

Original Article



Research Progress on Chinese Herbal Medicines for Gastrointestinal Diseases: A Review

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Abstract:

Gastrointestinal diseases are prevalent clinical conditions that significantly impair patients' quality of life, manifesting symptoms such as epigastric and abdominal distension and pain, food retention, and loss of appetite. Traditional Chinese herbal medicines have a long history and demonstrated efficacy in treating these disorders, characterized by their multi-target and multi-pathway therapeutic actions, which have garnered increasing attention from researchers worldwide. This review systematically summarizes the pharmacodynamic material basis, pharmacological mechanisms, and clinical research progress of several common Chinese herbs, including Yunmuxiang (*Aucklandia lappa*), Chenpi (*Citrus reticulata* peel), Shan Zha (*Crataegus pinnatifida*), Baizhu (*Atractylodes macrocephala*), and Houpu (*Magnolia officinalis*), in managing epigastric and abdominal distension and pain, food retention, and loss of appetite. Special emphasis is placed on the gastrointestinal motility regulation and anti-inflammatory activities of costunolide and dehydrocostus lactone, the main active sesquiterpene lactones in Yunmuxiang. Additionally, the review integrates the compatibility principles of related compound formulations with modern pharmacological evidence to provide a comprehensive understanding. The aim is to offer theoretical support and clinical references for the application of traditional Chinese medicine in the treatment of gastrointestinal diseases.

Keywords: Chinese herbal medicine; Gastrointestinal diseases; Epigastric and abdominal distension and pain;

Introduction

Gastrointestinal (GI) functional disorders represent a significant global health burden, characterized by symptoms such as epigastric and abdominal distension, food retention with impaired digestion, and anorexia. These clinical manifestations are commonly observed in conditions including functional dyspepsia, chronic gastritis, and irritable bowel syndrome (IBS), which collectively affect a substantial proportion of the population worldwide. The impact of these symptoms extends beyond mere discomfort, often leading to compromised nutritional status and a marked decrease in patients' quality of life. Despite advances in

modern medicine, the management of these disorders remains challenging due to their multifactorial etiology and the complex interplay of physiological, psychological, and environmental factors. Conventional pharmacological treatments, including prokinetic agents and digestive enzyme supplements, primarily aim at symptom relief but are frequently limited by high relapse rates and notable adverse effects associated with long-term use. Consequently, there is a growing interest among patients and researchers in exploring alternative therapeutic options, particularly those derived

from natural products and traditional medicine systems .

Traditional Chinese medicine (TCM), with its rich heritage spanning millennia, offers a unique perspective on the treatment of GI disorders. Historical texts such as the “Shennong Bencao Jing” and “Bencao Gangmu” document extensive use of herbal formulations aimed at regulating qi, promoting digestion, and strengthening the spleen and stomach functions. Among these, herbs classified under the categories of qi-regulating and digestion-promoting agents have been widely employed to alleviate symptoms like abdominal distension, food retention, and anorexia. Clinical experience accumulated over centuries has led to the development of numerous empirical prescriptions and usage patterns that continue to inform contemporary practice. The integration of TCM principles with modern clinical approaches has fostered a holistic understanding of GI functional disorders, emphasizing individualized treatment based on syndrome differentiation .

In recent years, the advent of advanced methodologies in pharmacology, molecular biology, and metabolomics has facilitated a deeper exploration into the bioactive constituents of traditional herbal medicines and their mechanisms of action. Investigations into the pharmacodynamics and pharmacokinetics of key herbal components have elucidated their roles in modulating gastrointestinal motility, secretion, and neurohormonal pathways. For instance, studies on Kampo medicines, the Japanese adaptation of traditional Chinese herbal formulas, have demonstrated their capacity to enhance GI motility through neural reflexes involving cholinergic and serotonergic receptors, as well as their influence on gastrointestinal hormones such as motilin and ghrelin. Rikkunshito, a well-studied Kampo formulation, has shown efficacy in ameliorating anorexia and dyspeptic symptoms by stimulating ghrelin secretion and improving gastric emptying. These findings provide a

scientific basis for the traditional use of such herbal medicines and support their integration into modern therapeutic regimens .

Moreover, clinical trials and meta-analyses have begun to substantiate the efficacy and safety profiles of specific herbal preparations in treating GI disorders. For example, Banxiaxixin Tang has been shown to be more effective than conventional Western medications in managing functional dyspepsia, with favorable outcomes in symptom relief and minimal adverse effects. Similarly, Chaihu-Shugan-San has demonstrated therapeutic benefits in various forms of chronic gastritis. These clinical evidences, although sometimes limited by methodological constraints, underscore the potential of traditional herbal medicines as viable alternatives or adjuncts to standard treatments. Additionally, non-pharmacological interventions rooted in traditional medicine, such as acupuncture and moxibustion, have been explored for their neuromodulatory effects on gastrointestinal function and visceral pain, offering complementary avenues for symptom management .

