, emerging techniques, particularly metabolomics and chemometrics, are being used. Harmonised pharmacopeial standards and metabolomics-driven quality controls are becoming essential for converting herbal candidates into clinically effective treatments, according to regulatory evaluations and comparative analyses [88, 89].

#### 7.2 Pharmacokinetic studies (ADME and interactions)

Systematic pharmacokinetic profiling of intricate plant preparations and their essential components has been a significant breakthrough. In order to determine which chemicals are accessible at target sites, their metabolic fates, and their potential for accumulation, studies now integrate in vitro (Caco-2 permeability, simulated gastric/intestinal fluids, liver microsomes), in vivo (plasma/tissue PK), and in silico modelling. Crucially, research on herb-drug interactions and multi-compound PK techniques has shed light on how components affect CYP enzymes, transporters recirculation. glycoprotein), and enterohepatic knowledge is essential for the safe co-administration of antibiotics or acid-suppressants. Integrated ADME pipelines are becoming more popular, giving bioavailable marker molecules top priority when determining therapeutic dose and safety limits [55, 90, 56]

# 7.3 Cellular and molecular mechanisms (target-based clarity)

Mechanistic resolution has been extended phenomenological anti-ulcer claims to identified molecular targets and pathways by preclinical research conducted between 2020 and 2025. For polyphenols, alkaloids, and polysaccharides, network-pharmacology and systems-biology techniques predict multi-target modalities and identify probable targets (such as NF-κB, Nrf2, COX-2, iNOS, and H+/K+-ATPase). Parallel experimental studies show decreased ROS, suppressed proinflammatory cytokines, increased mucin expression, and direct urease/adhesion inhibition, confirming antioxidant, anti-inflammatory, mucoprotective, and anti-H. pylori affects the cellular level. The sensible selection of potential botanicals for focused clinical research and combinations intended to work in concert on complementary pathways is made possible by these mechanistic facts [41,91].

#### 7.4 Drug delivery systems for herbal compounds

In plant formulation research, rapid innovation has been fuelled by poor solubility, low bioavailability, and stomach instability. Polymeric matrices, nanoparticle-based carriers, floating, mucoadhesive, and expanding gastroretentive systems, as well as 3D-printed gastroretentive designs, have all been used to extend gastric residence, safeguard labile phytochemicals, and accomplish controlled local release at the stomach lining. These technologies can lessen systemic side effects while increasing local exposure to gastroprotective substances (such as flavonoids and polysaccharides). Key actives given via GRDDS or nanoformulations have better PK profiles and increased mucosal effectiveness, according to recent reviews and proof-of-concept studies. These delivery systems serve as a crucial translational link between encouraging in vitro results and outcomes that have therapeutic significance [92, 57, 93].

### 7.5 Synergistic effects of herbal combinations

Instead of treating multi-herb formulations as simple combinations, modern research increasingly views them as

integrative, multi-target medicines. Combinations can result in true pharmacodynamic synergy (such as increased antioxidant capacity, complementary anti-inflammatory signalling, and potentiated anti-*H. pylori* activity) or allow dose-sparing of individual constituents, according to systems-pharmacology, isobolographic analyses, and combination-PK studies. However, interaction studies highlight the possibility of pharmacokinetic modulation, which is when one herb changes how another is absorbed or metabolised. This necessitates thorough interaction testing and logical combination design based on PK compatibility and mechanistic complementarity. A growing number of clinical combination trials and well-designed preclinical combination studies suggest that synergy can be used, but only with strong standardisation and safety assessment [94, 58].

#### 8. Challenges and future directions

### 8.1 Quality control and standardization issues

Why quality control and standardization matter for gastroprotective botanicals?

The same standards that apply to any therapy must be met by herbal preparations used for gastroprotection: repeatable chemistry, consistent pharmacology, proven safety, and clinically significant effect sizes. In contrast to single-molecule medications, botanicals are complex mixtures whose pharmacology is dependent on minor components, multi-constituent profiles, and matrix effects that differ depending on the species, processing method, and geographic location. Safety signals (contamination, adulteration, herb-drug interactions) may go unnoticed, and preclinical efficacy signals cannot be accurately translated to the clinic without strict Quality Control (QC) and standardisation. Therefore, enhancing QC is essential to the scientific and regulatory validity of herbal gastroprotectants and is not a side technical issue [59,60].

#### 8.2 Core challenges

# 8.2.1 Variability in raw materials, misidentification of species and adulteration

The number of active constituents in plants varies greatly based on the genotype, chemotype, soil, harvest time, drying, and storage conditions. In actuality, deliberate or inadvertent substitution (adulteration) and inadequate botanical authentication are common sources of product variations. Widespread substitution and mislabeling in commercial herbal products are documented by studies and reviews from many countries. This immediately compromises the reproducibility of pharmacological results and raises the risk of safety if dangerous substitutes are present. For treated materials, morphological authentication is insufficient and calls for molecular and chemical identity techniques [95,61].

## **8.2.2** Inconsistent marker selection and inadequate chemical standardisation:

Numerous herbal studies still lack quantitative markers and define extracts using imprecise terms like "ethanolic extract" or "aqueous extract." Even with multi-constituent preparations, when marker compounds are published, various studies frequently select different markers or employ single-marker standardisation, resulting in batches that are not comparable. This renders dose-response inference and meta-analysis untrustworthy for gastroprotective endpoints (*H. pylori* outcomes, ulcer healing, and mucosal biomarkers). There is increasing agreement that the minimal need for translational studies should be multi-marker fingerprints

paired with at least one bioactive or bioavailable marker [60, 62]

## **8.2.3** Manufacturing impurities, adulterants, and contaminants

Heavy metals, pesticides, mycotoxins, and microbiological infections can contaminate herbal goods; certain markets also report intentional adulteration using synthetic medications. Particularly in low- and middle-income nations, systematic reviews reveal a nontrivial incidence of pollutants that present both immediate toxicity risks and long-term safety issues. Because patients with gastric disease frequently get polypharmacy (antibiotics, PPI), which raises the risk of compound-drug interactions or compounded toxicity, this is crucial for gastroprotective purposes [96,63].

