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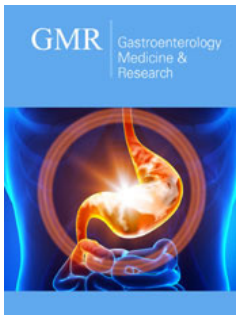
Traditional Chinese Medicine Therapeutic Strategies for *Helicobacter pylori* Associated Gastric Diseases: A Mini Review

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Abstract

H*elicobacter pylori* (*H. pylori*), a class-I carcinogen, induces the Correa cascade towards gastric carcinoma and infects over half the global population. Standard bismuthquadruple therapy faces challenges of antibiotic resistance, microbiota disturbance, sideeffects and high recurrence. TCM exerts multitarget effects including bacteriostasis, biofilm suppression, mucosal protection, microecology and inflammation regulation. This review summarizes TCM syndrome differentiation, formulas, active components and limitations. It highlights interactions between *H. pylori*, gastric dysbiosis and carcinogenesis, and prospects integrated therapy and nanodelivery for drugresistant *H. pylori*.

Keywords: *Helicobacter pylori*; Traditional Chinese medicine; Active herbal ingredients; Anti inflammation; Gastric mucosal protection

Introduction

Helicobacter pylori, a Gramnegative microaerophilic bacterium, colonises human gastric mucosa and acts as the initiating driver of the Correa pathological cascade toward gastric cancer [1,2]. More than 90 % of gastric carcinoma cases are associated with *H. pylori* infection, yet only 13 % of infected individuals develop malignant transformation, which implies that additional hostmicroecological cofactors participate in disease progression [3,4]. With disease aggravation from gastritis to intestinal metaplasia and gastric cancer [5], gastric acid secretion declines [6] and intragastric pH rises [7-10]. Such microenvironmental shifts reshape gastric microbiota composition: gastric microbial αdiversity increases significantly in gastric carcinoma tissues, while the dominating status of *H. pylori* weakens at the cancer stage, and opportunistic pathogens such as *Fusobacterium*, *Prevotella*, *Veillonella* proliferate abundantly [11-14]. Disturbed gastric microbiota further promotes carcinogenesis via altered metabolite profiles including nitrosamine compounds and shortchain fatty acids. Clinically, bismuth quadruple therapy combining two antibiotics, protonpump inhibitor and bismuth agent serves as standard eradication treatment [15-18]. Nevertheless, widespread antibiotic application gives rise to drugresistant *H. pylori* strains, damages commensal intestinal flora and causes adverse symptoms such as diarrhoea and bloating, and posttreatment relapse remains a clinical obstacle [19-22]. Therefore, exploring safe, multimodal alternative therapies is urgently required. Traditional Chinese medicine treats *H. pylori*associated gastropathy under the pattern of "gastric stuffiness" and "epigastric pain" [23-27]. TCM therapies follow syndromedifferentiated treatment principles, exhibiting comprehensive advantages:

inhibiting *H. pylori* viability, dismantling bacterial biofilms, repairing damaged gastric mucosa, regulating inflammatory cascades and remodelling gastric microecology. Classical formulas such as Banxia Xiexin Decoction have long been applied clinically for *H. pylori*related chronic gastritis [28-32]. This review focuses on syndrome classification, commonlyused prescriptions, bioactive constituents, pharmacological mechanisms, research bottlenecks and future directions of TCM against *H. pylori*related gastric diseases.

Characteristics of *H. pylori* Associated Gastric Diseases in TCM

H. pylori is interpreted as "dampheat pathogenic toxin" in TCM theory [33]. Pathogenic toxin invades the stomach, damages spleenstomach qi movement, induces stagnation, dampnessheat accumulation, blood stasis and deficiency syndromes [34]. The main clinical TCM patterns are summarised in Figure 1.