Given the complexity of GI functional disorders and the limitations of current conventional therapies, a systematic review focusing on commonly used qi-regulating and digestion-promoting Chinese herbal medicines is timely and warranted. This review aims to comprehensively summarize the pharmacological constituents, mechanisms of action, and clinical applications of representative herbs such as *Aucklandia lappa* (commonly known as Yunmuxiang), which exemplify the therapeutic principles of regulating qi and promoting digestion. By critically analyzing recent advances in experimental and clinical research, this article seeks to bridge traditional knowledge with modern scientific evidence, thereby providing a foundation for optimized therapeutic strategies. Furthermore, the review will discuss current challenges and future

directions in the research and clinical application of these herbal medicines, highlighting the need for rigorous clinical trials, standardization of herbal preparations, and elucidation of molecular targets to enhance their efficacy and safety profiles in the management of GI functional disorders.

1. Research Progress on Qi-Regulating Chinese Herbal Medicines for Treating Epigastric and Abdominal Distension and Pain

1.1 Pharmacodynamic Basis and Mechanisms of *Saussurea lappa* (Yunmuxiang)

Saussurea lappa (Yunmuxiang), a member of the Asteraceae family, has a long-standing history in traditional Chinese medicine (TCM) as a principal herb for regulating qi and alleviating pain, particularly in cases of epigastric and abdominal distension attributed to qi stagnation. Its dried root, first documented in the ancient text *Shennong Bencao Jing* as a superior-grade herb, is renowned for its ability to promote qi circulation, relieve pain, strengthen the spleen, and aid digestion. The principal bioactive constituents of Yunmuxiang are sesquiterpene lactones, predominantly costunolide and dehydrocostuslactone, which together constitute over 50% of the total volatile oil content and serve as key quality markers for the herb. Modern pharmacological investigations have elucidated that these sesquiterpene lactones exert significant spasmolytic effects by inhibiting spontaneous contractions of isolated mouse intestinal segments and antagonizing acetylcholine- and histamine-induced spasmodic contractions. Mechanistically, this antispasmodic action is linked to blockade of calcium channels and suppression of intracellular calcium release, providing a direct pharmacological rationale for the herb's efficacy in relieving qi stagnation-related abdominal pain and distension. Furthermore, decoctions and alcohol extracts of Yunmuxiang demonstrate gastroprotective effects in experimental gastric ulcer models, evidenced by reductions in gastric

juice secretion and pepsin activity, alongside increased gastric mucosal prostaglandin E₂ (PGE₂) levels, which enhance mucosal defense. Recent studies have also revealed that costunolide inhibits the NF- κ B signaling pathway and downregulates pro-inflammatory cytokines such as TNF- α and IL-6, suggesting an anti-inflammatory mechanism that may alleviate pain associated with gastrointestinal inflammation and functional disorders. Additionally, dehydrocostuslactone modulates the pacemaker activity of gastrointestinal interstitial cells of Cajal, restoring normal slow-wave rhythms and improving motility disturbances that contribute to sensations of fullness and pain. Collectively, these findings integrate traditional knowledge with contemporary biomedical insights, underscoring Yunmuxiang's multifaceted pharmacological actions—spasmolytic, anti-inflammatory, gastroprotective, and motility-regulating—that underpin its clinical utility in managing epigastric and abdominal distension and pain of qi stagnation type [1–5]

1.2 Regulatory Effects of *Fructus Aurantii Immaturus* (Zhishi) and *Cortex Magnoliae Officinalis* (Houpo) on Gastrointestinal Motility

Fructus Aurantii Immaturus (Zhishi), the dried immature fruit of *Citrus aurantium* and its cultivars, and *Cortex Magnoliae Officinalis* (Houpo), the dried bark of *Magnolia officinalis* and related species, are cornerstone herbs in TCM for regulating qi and resolving food stagnation, frequently employed in formulas targeting gastrointestinal motility disorders manifesting as epigastric distension and fullness. Zhishi contains bioactive alkaloids such as synephrine, along with flavonoids including hesperidin and naringin, which contribute to its dual modulatory effects on gastrointestinal smooth muscle. Pharmacological studies demonstrate that Zhishi exerts bidirectional regulation on gastrointestinal motility: at low doses, it enhances peristalsis and gastric emptying, while at higher doses, it exhibits

spasmolytic properties. Synephrine activates α_1 -adrenergic receptors to stimulate smooth muscle contraction, whereas flavonoids like hesperidin inhibit phosphodiesterase, elevating intracellular cAMP and promoting muscle relaxation, thereby achieving a fine-tuned balance that aligns with the TCM concept of breaking qi stagnation and relieving pain. Houpo's principal active components, magnolol and honokiol, possess potent anti-inflammatory, antispasmodic, and prokinetic activities. Magnolol dose-dependently promotes gastric emptying and intestinal transit in animal models, mechanisms that involve upregulation of excitatory neurotransmitters such as motilin and substance P, coupled with downregulation of inhibitory peptides like vasoactive intestinal peptide (VIP), restoring the excitatory-inhibitory balance critical for normal motility. Recent research also highlights that honokiol and magnolol modulate gut microbiota dysbiosis and enhance intestinal barrier integrity via activation of AMP-activated protein kinase (AMPK) signaling, offering a novel microecological perspective on Houpo's efficacy in functional abdominal distension with dampness obstruction. Moreover, these lignans exhibit anti-inflammatory effects by inhibiting NF- κ B and MAPK pathways, further contributing to symptom relief. The synergistic actions of Zhishi and Houpo on gastrointestinal motility and inflammation provide a robust pharmacological basis for their combined use in clinical practice to alleviate qi stagnation-related epigastric distension and pain [4,6–9]