#### 8.2.4 Limitations in analysis and methodology

Analytical platforms (HPLC, UHPLC-MS, NMR, GC-MS, IR, etc.) and procedure sensitivity/specificity vary throughout laboratories. Many botanicals utilised in gastroprotection (e.g., certain polysaccharide fractions) do not have widely available fingerprint standards, reference materials, and validated assays. Cross-study comparability and batch release testing are made more difficult by this heterogeneity. Although metabolomics and chemometrics have advanced, their adoption has been inconsistent, and many regulatory regimes continue to prioritise older, single-marker assays [60, 62].

## 8.2.5 Herb-drug interactions and pharmacokinetic complexity

The ADME profiles of the ingredients in complex mixes vary greatly; some bioactive chemicals have limited oral bioavailability, while other minor constituents alter the primary actives' absorption and metabolism. Importantly, components may change the PK of co-administered medications (such as PPIs, clarithromycin, and amoxicillin) used in peptic ulcer and *H. pylori* regimens by inhibiting or inducing CYP enzymes and transporters (P-gp). Unexpected interactions and changed efficacy or toxicity in actual patients are hazards associated with incomplete PK characterisation of botanical products [64, 65].

# 8.3 Implications for clinical translation and gastroprotection research

Three specific issues emerge as a result of the aforementioned difficulties. First, variable products make it difficult to combine evidence and yield inconsistent clinical results (meta-analyses frequently indicate substantial heterogeneity). Second, experiments that seem harmless at first glance may be harmed by unidentified pollutants or interactions. Third, a lack of PK/PD linkage makes it impossible to choose doses sensibly and optimise delivery for actions that target the stomach (such as gastroretentive exposure). Despite encouraging preclinical findings, these issues collectively impede the integration of herbal gastroprotectants into evidence-based treatment [66,67].

### 8.4 Emerging solutions and translational pathways 8.4.1 Metabolomics and multivariate chemical

### 6.4.1 Metabolomics and multivariate chemical fingerprints

When paired with chemometrics, metabolomics (NMR, LC-MS-based) allows for comprehensive fingerprints that capture hundreds of features, enhancing batch comparability and authentication. By making it easier to correlate particular chemical profiles with bioactivity (bioactivity-fingerprint coupling), fingerprinting makes it possible to choose batch

release conditions logically that go beyond a single marker. Metabolomics significantly enhances the ability to distinguish authentic from contaminated material, and it can help choose bioactive marker panels for gastroprotective extracts, according to reviews and proof-of-concept research conducted between 2020 and 2025  $^{[60,59]}$ .

#### 8.4.2 Bioassay-guided standardisation and multi-marker

Combining chemical markers (multi-marker panels) with at least one functional bioassay (such as antioxidant capacity, urease inhibition, or mucin-stimulating test) in place of single-marker assays offers a more pertinent standardisation that connects chemistry to anticipated gastric biology. Bioassay-guided standardisation is a crucial step in converting *in vitro* results into in vivo gastric endpoints by ensuring that batches that satisfy QC are also biologically comparable [60, 62]

# **8.4.3** Combined ADME/PK profiling of important metabolites and marker chemicals

*In vitro-in vivo* extrapolation (IVIVE) is being used by a number of groups to flag probable herb-drug interactions, measure plasma/tissue exposure of prioritised marker chemicals, and identify human metabolites. By selecting indicators that are not only plentiful but also bioavailable or present at the site of action (gastric mucosa), developers can improve dosage selection and safety prediction using this integrated ADME approach [64, 68].

# 8.4.4 Using gastroretentive delivery and sophisticated formulations to lessen exposure variability

In addition to decreasing systemic variability, formulation science (gastroretentive systems, mucoadhesives, and nanoparticle carriers) can improve local efficacy and promote consistency in gastrointestinal exposure to important actives. A number of proof-of-concept studies show that using gastroretentive or nano-formulations improves mucosal retention and improves local pharmacodynamic effects. This is a crucial translational technique to address the low systemic bioavailability of certain phytochemals [97,98].

# 8.4.5 Enhanced supply-chain traceability and contamination testing

Good Agricultural and Collection Practices (GACP), supplychain traceability (barcoding, blockchain pilot projects), and routine testing for heavy metals, pesticides, and mycotoxins all help to minimise contamination and variability at the source. The benefit of upstream controls in reducing the prevalence of contaminants in marketed products is documented by systematic surveillance studies conducted between 2020 and 2024 [96,69].

### 9. Challenges and future directions

# **9.1 Regulatory hurdles: Fragmented frameworks and unmet quality expectations**

Jurisdictions continue to have very different regulatory oversight policies for herbal medical products, ranging from food-like registration with few evidence requirements to full drug-like routes requiring defined pharmacology and randomised clinical data. This regulatory fragmentation undermines physician confidence and makes international research more difficult by allowing goods with vastly disparate quality and evidence bases to reach the market. Furthermore, a lot of regulatory regimes lack consistent contaminant limits (heavy metals, pesticides, and mycotoxins), validated multi-marker quality standards, and

strong, harmonised monographs all of which are necessary to guarantee repeatable clinical results in gastroprotection investigations. Larger, interoperable clinical programs would be made possible by strengthened, standardised regulatory guidance, which would ideally be supported by pharmacopeial monographs and the recognition of metabolomics-driven fingerprints as part of batch release criteria [70, 99].

# 9.2 Evidence requirements and the gap to drug-like approval

Clinicians and regulators look for unambiguous proof of safety and effectiveness. Preclinical research, tiny single-center trials, or heterogeneous open-label studies with varying formulations, standardisations, and outcomes continue to dominate the evidence base for the majority of herbal gastroprotective candidates. Without sufficiently powered, carefully monitored trials that employ standardised products and objective endpoints (endoscopic healing, validated symptom scales, urea breath test/culture for *H. pylori*), agencies cannot confidently recommend or endorse herbal therapies for gastroprotection, which leads to regulatory inertia. Creating regulatory pathways that allow staged evidence generation (phased approvals, conditional use with post-marketing commitments) could accelerate responsible translation while preserving safety oversight [70,71].

# 9.3 Need for large-scale clinical trials design, funding, and feasibility challenges

Obtaining standardised study materials (consistent batches with chemical fingerprints and bioassay-linked potency), choosing suitable comparators (placebo, standard-of-care, or add-on designs), blinding when organoleptic properties differ, and guaranteeing adequate statistical power given variable effect sizes are barriers to conducting large-scale RCTs, which are the foundation for proving clinical effectiveness and safety. Major obstacles include funding and infrastructure; small businesses and university institutions sometimes lack the means to conduct multicenter studies. Feasibility can be increased by public-private collaborations, grant financing for high-priority botanicals, and practical trial designs that include objective outcomes in standard clinical procedures. Additionally, several botanical candidates or combinations may be effectively evaluated in parallel using adaptive and platform trial designs, saving resources while generating high-quality comparative evidence [70,72].

# 9.4 Integration into mainstream healthcare models, training, and policy levers

Evidence-based therapeutic approaches, practitioner education, and institutional policies that acknowledge the importance of herbal choices (e.g., adjuncts for H. pylori eradication, mucoprotective adjuvants to lower PPI load) are necessary for successful integration. Examples from China, India, and Brazil demonstrate how policy support, covered reimbursement pathways, and integrated education can promote appropriate use. However, quality standards must be met by products, interactions must be understood, and electronic health records must record herbal use to guide safety surveillance for integration to be sustainable. Clinician acceptance and safer uptake will be facilitated by professional guidelines that specifically address standardised herbal choices, checklists of herb-drug interactions, and the incorporation of herbal medicines in clinical decision-support tools [73, 74].

## 9.5 Safety governance and pharmacovigilance closing the surveillance gap

There are frequently few post-marketing safety data available for herbal products. The capacity to identify uncommon but important effects (hepatotoxicity, idiosyncratic reactions, or interactions with antibiotics/PPIs) is diminished by underreporting, imprecise causality attribution, and a lack of product-lot connection in adverse-event data. Mandating batch-identified reporting fields, active surveillance programs (sentinel sites), and integrating PV databases with chemical fingerprint repositories are necessary to strengthen pharmacovigilance for botanicals. This will allow signals to be linked to specific product batches or adulterants. As items become more widely used in clinical settings, these technologies would also facilitate reevaluating the risks and benefits [100,61].

# 9.6 Standardization and supply-chain reliability as prerequisites for scale-up

Reproducible product chemistry is necessary for trustworthy clinical evidence. Good Agricultural and Collection Practices (GACP), validated extraction techniques, multi-marker chemical fingerprints (metabolomics/chemometrics), and validated bioassays linked to mechanisms of action (e.g., urease inhibition, mucin stimulation) are all necessary for botanicals to be useful at scale. In order to avoid batch failures or public health problems that could impede wider supply-chain acceptance, traceability and upstream contamination management are equally important. Reproducible research and regulatory review will be expedited by investments in open-access fingerprint databases and recognised supply networks [75, 76].

### 9.7 Scientific opportunities and future research directions

High translational yield can be obtained from several strategic research avenues, including

- a) Giving priority to botanicals with strong preclinical mechanistic validation and demonstrable bioavailable markers for clinical development;
- b) Incorporating early ADME/PK and herb-drug interaction studies into development plans to minimise surprises later on
- Advancing gastro-targeted delivery (gastroretentive systems, mucoadhesives, and inhalable/sublingual alternatives where appropriate) to improve mucosal exposure and lower systemic variability
- d) Using systems-pharmacology and network medicine to logically design synergistic combinations and predict interactions
- e) Carrying out practical, registry-linked effectiveness studies to assess safety, adherence, and real-world outcomes after initial efficacy is demonstrated in RCTs.

These strategies will preserve patient safety while expediting the integration of evidence-based practice [71,77].

### 9.8 Policy, funding, and collaborative models to accelerate progress

New funding and governance models will be needed to meet the scale and quality requirements of large trials and regulatory validation. These include collaborative consortia that share validated chemical reference materials and SOPs, pooled public research funds that prioritise high-impact herbal candidates, and innovative regulatory measures like conditional approvals linked to the creation of post-marketing evidence. Regional pharmacopeial cooperation and the WHO Traditional Medicine Strategy are two examples of international harmonisation efforts that can reduce obstacles to cross-border trials and establish internationally recognised quality standards. Large, conclusive trials are made possible by such collaborative approaches, which also distribute expenses and minimise repetition [78, 100].

### 9.9 Equity, access, and cultural considerations

Lastly, while guaranteeing fair access to standardised, safe goods, integration must preserve cultural contexts in which herbal medicines are a part of long-standing health practices. This calls for policies that prevent the creation of two-tiered systems in which only high-resource settings have access to standardised, evidence-based botanicals, the preservation of traditional knowledge, benefit sharing with communities, and the development of local capacity (laboratory QC, surveillance). To guarantee that scientific discoveries are translated into wider public health benefits, inclusive research collaborations and community-engaged implementation science will be essential [79, 101].

### 10. Conclusion

Despite the availability of standard pharmaceutical and surgical therapies, gastrointestinal disorders particularly peptic and gastric ulcers remain a significant global health burden. The ongoing problems with antibiotic resistance, proton pump inhibitor side effects, and the short-term effectiveness of traditional medications underscore the pressing need for complementary or alternative medicines. Because of their multi-targeted modes of action, which include anti-inflammatory, antioxidant, anti-secretory, mucosal protecting, and anti-Helicobacter pylori activity, herbal medications have become attractive options.

Recent developments in pharmacokinetic profiling, gastroretentive drug delivery technologies, and phytochemical standardisation between 2020 and 2025 have reinforced the scientific basis for the application of herbal plants in gastroprotection. By altering important molecular pathways like NF-κB, MAPK, and prostaglandin signalling, medicinal herbs like *Glycyrrhiza glabra*, *Curcuma longa*, Aloe vera, *Zingiber officinale*, and *Camellia sinensis* show great promise for restoring gastric mucosal equilibrium. Additionally, preclinical and clinical research confirms their effectiveness in preventing ulcers, repairing mucosal tissue, and enhancing gastrointestinal function.