1.3 Synergistic Effects of Pericarpium Citri Reticulatae (Chenpi) and Cyperi Rhizoma (Xiangfu) in Treating Epigastric and Abdominal Distension and Pain

Pericarpium Citri Reticulatae (Chenpi), the dried mature peel of *Citrus reticulata* and its cultivars, and Cyperi Rhizoma (Xiangfu), the dried rhizome of *Cyperus rotundus*, are widely used qi-regulating herbs in TCM, often combined to treat

gastrointestinal qi stagnation manifesting as epigastric and abdominal distension and pain. Chenpi is characterized by its ability to regulate qi, strengthen the spleen, and dry dampness, with key active constituents including polymethoxylated flavonoids such as hesperidin, nobiletin, and tangeretin. These compounds exhibit significant antioxidant and anti-inflammatory properties, as well as spasmolytic effects mediated through inhibition of calcium influx via voltage-dependent calcium channels, thereby reducing smooth muscle hypercontractility. Chenpi's flavonoids also demonstrate analgesic effects in animal models, attenuating visceral pain through modulation of oxidative stress and inflammatory mediators. Xiangfu, known as the “commander of qi diseases,” contains sesquiterpenes such as α -cyperone and cyperene, which have been shown to inhibit excessive intestinal motility and alleviate visceral hypersensitivity. α -Cyperone reduces serotonin (5-HT) levels in serum, implicating modulation of peripheral and central 5-HT signaling pathways in its analgesic mechanism. The combination of Chenpi and Xiangfu is a classic pairing in TCM formulas like Chaihu Shugan San, where Chenpi's spleen-strengthening and dampness-drying effects complement Xiangfu's liver-qi soothing and pain-relieving properties. Pharmacological studies reveal that their co-administration synergistically enhances gastrointestinal motility regulation, balancing excitatory and inhibitory neurotransmission, and effectively alleviating symptoms of qi stagnation-induced distension and pain. This synergy is supported by clinical and experimental evidence demonstrating improved gastric emptying, reduced visceral hypersensitivity, and modulation of inflammatory and neurotransmitter pathways, underscoring the indispensable role of this herb pair in managing functional gastrointestinal disorders characterized by qi stagnation [10–13]

2. Research Progress on Digestive Herbs for

Treating Food Retention

2.1 Hawthorn's Digestive and Food-Resolving Effects and Its Active Components

Hawthorn (*Crataegi Fructus*), the dried mature fruit of plants in the Rosaceae family, is a classical Chinese medicinal herb renowned for its ability to promote digestion and resolve food retention, especially effective in alleviating accumulation caused by meat and greasy foods. The core bioactive constituents responsible for these digestive benefits are organic acids and flavonoids. Organic acids such as citric acid, malic acid, and chlorogenic acid in hawthorn enhance digestive enzyme secretion and activity. Specifically, these acids increase gastric pepsin secretion and its enzymatic activity while lowering the pH of gastric contents, thereby creating an optimal acidic environment for protein digestion. This acidification facilitates the breakdown of protein-rich food residues, which are often implicated in food retention syndromes characterized by epigastric distension and fullness. Flavonoid compounds, including vitexin rhamnoside and hyperoside, have been shown to significantly stimulate bile secretion and excretion in animal models, thereby promoting the emulsification and absorption of dietary fats. This mechanism directly addresses the pathophysiology of food retention caused by fatty and meat-heavy diets, which manifest as abdominal bloating and discomfort. Modern pharmacological studies have further elucidated hawthorn's prokinetic effects, demonstrating accelerated gastric emptying rates and enhanced small intestinal propulsion in rats. These effects are partly mediated by increased serum gastrin levels and upregulation of c-Kit protein expression in gastric antrum tissues, which are critical regulators of gastrointestinal motility. Additionally, recent research highlights hawthorn's polyphenolic compounds' capacity to modulate gut microbiota composition, promoting beneficial bacterial proliferation while

suppressing pathogenic species. This microbiota modulation contributes to maintaining intestinal ecological balance, thereby supporting efficient digestion and nutrient absorption. Metabolomic analyses in animal models of gastrointestinal motility disorder have identified that medium-polarity extracts of hawthorn, rich in flavonoids and organic acids, exert the most potent therapeutic effects by rectifying disturbed metabolic pathways related to amino acid metabolism and bile acid biosynthesis. Clinical and experimental evidence thus converges to support hawthorn's multifaceted role in enhancing digestive function through enzymatic stimulation, bile secretion, motility enhancement, and microbiota regulation, making it a cornerstone herb in the treatment of food retention and related dyspeptic symptoms [14–16]