However, significant obstacles such as raw material variability, lack of standardisation, irregular dosing, and a lack of large-scale clinical studies must be overcome before these findings can be applied in clinical practice. To guarantee product safety and reproducibility, pharmacovigilance systems, metabolomics-based standardisation, multi-marker quality control, and strengthened regulatory frameworks are crucial. Herbal gastroprotective medicines will be included in evidence-based healthcare more quickly thanks to cooperative research projects and flexible clinical trial designs.

In summary, herbal remedies have great potential as sustainable, safe, and mechanistically adaptable treatment choices for ulcer prevention and stomach protection. These botanicals have the potential to transform from traditional medicines into standardised, scientifically validated treatments that support and improve contemporary gastroenterological care with sustained investment in quality assurance, clinical validation, and international regulatory harmonisation.

#### References

- 1. Mule VS, Manjarekar TN, Mohite MS, Gawade CS, Kakade SV, Sawant SS, Jagtap VA. Medicinal plants with gastroprotective activity for treatment of peptic ulcer disease. Indian J Pharm Sci Res. 2020;2:40-46. Available from: https://www.ijpsrjournal.com
- 2. Sperber AD. Advances in IBS. In: Chey WD, editor. Gastroenterology & Hepatology. 2023;19(9).
- 3. Deshpande M, Dighe P, Nagare S. A review of antiulcer activity of some medicinal plants. J Drug Deliv Ther. 2024;14(8):201-213. DOI:10.22270/jddt.v14i8.6722
- 4. Ray G, Ghoshal UC. Epidemiology of disorders of the gut-brain interaction: An appraisal of the Rome IV criteria and beyond. Gut Liver. 2024;18(4):578-592. DOI:10.5009/gnl230396
- Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, *et al*. Worldwide prevalence and burden of functional gastrointestinal disorders: Results of Rome Foundation global study. Gastroenterology. 2020;160(1):99-114.e3.
   DOI:10.1053/j.gastro.2020.04.014
- Loh JS, Mak WQ, Tan LKS, Ng CX, Chan HH, Yeow SH, et al. Microbiota-gut-brain axis and its therapeutic applications in neurodegenerative diseases. Signal Transduct Target Ther. 2024;9(1). DOI:10.1038/s41392-024-01743-1
- 7. Mandarino FV, Sinagra E, Raimondo D, Danese S. The role of microbiota in upper and lower gastrointestinal functional disorders. Microorganisms. 2023;11(4):980. DOI:10.3390/microorganisms11040980
- 8. Dudzińska E, Grabrucker AM, Kwiatkowski P, Sitarz R, Sienkiewicz M. The importance of visceral hypersensitivity in irritable bowel syndrome Plant metabolites in IBS treatment. Pharmaceuticals. 2023;16(10):1405. DOI:10.3390/ph16101405
- Tian S, Zhang H, Chen S, Wu P, Chen M. Global research progress of visceral hypersensitivity and irritable bowel syndrome: bibliometrics and visualized analysis. Front Pharmacol. 2023;14. DOI:10.3389/fphar.2023.1175057
- Zhou L, Zeng Y, Zhang H, Ma Y. The role of gastrointestinal microbiota in functional dyspepsia: a review. Front Physiol. 2022;13. DOI:10.3389/fphys.2022.910568
- 11. Petrut S, Bragaru AM, Munteanu AE, Moldovan A, Moldovan C, Rusu E. Gut over mind: Exploring the powerful gut-brain axis. Nutrients. 2025;17(5):842. DOI:10.3390/nu17050842
- 12. Ullah H, Arbab S, Chang C, Bibi S, Muhammad N, Rehman SU, *et al.* Gut microbiota therapy in gastrointestinal diseases. Front Cell Dev Biol. 2025;13. DOI:10.3389/fcell.2025.1514636
- 13. Peery AF, Crockett SD, Murphy CC, Jensen ET, Kim HP, Egberg MD, *et al.* Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update; 2021. Gastroenterology. 2021;162(2):621-644. DOI:10.1053/j.gastro.2021.10.017
- 14. Almario CV, Sharabi E, Chey WD, Lauzon M, Higgins CS, Spiegel BM. Prevalence and burden of illness of Rome IV irritable bowel syndrome in the United States. Gastroenterology. 2023;165(6):1475-1487. DOI:10.1053/j.gastro.2023.08.010
- 15. Baklola M, Terra M, Badr A, Fahmy FM, Elshabrawy E, Hawas Y, *et al.* Prevalence of gastro-oesophageal reflux disease and its associated risk factors among medical

Journal of Medicinal Plants Studies <a href="https://www.plantsjournal.com">https://www.plantsjournal.com</a>