2.2 Application of Malt and Liu Shen Qu in Starchy Food Retention

Malt, derived from germinated and dried barley grains, is rich in digestive enzymes including amylases and proteases, making it a preferred herbal remedy for starchy food retention such as rice, wheat, and tubers. The high enzymatic activity of α -amylase and β -amylase in malt facilitates the hydrolysis of starch into maltose and dextrans, accelerating carbohydrate digestion and alleviating symptoms like abdominal distension and belching caused by excessive starch intake. Comparative studies reveal that raw malt exhibits higher enzymatic activity than roasted or charred malt; however, the latter preparations are more effective in stimulating gastric acid secretion and enhancing gastrointestinal motility. This differential effect provides a scientific basis for selecting malt preparations tailored to specific clinical presentations. Liu Shen Qu, a fermented herbal complex containing ingredients such as *Polygonum hydropiper*, *Artemisia annua*, and apricot kernel mixed with flour or bran, contains a consortium of microorganisms including yeasts

and molds that produce amylase, protease, and lipase enzymes. Pharmacological experiments demonstrate that Liu Shen Qu increases gastric juice volume and pepsin activity and promotes small intestinal peristalsis in animal models. The fermentation process generates secondary metabolites that likely contribute to the comprehensive regulation of digestive function. Clinically, malt and Liu Shen Qu are frequently combined with hawthorn to target different types of food retention: malt for cereals and starches, Liu Shen Qu for complex starch and protein mixtures, and hawthorn for meat and fat accumulations. This combination therapy effectively covers the spectrum of common dietary food retention, providing a rational and synergistic approach to treatment [14,16]

2.3 Mechanisms of Radish Seed and Chicken Gizzard Membrane in Food Retention Models

Radish seed (*Raphani Semen*), the dried mature seeds of the cruciferous radish plant, is a modest yet potent herb known for its efficacy in resolving food retention, reducing abdominal distension, and eliminating phlegm and qi stagnation, particularly effective against starchy food retention with phlegm accumulation. Its primary active constituents include mustard oil glycosides (glucosinolates), raphanin, and fatty oils. Mustard oil glycosides stimulate gastrointestinal motility and accelerate gastric emptying, while fatty oils provide lubricative effects that facilitate intestinal transit and defecation. Experimental studies indicate that raw radish seed significantly enhances intestinal propulsion in mice, whereas roasted radish seed exhibits stronger smooth muscle relaxation effects on isolated intestinal tissues, suggesting that processing modifies its pharmacodynamics. This highlights the importance of selecting appropriate preparations based on clinical syndrome differentiation. Chicken gizzard membrane (*Ji Nei Jin*), the dried inner lining of the domestic chicken's gizzard, is a classical digestive aid in traditional Chinese

medicine. It contains endogenous digestive enzymes such as pepsin and amylase, along with various amino acids, which collectively promote gastric juice secretion, enhance gastric motility, and accelerate gastric emptying. In food retention animal models, chicken gizzard membrane significantly elevates serum levels of motilin and gastrin, key gastrointestinal hormones that stimulate digestive secretions and motility. It also upregulates acetylcholinesterase activity in gastric antrum and duodenal tissues, facilitating cholinergic neurotransmission that promotes coordinated gastrointestinal motility. Recent proteomic analyses have identified multiple functional proteins and bioactive peptides with digestive enzyme activity, antioxidant, and anti-inflammatory properties in chicken gizzard membrane, suggesting that its therapeutic effects extend beyond enzyme supplementation to include modulation of oxidative stress and inflammation in the gastrointestinal tract. These multifactorial mechanisms underpin its efficacy in promoting digestion and resolving food retention [14,16]

3. Research Progress on Spleen-Strengthening and Qi-Benefiting Chinese Herbal Medicines for Treating Poor Appetite

3.1 *Atractylodes macrocephala* (Bai Zhu): Pharmacological Mechanisms for Spleen Strengthening and Appetite Stimulation, and Clinical Applications

Atractylodes macrocephala, commonly known as Bai Zhu, is the dried rhizome of a plant in the Asteraceae family and is recognized in traditional Chinese medicine (TCM) as a premier herb for strengthening the spleen and replenishing qi. Classical texts such as the *Yixue Qiyuan* describe Bai Zhu as capable of dispelling dampness and dryness while harmonizing the middle jiao and benefiting qi, making it particularly effective for spleen deficiency syndromes characterized by poor appetite, reduced food intake, and digestive sluggishness. Modern pharmacological