students. BMC Gastroenterol. 2023;23(1). DOI:10.1186/s12876-023-02899-w

- Lu M, Chiang H. Turn over the new leaf of the treatment in peptic ulcer bleeding: a review of the literature. Ther Adv Gastroenterol. 2024;17. DOI:10.1177/17562848241275318
- 17. Naseer M, Lambert K, Hamed A, Ali E. Endoscopic advances in the management of non-variceal upper gastrointestinal bleeding: a review. World J Gastrointest Endosc. 2019;12(1):1-16. DOI:10.4253/wjge.v12.i1.1
- 18. Yuan C, Yu C, Sun Q, Xiong M, Zhou S, Zeng M, Song H. Research on antibiotic resistance in *Helicobacter pylori*: A bibliometric analysis. Front Microbiol. 2023;14. DOI:10.3389/fmicb.2023.1208157
- 19. Salahi-Niri A, Nabavi-Rad A, Monaghan TM, Rokkas T, Doulberis M, Sadeghi A, *et al.* Global prevalence of *Helicobacter pylori* antibiotic resistance among children: A systematic review and meta-analysis. BMC Med. 2024;22:598. DOI:10.1186/s12916-024-03816-y
- 20. Davis TA, Gyawali CP. Refractory gastroesophageal reflux disease: Diagnosis and management. J Neurogastroenterol Motil. 2024;30(1):17-28. DOI:10.5056/jnm23145
- 21. Maideen NMP. Adverse effects associated with long-term use of proton pump inhibitors. Chonnam Med J. 2023;59(2):115. DOI:10.4068/cmj.2023.59.2.115
- 22. Vatcharavongvan P, Puttawanchai V. Elderly patients in primary care are still at risks of receiving potentially inappropriate medications. J Prim Care Community Health. 2021;12. DOI:10.1177/21501327211035088
- 23. Tassone D, Kazi S, Lee T, Gilmore R, Ding N. Endoscopic versus medical management of peptic ulcers with adherent clots: a systematic review and meta-analysis. J Gastroenterol Hepatol. 2024;39(10):2031-2042. doi:10.1111/jgh.16611
- 24. Hossa K, Małecka-Wojciesko E. Advances in gastroesophageal reflux disease management: exploring the role of potassium-competitive acid blockers and novel therapies. Pharmaceuticals. 2025;18(5):699. DOI:10.3390/ph18050699
- 25. Yao Y, Habib M, Bajwa HF, Qureshi A, Fareed R, Altaf R, *et al*. Herbal therapies in gastrointestinal and hepatic disorders: An evidence-based clinical review. Front Pharmacol. 2022;13. DOI:10.3389/fphar.2022.962095
- 26. Kim YS, Kim JW, Ha NY, Kim J, Ryu HS. Herbal therapies in functional gastrointestinal disorders: a narrative review and clinical implication. Front Psychiatry. 2020;11:601. DOI:10.3389/fpsyt.2020.00601
- 27. Kim M, Park C, Park JW, Kim J, Ko SJ. Herbal medicine for the treatment of non-erosive reflux disease: A systematic review and meta-analysis. Medicine (Baltimore). 2024;103(45). DOI:10.1097/MD.00040269
- 28. Prayoga DK, Aulifa DL, Budiman A, Levita J. Plants with anti-ulcer activity and mechanism: a review of preclinical and clinical studies. Drug Des Devel Ther. 2024;193-213. Available from: https://www.dovepress.com
- 29. Abdi S, Ataei S, Abroon M, Sanaye PM, Abbasinazari M, Farrokhian A. Complementary and dietary medicines in eradicating *Helicobacter pylori*: A comprehensive review. Iran J Pharm Res. 2022;21(1). DOI:10.5812/ijpr-127030
- 30. Yang L, Fang Z, Zhu J, Li X, Yang B, Liu H, Lou F. The potential of Sijunzi decoction in the fight against gastrointestinal disorders: a review. Front Pharmacol. 2025;16. DOI:10.3389/fphar.2025.1464498
- 31. Park C, Kim M, Park JW, Kim J, Bu Y, Ko SJ. Effect of

- Bojanggunbi-tang and its primary constituent herbs on the gastrointestinal tract: A scoping review. Front Pharmacol. 2025;16:1543194. DOI:10.3389/fphar.2025.1543194
- 32. Cherrada N, Elkhalifa Chemsa A, Gheraissa N, Laib I, Gueboudji Z, El-Shazly M, *et al.* Gastroprotective efficacy of North African medicinal plants: a review on their therapeutic potential for peptic ulcers. Food Sci Nutr. 2024;12:8793-8824. DOI:10.1002/fsn3.4536
- 33. Komolafe K, Komolafe TR, Crown OO, Ajiboye B, Noubissi F, Ogungbe IV, *et al.* Natural products in the management of gastroesophageal reflux disease: mechanisms, efficacy, and future directions. Nutrients. 2025;17:1069. DOI:10.3390/nu17061069
- 34. Lee YM, Jo K, Kim SY, Seo C, Son E, Kim A, *et al.* Yeokwisan: standardised herbal formula enhancing gastric mucosal protection against gastric ulcers in mice. Pharmaceuticals. 2025;18(1):44. DOI:10.3390/ph18010044
- 35. Sanpinit S, Chonsut P, Punsawad C, Wetchakul P. Gastroprotective and antioxidative effects of the traditional Thai polyherbal formula Phy-Blica-D against ethanol-induced gastric ulcers in rats. Nutrients. 2021;14(1):172. DOI:10.3390/nu14010172
- 36. Shahzad N, Ibrahim IA, Alzahrani AR, Al-Ghamdi SS, Alanazi IMM, Ahmad MP, *et al.* Phytochemicals as potential therapeutic agents for stress-induced gastric ulcer: a comprehensive review. J Umm Al-Qura Univ Appl Sci. 2024. DOI:10.1007/s43994-024-00140-2
- 37. Yigit S, Kaci FN, Gezer A, Yayla M, Duysak L, Kilicle PA, *et al.* Gastroprotective and antioxidant effects of Ferula plant extract against indomethacin-induced gastric ulcer in rats. Food Sci Nutr. 2025;13(8). DOI:10.1002/fsn3.70730
- 38. Xu K, Li J, Guo S, Zhang J, Zhang X. Gastric mucosal repair by Men's Huwei powder via EGF-NO/PGE2-PI3K-TLR4 in RELISH. Front Pharmacol. 2025;16. DOI:10.3389/fphar.2025.1594089
- 39. Wang L, Lian Y, Dong J, Liu M, Liu H, Cao Z, *et al.*Traditional Chinese medicine for chronic atrophic gastritis: efficacy, mechanisms and targets. World J Gastroenterol.