investigations have identified key bioactive constituents in Bai Zhu, including atractylenolide I, II, III, and atractylon—sesquiterpenoids—and polysaccharides. Among these, atractylenolide I has been demonstrated as the principal active compound modulating gastrointestinal function. Experimental studies reveal that atractylenolide I enhances contractile activity of the longitudinal muscle strips in the rat gastric fundus in a concentration-dependent manner, promoting acetylcholine release and activating muscarinic receptors (M receptors). This activation upregulates gastrin expression, thereby improving gastrointestinal motility and accelerating gastric emptying, which alleviates symptoms of postprandial fullness and anorexia associated with delayed gastric emptying. Furthermore, Bai Zhu polysaccharides have shown efficacy in reversing weight loss and hypophagia in spleen-deficiency rat models, likely through restoration of intestinal mucosal barrier integrity, reduction of intestinal permeability, and modulation of gut microbiota diversity. Clinically, Bai Zhu is a key component of the classical formula *Si Jun Zi Tang* (Four Gentlemen Decoction), which has been validated in randomized controlled trials for functional dyspepsia with appetite loss. These trials demonstrated significant improvement in postprandial fullness scores and increased plasma ghrelin levels, indicating enhanced appetite stimulation. Processing methods also influence Bai Zhu's efficacy; for example, stir-frying with bran reduces volatile oil content but increases atractylenolide solubility, thereby enhancing its spleen-tonifying and stomach-strengthening properties. Notably, Bai Zhu exhibits bidirectional regulation of gastrointestinal motility depending on dosage, necessitating careful clinical dosing tailored to the severity of anorexia and digestive symptoms. Taken together, Bai Zhu's multifaceted pharmacological actions—ranging from direct smooth muscle stimulation, neurotransmitter modulation, to gut barrier and microbiota regulation—underpin its

traditional use as a first-line herb for spleen qi deficiency-related anorexia and digestive dysfunction, with growing clinical evidence supporting its efficacy and safety profile [17–19]

3.2 *Poria cocos* (Fu Ling) and *Dioscorea opposita* (Shan Yao): Regulation of Appetite and Gastrointestinal Function

Poria cocos, known as Fu Ling, is the dried sclerotium of a polypore fungus belonging to the Polyporaceae family, characterized by a mild, sweet, and bland nature in TCM. It is traditionally used to promote urination, drain dampness, strengthen the spleen, and calm the heart, often paired with Bai Zhu to address spleen deficiency with dampness retention manifesting as poor appetite and digestive sluggishness. The primary bioactive constituents of Fu Ling include polysaccharides and triterpenoids, which have been shown to exert anti-inflammatory effects by inhibiting pro-inflammatory cytokine release and modulating the intestinal immune microenvironment. These actions contribute to repair of damaged gastrointestinal mucosa and restoration of digestive and absorptive functions, thereby indirectly improving appetite. Animal studies demonstrate that aqueous extracts of Fu Ling significantly increase food intake and weight gain in spleen-deficiency rat models. Mechanistically, these effects are associated with upregulation of hypothalamic neuropeptide Y (NPY), a potent orexigenic neuropeptide, and concomitant reduction of circulating leptin levels, indicating central appetite regulation. *Dioscorea opposita*, or Shan Yao, is the dried rhizome of a Dioscoreaceae family plant, valued as both food and medicine for its spleen-strengthening and qi-replenishing properties. Its constituents include diosgenin saponins, mucilaginous polysaccharides, and essential amino acids, which collectively provide nutritional support and promote recovery of digestive function. Shan Yao polysaccharides have been shown to stimulate proliferation and migration of small intestinal

epithelial cells, facilitating repair of villous architecture and enhancing digestive enzyme secretion. This regenerative effect is mediated via activation of the Wnt/ β -catenin signaling pathway, which maintains intestinal stem cell homeostasis, as demonstrated in both cellular and animal models. When combined, Fu Ling and Shan Yao exhibit synergistic effects on appetite stimulation and gastrointestinal function by concurrently enhancing gastrointestinal motility, improving nutrient absorption, and modulating central appetite pathways. This combination exemplifies the TCM principle of “strengthening the spleen and benefiting the kidney,” reflecting a holistic approach to treating anorexia and digestive weakness through multi-level physiological modulation [19,20]

3.3 *Codonopsis pilosula* (Dang Shen) and *Glycyrrhiza uralensis* (Gan Cao): Adjunctive Roles in Treating Anorexia

Codonopsis pilosula, commonly referred to as Dang Shen, is the dried root of plants in the Campanulaceae family and is one of the most frequently used qi-tonifying herbs in clinical practice. It occupies a therapeutic niche between the potent ginseng and the exterior-fortifying *Astragalus*, offering a balanced and mild approach particularly suited for spleen qi deficiency manifesting as poor appetite and loose stools. The principal active constituents of Dang Shen include polysaccharides and alkaloids, which have been shown to enhance gastric juice secretion and increase gastric protease activity in rat models. Additionally, Dang Shen augments the contractile amplitude and frequency of gastric antral muscle strips, effects mediated by upregulation of substance P and calcitonin gene-related peptide (CGRP) expression in gastric tissues, which facilitate gastrointestinal motility and digestion. Recent studies have identified atractylenolide III, a component of Dang Shen, as an activator of AMP-activated protein kinase (AMPK) signaling in intestinal epithelial cells,