  DOI:10.3748/wjg.v31.i9.102053
- 40. Liu M, Gao H, Miao J, Zhang Z, Zheng L, Li F, *et al. Helicobacter pylori* infection in humans and phytotherapy, probiotics, and emerging therapeutic interventions: A review. Front Microbiol. 2024;14. DOI:10.3389/fmicb.2023.1330029
- 41. Deng R, Chen X, Zhao S, Zhang Q, Shi Y. Effects and mechanisms of natural products on *Helicobacter pylori* eradication. Front Cell Infect Microbiol. 2024;14. DOI:10.3389/fcimb.2024.1360852
- 42. Czigle S, Fialová SB, Tóth J, Mučaji P, Nagy M. Treatment of gastrointestinal disorders Plants and potential mechanisms of action of their constituents. Molecules. 2022;27(9):2881. DOI:10.3390/molecules27092881
- 43. Alves NM, Nunes PHM, Garcez AM, De Freitas MCL, Oliveira IS, Da Silva FV, *et al.* Antioxidant mechanisms underlying the gastroprotective effect of menthofuran on experimentally induced gastric lesions in rodents. Evid Based Complement Alternat Med. 2023;2023:9192494. DOI:10.1155/2023/9192494
- 44. Chaudhary P, Janmeda P, Docea AO, Yeskaliyeva B, Razis AFA, Modu B, *et al.* Oxidative stress, free radicals

Journal of Medicinal Plants Studies https://www.plantsjournal.com

and antioxidants: Potential crosstalk in the pathophysiology of human diseases. Front Chem. 2023;11. DOI:10.3389/fchem.2023.1158198

- 45. Sharma A, Sood C, Chaudhary S, Devi M, Sharma G, Sharma K. Gastroprotective mechanisms and its augmentation by external agents: A review. YMER. 2024;533. Available from: https://www.researchgate.net/publication/379023644
- 46. Sun Y, Zhou F, Zheng H, Xiao J. Clinical efficacy and mechanism of *Bletilla striata* and Chinese herbal compounds in treatment of peptic ulcer. World J Gastroenterol. 2025;31(30). DOI:10.3748/wjg.v31.i30.110145
- 47. Jiang Z, Deng B, Zhang Y, Li Y, Yu Z, Deng H, *et al*. Efficacy and safety of seven Chinese patent medicines combined with conventional therapy for *Helicobacter pylori*-positive peptic ulcers: a network meta-analysis. BMJ Open. 2024;14(4):e074188. DOI:10.1136/bmjopen-2023-074188
- 48. Chen D, Wang W, Chen X, Liang N, Li J, Ding W, et al. Plant-derived extracts or compounds for Helicobacter-associated gastritis: A systematic review. Chin Med. 2025;20(1). DOI:10.1186/s13020-025-01093-2
- 49. Thavorn K, Wolfe D, Faust L, Shorr R, Akkawi M, Isaranuwatchai W, *et al.* Efficacy and safety of turmeric in the treatment of digestive disorders: A systematic review and meta-analysis. Phytother Res. 2024;38(6):2687-2706. DOI:10.1002/ptr.8189
- 50. Sperber AD, Freud T, Aziz I, Palsson OS, Drossman DA, Dumitrascu DL, *et al.* Greater overlap of Rome IV disorders of gut-brain interactions leads to increased disease severity and poorer quality of life. Clin Gastroenterol Hepatol. 2022;20(5):e945-e956. DOI:10.1016/j.cgh.2021.05.042
- 51. Wang X, Yin J, Hu J, Nie S, Xie M. Gastroprotective polysaccharide from natural sources: Review on structure, mechanism, and structure-activity relationship. Food Frontiers. 2022;3(4):560-591. https://doi.org/10.1002/fft2.172
- 52. Kongkaew C, Phan DTA, Janusorn P, Mongkhon P. Estimating adverse events associated with herbal medicines using pharmacovigilance databases:

  Systematic review and meta-analysis. JMIR Public Health and Surveillance. 2024;10:e63808. https://doi.org/10.2196/63808
- 53. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, *et al.* Worldwide prevalence and burden of functional gastrointestinal disorders, results of Rome Foundation Global Study. Gastroenterology. 2021;160(1):99-114.e3. https://doi.org/10.1053/j.gastro.2020.04.014
- 54. Oka P, Parr H, Barberio B, Black CJ, Savarino EV, Ford AC. Global prevalence of irritable bowel syndrome according to Rome III or IV criteria: a systematic review and meta-analysis. Lancet Gastroenterology & Hepatology. 2020;5(10):908-917. https://doi.org/10.1016/S2468-1253(20)30217-X
- 55. Jia W, Lu C, Lin G, Ge G. Editorial: Pharmacokinetics of herbal medicines and herb-drug interactions. Frontiers in Pharmacology. 2022;13:1107777. https://doi.org/10.3389/fphar.2022.1107777
- 56. De Jesus PC, Silva DMRR, Moura PHM, Gopalsamy RG, Silva EED, Barreto MS, *et al.* The *in vitro* pharmacokinetics of medicinal plants: A review. Pharmaceuticals. 2025;18(4):551. https://doi.org/10.3390/ph18040551
- 57. Turac I, Porfire A, Iurian S, Crișan AG, Casian T,