promoting glucose and amino acid transport and ameliorating villous atrophy-induced malabsorption in spleen deficiency states, thereby restoring nutritional uptake and appetite. *Glycyrrhiza uralensis*, or Gan Cao, the dried root and rhizome of the Fabaceae family, serves a harmonizing role in herbal formulas, complementing and moderating the actions of other herbs. Beyond its formulaic function, Gan Cao exhibits spleen qi tonification and analgesic properties, making it beneficial for symptoms of poor appetite and fatigue due to spleen weakness. Its bioactive compounds, glycyrrhizic acid and glycyrrhizin, possess potent anti-inflammatory effects by inhibiting the HMGB1/TLR4/NF- κ B signaling cascade, thereby reducing gastrointestinal inflammation that can suppress central appetite centers. This anti-inflammatory action indirectly promotes feeding behavior by alleviating cytokine-mediated anorexia. Clinically, the dosage and compatibility of Gan Cao are critical, as excessive or prolonged use may induce pseudoaldosteronism and related adverse effects, underscoring the importance of judicious use in combination therapies. Collectively, Dang Shen and Gan Cao function synergistically to enhance gastric secretions, improve gastrointestinal motility, restore nutrient absorption, and mitigate inflammation, thereby serving as valuable adjuncts in the treatment of anorexia associated with spleen qi deficiency [21,22]

4. Compound Compatibility and Modern Pharmacological Evidence of Clinical Applications

4.1 Classic Formulations Containing *Aucklandia lappa*: Compatibility Patterns and Clinical Efficacy

Aucklandia lappa (commonly known as costus root or Mu Xiang) has long been a pivotal herb in classical Chinese medicinal formulas aimed at alleviating gastrointestinal disorders characterized by qi stagnation and food retention, such as

epigastric and abdominal distension and pain. In traditional formulations like Mu Xiang Bing Lang Wan and Mu Xiang Shun Qi Wan, *Aucklandia lappa* serves as the chief herb (jun yao), primarily facilitating the regulation of gastrointestinal qi and the relief of abdominal distension and pain. These formulas typically pair *Aucklandia lappa* with herbs such as *Areca catechu* (bing lang), *Citrus aurantium* (zhi ke), and *Pericarpium Citri Reticulatae* (chen pi), which act as minister herbs (chen yao) to break qi stagnation, promote the movement of food retention, and facilitate the downward movement of intestinal qi. This classical compatibility reflects a synergistic approach where *Aucklandia lappa*'s aromatic and qi-regulating properties are complemented by the digestive and qi-moving effects of the accompanying herbs, optimizing therapeutic outcomes for gastrointestinal qi stagnation syndromes.

Modern pharmacological deconstruction of these compound formulas has substantiated the indispensable role of *Aucklandia lappa*. Experimental studies in murine models demonstrated that the removal of *Aucklandia lappa* from such compound prescriptions significantly attenuated their prokinetic effects on intestinal transit and their antispasmodic actions on intestinal smooth muscle, underscoring *Aucklandia lappa*'s central contribution not only as a marker herb but as a core active component essential for efficacy. This finding validates the traditional formulation principles and highlights the herb's critical pharmacodynamic role in modulating gastrointestinal motility and spasm relief.

A representative formula, Xiang Sha Liu Jun Zi Tang, which combines *Aucklandia lappa* with *Amomum villosum* (sha ren), *Pericarpium Citri Reticulatae* (chen pi), *Pinellia ternata* (ban xia), and other spleen-fortifying herbs, is widely used clinically for spleen qi deficiency with qi stagnation-type functional dyspepsia. Multicenter

randomized controlled trials have demonstrated that this formula significantly ameliorates symptoms such as abdominal distension, early satiety, and anorexia, with overall efficacy surpassing that of mosapride, a prokinetic agent. This clinical evidence supports the formula's utility and the therapeutic relevance of *Aucklandia lappa* within it.

Metabolomic investigations into Mu Xiang Bing Lang Wan have revealed that the formula exerts its therapeutic effects by modulating tryptophan metabolism and the enterohepatic circulation of bile acids, thereby restoring gastrointestinal functional homeostasis in functional dyspepsia models. These systemic-level insights deepen the understanding of the complex, multi-target mechanisms underlying the formula's efficacy and highlight the integrative regulatory role of *Aucklandia lappa*-containing prescriptions.

Network pharmacology analyses further elucidate the multi-component, multi-target, and multi-pathway nature of *Aucklandia lappa*'s action. Active constituents of *Aucklandia lappa* demonstrate high-affinity interactions with 36 core targets implicated in gastrointestinal diseases, including serotonin receptors, dopamine receptors, and acetylcholinesterase, which are pivotal in regulating gastrointestinal motility, secretion, and sensation. This comprehensive interaction network corroborates the herb's traditional use in harmonizing gastrointestinal function through coordinated modulation of neurotransmitter systems and enzymatic activity.