- Iovanov R, *et al.* Expanding the manufacturing approaches for gastroretentive drug delivery systems with 3D printing technology. Pharmaceutics. 2024;16(6):790. https://doi.org/10.3390/pharmaceutics16060790
- 58. Gamil NM, Elsayed HA, Hamed RM, Salah ET, Ahmed AM, Mostafa HA, *et al.* Insights from herb interactions studies: A foundational report for integrative medicine. Future Journal of Pharmaceutical Sciences. 2025;11(1). https://doi.org/10.1186/s43094-025-00794-7
- 59. Wang H, Chen Y, Wang L, Liu Q, Yang S, Wang C. Advancing herbal medicine: Enhancing product quality and safety through robust quality control practices. Frontiers in Pharmacology. 2023;14:1265178. https://doi.org/10.3389/fphar.2023.1265178
- Noviana E, Indrayanto G, Rohman A. Advances in fingerprint analysis for standardization and quality control of herbal medicines. Frontiers in Pharmacology. 2022;13:853023. https://doi.org/10.3389/fphar.2022.853023
- 61. Balkrishna A, Sharma N, Srivastava D, Kukreti A, Srivastava S, Arya V. Exploring the safety, efficacy, and bioactivity of herbal medicines: bridging traditional wisdom and modern science in healthcare. Future Integrative Medicine. 2024;3(1):35-49. https://doi.org/10.14218/fim.2023.00086
- 62. Edo GI, Obasohan P, Makia RS, O TA, Umelo EC, Jikah AN, *et al.* The use of quality control parameters in the evaluation of herbal drugs: A review. Deleted Journal. 2024;1(1). https://doi.org/10.1007/s44337-024-00177-6
- 63. Jităreanu A, Trifan A, Vieriu M, Caba I, Mârţu I, Agoroaei L. Current trends in toxicity assessment of herbal medicines: A narrative review. Processes. 2022;11(1):83. https://doi.org/10.3390/pr11010083
- 64. Czigle S, Nagy M, Mladěnka P, Tóth J. Pharmacokinetic and pharmacodynamic herb-drug interactions Part I. Herbal medicines of the central nervous system. PeerJ. 2023;11:e16149. https://doi.org/10.7717/peerj.16149
- 65. Lippert A, Renner B. Herb-drug interaction in inflammatory diseases: review of phytomedicine and herbal supplements. Journal of Clinical Medicine. 2022;11(6):1567. https://doi.org/10.3390/jcm11061567
- 66. Sartori D, Aronson JK, Brand JS, Gauffin O, Vidlin SH, Norén GN, Onakpoya IJ. Signals of adverse reactions to herbal medicines: Evidence and document analysis based on a scoping review. Drug Safety; 2025. https://doi.org/10.1007/s40264-025-01580-3
- 67. Bukowska B, Grzegorowska A, Szczerkowska-Majchrzak E, Bukowski K, Kadac-Czapska K, Grembecka M, *et al.* Hazardous interactions between food, herbs, and drugs in the first stage of biotransformation: case reports of adverse drug interactions in humans. International Journal of Molecular Sciences. 2025;26(11):5188. https://doi.org/10.3390/ijms26115188
- 68. Belwal C, Bisht D, Bharadwaj M, Bisht M. Targeted nano delivery systems for natural antioxidants in ferulic acid gastric ulcer management: Insights and innovations. Journal of Neonatal Surgery. 2025;14(31s):721. https://www.jneonatalsurg.com
- 69. Jităreanu A, Trifan A, Vieriu M, Caba I-C, Mârt I, Agoroaei L. Current trends in toxicity assessment of herbal medicines: A narrative review. Processes; 2022. https://doi.org/10.3390/pr11010083
- 70. Koonrungsesomboon N, Sakuludomkan C, Takuathung MN, Klinjan P, Sawong S, Perera PK. Study design of

Journal of Medicinal Plants Studies <a href="https://www.plantsjournal.com">https://www.plantsjournal.com</a>

herbal medicine clinical trials: a descriptive analysis of published studies investigating the effects of herbal medicinal products on human participants. BMC Complementary Medicine and Therapies. 2024;24(1). https://doi.org/10.1186/s12906-024-04697-7

- 71. Salm S, Rutz J, Van Den Akker M, Blaheta RA, Bachmeier BE, *et al.* Current state of research on the clinical benefits of herbal medicines for non-life-threatening ailments. Frontiers in Pharmacology. 2023;14:1234701. https://doi.org/10.3389/fphar.2023.1234701
- 72. Wang Z, Xu D, Chen X. Rigorous clinical trials for traditional Chinese herbal medicine: Challenge and opportunity. The Innovation Medicine. 2025;100117. https://doi.org/10.59717/j.xinn-med.2025.100117
- 73. Thamizhoviya G. Global integration of traditional and modern medicine: Policy developments, regulatory frameworks, and clinical integration model. Future Integrative Medicine. 2025;000(000):000. https://doi.org/10.14218/fim.2025.00033
- 74. Ikhoyameh M, Okete WE, Ogboye RM, Owoyemi OK, Gbadebo OS. Integrating traditional medicine into the African healthcare system post-Traditional Medicine Global Summit: challenges and recommendations. Pan African Medical Journal. 2024;47. https://doi.org/10.11604/pamj.2024.47.146.43011
- 75. Patel R, Jawaid T, Gautam P, Dwivedi P. Herbal remedies for gastroprotective action: A review. International Journal of Phytopharmacy. 2012;2(2). https://doi.org/10.7439/ijpp.v2i2.388
- 76. Hoenders R, Ghelman R, Portella C, Simmons S, Locke A, Cramer H, *et al.* A review of the WHO strategy on traditional, complementary, and integrative medicine from the perspective of academic consortia for integrative medicine and health. Frontiers in Medicine. 2024;11:1395698. https://doi.org/10.3389/fmed.2024.1395698
- 77. Raja M, Cramer H, Lee MS, Wieland LS, Ng JY. Addressing the challenges of traditional, complementary, and integrative medicine research: an international perspective and proposed strategies moving forward. Perspectives on Integrative Medicine. 2024;3(2):86-97. https://doi.org/10.56986/pim.2024.06.004
- 78. Tan N, Gwee KA, Tack J, Zhang M, Li Y, Chen M, *et al*. Herbal medicine in the treatment of functional gastrointestinal disorders: A systematic review with meta-analysis. Journal of Gastroenterology and Hepatology. 2019;35(4):544-556. https://doi.org/10.1111/jgh.14905
- 79. Ikhoyameh M, Okete WE, Ogboye RM, Owoyemi OK, Gbadebo OS. Integrating traditional medicine into the African healthcare system post-Traditional Medicine Global Summit: challenges and recommendations. Pan African Medical Journal. 2024;47. https://doi.org/10.11604/pamj.2024.47.146.43011
- 80. Qian JN, Kang YL, He YC, Hu HY. Topic modeling analysis of Chinese medicine literature on gastroesophageal reflux disease: insights into potential treatment. Chinese Journal of Integrative Medicine. 2024;30(12):1128-1136. https://doi.org/10.1007/s11655-024-3800-y
- 81. Khorasani EZ, Amirian T, Formi EN, Mahjoub F, Sadeghi M. Efficacy of *Glycyrrhiza glabra* on peptic ulcer disease: a systematic review and meta-analysis. Advances in Integrative Medicine. 2025;12(4):100485. https://doi.org/10.1016/j.aimed.2025.100485
- 82. Sandu R, Pandy V. Capsaicin: A review of its