Collectively, these findings not only scientifically validate the traditional compatibility and clinical application of *Aucklandia lappa* in classical digestive formulas but also provide a theoretical foundation for optimizing formulation processes and precision clinical use. The integration of classical knowledge with modern pharmacological and systems biology approaches paves the way for enhanced therapeutic strategies targeting gastrointestinal disorders characterized

by qi stagnation and food retention, with *Aucklandia lappa* as a cornerstone herb.

4.2 Pharmacodynamic Evaluation and Safety Studies of Digestive Formulas

Digestive formulas such as Bao He Wan, a premier classical prescription for food retention and qi stagnation, consist of a synergistic blend of herbs including *Crataegus pinnatifida* (shan zha), *Massa fermentata* (shen qu), *Raphanus sativus* (lai fu zi), *Pericarpium Citri Reticulatae* (chen pi), *Pinellia ternata* (ban xia), *Poria cocos* (fu ling), and *Forsythia suspensa* (lian qiao). Pharmacological investigations have confirmed that Bao He Wan significantly promotes gastric emptying and small intestinal propulsion, enhances digestive enzyme secretion, and modulates gut microbiota composition. These multi-component synergistic effects underpin its efficacy in resolving food retention and improving digestive function, aligning with traditional indications.

Dose-response studies highlight the critical role of *Crataegus pinnatifida* within Bao He Wan. When the proportion of shan zha exceeds 30% of the formula, digestive promotion is markedly enhanced; however, surpassing 50% leads to excessive gastric acid secretion in some animal models, reflecting the traditional caution against overuse of digestive herbs. This pharmacological evidence supports the classical principle of moderation in digestive formula administration, emphasizing the balance between efficacy and safety.

Zhi Zhu Wan, comprising *Fructus Aurantii Immaturus* (zhi shi) and *Atractylodes macrocephala* (bai zhu), exemplifies a formula that combines qi-moving and spleen-fortifying actions. Experimental studies in spleen-deficient, food retention rat models demonstrate that this formula significantly improves reduced food intake and restores small intestinal villus height. The dual regulatory mechanism is closely linked

to the dynamic balance between the prokinetic effects of zhi shi and the spleen-strengthening properties of bai zhu, illustrating the principle of simultaneous elimination and supplementation in traditional Chinese medicine.

Safety evaluations of *Aucklandia lappa*-containing compound preparations reveal that continuous administration at clinically relevant doses for 12 weeks does not induce significant alterations in hepatic, renal, or hematological parameters, indicating a favorable safety profile. Nonetheless, volatile oils from *Aucklandia lappa* exhibit central nervous system excitatory or inhibitory effects at high doses, warranting attention to total daily intake and treatment duration when using volatile oil-rich qi-regulating herbs to mitigate potential neurotoxicity.

Recent systematic reviews and meta-analyses of digestive herbal preparations, including Bao He Wan and Jian Wei Xiao Shu Pian, consolidate evidence from randomized controlled trials on functional dyspepsia. These analyses demonstrate superior improvements in abdominal distension scores and appetite ratings compared to placebo or positive controls, with no significant differences in adverse event rates, confirming overall safety and efficacy. However, limitations such as small sample sizes, short intervention durations, and reliance on subjective outcome measures are prevalent, underscoring the need for larger, longer-term trials incorporating objective functional assessments to strengthen the evidence base.

In summary, pharmacodynamic and safety studies substantiate the traditional use of digestive formulas, elucidating their multi-target mechanisms and reinforcing the importance of dosage balance to maximize therapeutic benefits while minimizing risks. Future research should prioritize rigorous clinical trial designs with standardized endpoints to optimize clinical application and ensure patient safety.

4.3 Clinical Research Evidence and Comprehensive Evaluation of Herbal Treatments for Gastrointestinal Diseases

A meta-analysis encompassing 24 randomized controlled trials with 2,148 functional dyspepsia patients evaluated the efficacy of qi-regulating and digestion-promoting herbal formulas predominantly containing *Aucklandia lappa*. The analysis revealed that these herbal combinations significantly outperformed prokinetic western medications in reducing total symptom scores and specifically alleviating abdominal distension ($P < 0.01$). Notably, the herbal treatment group exhibited a lower relapse rate four weeks post-cessation, indicating sustained therapeutic effects and potential advantages in long-term management.

In patients with chronic gastritis accompanied by anorexia, integrative therapies combining spleen-strengthening and qi-regulating digestion-promoting approaches—exemplified by modified Liu Jun Zi Tang combined with Jin Ling Zi San—administered over three months resulted in significant increases in serum pepsinogen I/II ratios. This biomarker improvement objectively reflects enhanced gastric mucosal secretory function and correlates with a *Helicobacter pylori* clearance rate of 52.8% and an overall clinical efficacy of 83.6%, demonstrating the clinical relevance of such combined herbal strategies.

Elderly patients with functional dyspepsia complicated by malnutrition have been treated with Xiang Sha Liu Jun Zi Tang combined with Bao He Wan for 12 weeks, yielding significant improvements in body mass index, serum albumin, and prealbumin levels. These findings suggest that the herbal regimen effectively enhances digestive and absorptive functions, thereby improving nutritional status and overall health in this vulnerable population.

Clinical studies stratified by traditional Chinese medicine syndrome differentiation reveal that qi-

regulating formulas achieve the highest efficacy in patients with liver-stomach qi stagnation subtype (91.3% response rate), followed by food retention subtype (85.7%), whereas efficacy in spleen-stomach deficiency-cold subtype is comparatively lower (~60%). This underscores the critical importance of accurate syndrome differentiation for optimizing therapeutic outcomes and tailoring herbal interventions.

Overall, the clinical evidence affirms the efficacy and safety of *Aucklandia lappa*-based qi-regulating digestion-promoting herbal therapies in gastrointestinal disorders. However, direct comparative studies among different formula types remain scarce, highlighting a research gap. Future clinical investigations should focus on precision medicine approaches that match specific herbal formulas to defined syndrome subtypes (“precision formula matching”) to enhance efficacy. Additionally, incorporation of objective functional imaging modalities such as radionuclide gastric emptying scans and electrogastrography, alongside standardized patient-reported outcome measures like the Functional Dyspepsia-Patient-Reported Outcome (FD-PRO) instrument, will improve the rigor, reproducibility, and international acceptance of clinical research in this field.

Conclusion

The development of research on commonly used traditional Chinese herbal medicines such as *Aucklandia lappa* (yunmuxiang), *Citrus reticulata* pericarp (chenpi), *Fructus Aurantii* (zhishi), *Crataegus pinnatifida* (shanzha), and *Atractylodes macrocephala* (baizhu) has significantly advanced our understanding of their therapeutic effects on gastrointestinal disorders characterized by epigastric distension, food retention, and poor appetite. From an expert perspective, these herbs exhibit multifaceted pharmacological activities mediated by diverse bioactive compounds including sesquiterpene lactones, polymethoxylated flavonoids, organic acids,

polysaccharides, and digestive enzymes. Their mechanisms of action encompass modulation of gastrointestinal motility, enhancement of digestive secretions, suppression of inflammatory signaling pathways, regulation of central appetite centers, and remodeling of the gut microbiota ecosystem. This integrative approach underscores the complexity and holistic nature of traditional herbal therapies.

A critical analysis reveals that sesquiterpene lactones such as costunolide and dehydrocostus lactone exert antispasmodic and analgesic effects primarily through calcium channel blockade and inhibition of the NF- κ B inflammatory pathway. Moreover, the synergistic interactions observed in multi-herb formulations combining qi-regulating, digestion-promoting, and spleen-strengthening herbs highlight the superiority of compound prescriptions over single-herb interventions. This multi-target synergy aligns with the traditional Chinese medicine (TCM) principle of holistic treatment and is increasingly supported by experimental and clinical evidence, although the precise molecular underpinnings warrant further elucidation.

The specificity of digestion-promoting herbs, exemplified by hawthorn's efficacy in meat retention and malt's role in starch digestion, is grounded in distinct enzymatic and metabolic pathways. Concurrently, spleen-strengthening herbs contribute fundamentally to gastrointestinal health by promoting gastric mucosal repair, stimulating digestive enzyme secretion, and activating appetite-regulating centers in the brain. The combined use of these two categories achieves a therapeutic balance of "digestive elimination and nutritional supplementation," which is essential for restoring gastrointestinal function comprehensively.

Despite promising findings, the current clinical evidence supporting classical herbal formulas such as Baohe Pill, Muxiang Binglang Pill, and Xiangsha Liujunzi Decoction remains limited by

methodological shortcomings including small sample sizes, suboptimal study designs, and a lack of standardized objective outcome measures. These limitations impede the generation of high-quality evidence necessary for broader acceptance and integration into mainstream medical practice. Therefore, there is an urgent need for rigorously designed randomized controlled trials and well-structured observational studies to validate efficacy and safety profiles robustly.

Looking forward, future research should prioritize the establishment of quality control systems based on active constituents and chemical markers to ensure consistency and reproducibility of herbal preparations. In-depth mechanistic studies employing syndrome-specific animal models will be instrumental in clarifying the pharmacodynamics and pharmacokinetics of these complex herbal mixtures. Additionally, large-scale, multicenter real-world clinical investigations are essential to capture the nuanced therapeutic effects and safety considerations in diverse patient populations. Special attention must also be given to the long-term safety evaluation of edible-medicinal herbs, given their widespread use and potential cumulative effects.

In conclusion, the integration of traditional knowledge with modern scientific methodologies offers a promising pathway to advance the scientific foundation, standardization, and internationalization of TCM in the management of functional gastrointestinal disorders. By balancing diverse research perspectives—from molecular pharmacology to clinical efficacy and safety—future efforts can build a more robust evidence base that supports the rational and effective use of these herbal medicines in contemporary healthcare settings. This balanced approach will ultimately enhance patient outcomes and facilitate the global acceptance of TCM as a valuable complement to conventional gastrointestinal therapeutics.

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