- pharmacology in gastrointestinal health and disorders. Pharmacological Research Natural Products. 2024;5:100103.
- https://doi.org/10.1016/j.prenap.2024.100103
- 83. Xiang ZD, Guan HD, Zhao X, Xie Q, Cai FJ, Xie ZJ, *et al.* Protoberberine alkaloids: A review of the gastroprotective effects, pharmacokinetics, and toxicity. Phytomedicine. 2024;126:155444. https://doi.org/10.1016/j.phymed.2024.155444
- 84. Xie T, Ren J, Ren L, *et al*. The global, regional, and national burden of peptic ulcer disease from 1990 to 2019: a population-based study. BMC Gastroenterology. 2022;22(1):58. https://doi.org/10.1186/s12876-022-02137-0
- 85. Xie X, Ren K, Zhou Z, Dang C, Zhang H. The global, regional, and national burden of peptic ulcer disease from 1990 to 2019: A population-based study. BMC Gastroenterology. 2022;22(1):58. https://doi.org/10.1186/s12876-022-02130-2
- 86. Adinortey MB, Ansah C, Asiedu-Larbi J, Kwofie SK, Bockarie AS, Barnes P, *et al.* Dissotis rotundifolia extract inhibits gastric acid secretion and H<sup>+</sup>/K<sup>+</sup>-ATPase activity and enhances mucin activity in vivo. Scientific African. 2022;17:e01317. https://doi.org/10.1016/j.sciaf.2022.e01317
- 87. Shojaeian A, Khalilian A, Mehrpoya M, Poorolajal J, Dastan D. Efficacy of a standardised herbal formulation in *Helicobacter pylori*-positive patients with gastritis or peptic ulcer: a triple-blind randomised clinical trial. Journal of Herbal Medicine. 2023;41:100706. https://doi.org/10.1016/j.hermed.2023.100706
- 88. Indrayanto G. Regulation and standardization of herbal drugs: current status, limitation, challenges, and future perspectives. In: Al-Majed AA, editor. Profiles of Drug Substances, Excipients and Related Methodology. Vol. 49. Academic Press; c2024, p. 153-199. https://doi.org/10.1016/bs.podrm.2023.11.003
- 89. Wang Z, Guo S, Cai Y, Yang Q, Wang Y, Yu X, *et al.* Decoding active compounds and molecular targets of herbal medicine by high-throughput metabolomics technology: a systematic review. Bioorganic Chemistry. 2024;144:107090. https://doi.org/10.1016/j.bioorg.2023.107090
- 90. Li C, Jia WW, Yang JL, Cheng C, Olaleye OE. Multi-compound and drug-combination pharmacokinetic research on Chinese herbal medicines. Acta Pharmacologica Sinica. 2022;43(12):3080-3095. https://doi.org/10.1038/s41401-022-00983-7
- 91. Xiang ZD, Guan HD, Zhao X, Xie Q, Cai FJ, Xie ZJ, et al. Protoberberine alkaloids: A review of the gastroprotective effects, pharmacokinetics, and toxicity. Phytomedicine. 2024;126:155444. https://doi.org/10.1016/j.phymed.2024.155444
- 92. Omidian H. Gastroretentive drug delivery systems: A holy grail in oral delivery. Drug Discovery Today. 2025;30(4):104340. https://doi.org/10.1016/j.drudis.2025.104340
- 93. Mora-Castaño G, Domínguez-Robles J, Himawan A, Millán-Jiménez M, Caraballo I. Current trends in 3D printed gastroretentive floating drug delivery systems: A comprehensive review. International Journal of Pharmaceutics. 2024;663:124543. https://doi.org/10.1016/j.ijpharm.2024.124543
- 94. Li C, Jia WW, Yang JL, Cheng C, Olaleye OE. Multicompound and drug-combination pharmacokinetic

- research on Chinese herbal medicines. Acta Pharmacologica Sinica. 2022;43(12):3080-3095. https://doi.org/10.1038/s41401-022-00983-7
- 95. Kaundal R, Kumar D. Current demands for standardization of Indian medicinal plants: A critical review. Medicine in Drug Discovery. 2025;27:100211. https://doi.org/10.1016/j.medidd.2025.100211
- 96. Opuni KFM, Kretchy JP, Agyabeng K, Boadu JA, Adanu T, Ankamah S, *et al.* Contamination of herbal medicinal products in low-and-middle-income countries: A systematic review. Heliyon. 2023;9(9):e19370. https://doi.org/10.1016/j.heliyon.2023.e19370
- 97. Yan X, Huang Z, Wu Y, Yu Z, Yang K, Chen Z, *et al.* Sequential loading of inclusion complex/nanoparticles improves gastric retention of Vladimiriae Radix essential oil to promote protection of acute gastric mucosal injury. International Journal of Pharmaceutics. 2021;610:121234.
  - https://doi.org/10.1016/j.ijpharm.2021.121234
- 98. Sen O, Manna S, Nandi G, Jana S, Jana S. Recent advances in alginate-based gastroretentive technologies for drug delivery applications. Medicine in Novel Technology and Devices. 2023;18:100236. https://doi.org/10.1016/j.medntd.2023.100236
- 99. World Health Organization. Traditional medicine: Questions and answers; 2024. Available from: https://www.who.int/news-room/questions-and-answers/item/traditional-medicine
- 100. World Health Organization. Traditional, complementary and integrative medicine; 2024. Available from: https://www.who.int/health-topics/traditional-complementary-and-integrative-medicine
- 101.Health Policy Watch. WHO's big push to integrate traditional medicine into global healthcare framework; 2024. Available from: https://
- 102. Juee LY, Sofi SH, Adham AN. Melissa officinalis gastroprotective and antioxidant efficacy. Journal of Functional Foods. 2023;105:105550. https://doi.org/10.1016/j.jff.2023.105550