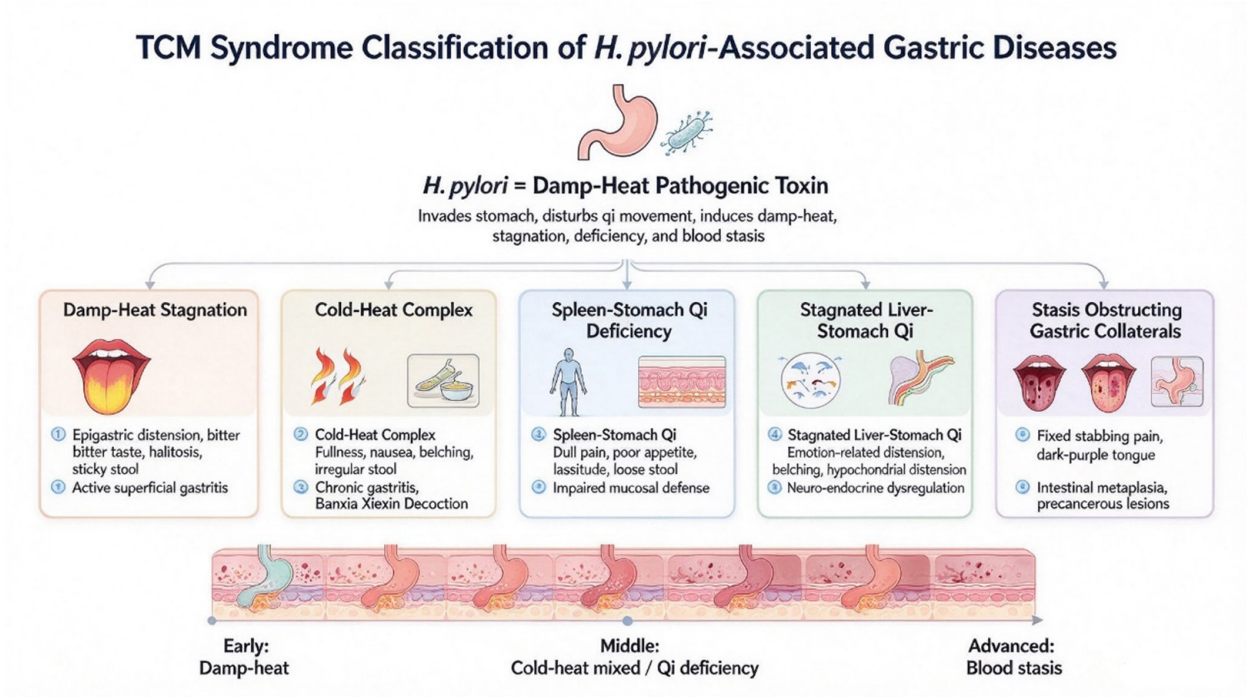


Figure 1: TCM syndrome classification of *H. pylori*-associated gastric diseases and their correlation with pathological progression.

Dampheat stagnation in spleenstomach

Epigastric distending pain, bitter taste in mouth, halitosis, sticky stool, red tongue with yellowgreasy coating. This pattern corresponds to active *H. pylori*positive superficial gastritis with obvious local inflammatory response [35].

Coldheat complex intermingling

Alternating coldheat manifestations, epigastric fullness and stuffiness, nausea, belching, loose stool or constipation. It is the representative syndrome treated by Banxia Xiexin Decoction, frequently observed in *H. pylori*positive chronic gastritis [36-39].

Spleenstomach qi deficiency

Dull epigastric ache, poor appetite, lassitude, loose stool, pale tongue with thinwhite coating, reflecting longterm infectioninduced mucosal injury and declining defensive capability [40,41].

Stagnated liverstomach qi

Epigastric distending pain fluctuating with emotional changes, frequent belching, distending hypochondrium, closely related to neuroendocrine dysregulation under chronic *H. pylori*triggered inflammation [42].

Stasis obstructing gastric collaterals

Fixed stabbing epigastric pain, darkpurple tongue with ecchymosis, mostly seen in advanced lesions including intestinal metaplasia and precancerous gastric mucosal changes [43]. Syndrome distribution is tightly linked with pathological severity: dampheat pattern dominates at earlystage gastritis; coldheat mixed and qideficiency patterns increase during disease progression; bloodstasis pattern prevails in precancerous and cancerous gastric mucosal lesions.

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Classical TCM Prescriptions for Anti *H. pylori* Therapy

Banxia Xiexin decoction

Banxia Xiexin Decoction originates from Treatise on Febrile Diseases, composed of *Pinelliae Rhizoma*, *Scutellariae Radix*, *Coptidis Rhizoma*, *Zingiberis Rhizoma*, *Ginseng Radix*, *Glycyrrhizae Radix et Rhizoma Praeparata cum Melle*, *Jujubae Fructus*. The formula harmonises cold and heat, dissipates focal distention. Modern researches demonstrate that it can suppress *H. pylori* urease activity, disrupt biofilm formation, inhibit PI3K/Akt/NFκB inflammatory signalling pathway, lower proinflammatory factors TNFα, IL6, IL1β and ameliorate gastric mucosal erosion. It achieves dual effects of eliminating pathogenic bacteria and protecting gastric epithelium. Currently multiple studies explore nanoselfassembly modification strategies for Banxia Xiexin Decoction active components to improve gastric stability and bioavailability [44-48].

Qingwei San

Qingwei San clears stomach heat and cools blood, mainly applicable for dampheat accumulation pattern *H. pylori*positive gastritis. *Coptidis Rhizoma* and *Rehmanniae Radix* in the formula exert direct bacteriostatic effects on *H. pylori*, relieve gastric mucosal congestion and inflammatory infiltration [49].

Sijunzi decoction combined with heatclearing herbs

Sijunzi Decoction tonifies spleenstomach qi. Combined with heatdetoxifying herbs (*Coptidis Rhizoma*, *Scutellariae Radix*, *Forsythiae Fructus*), it treats spleendeficiency complicated with damptoxin pattern. It does not produce strong direct bactericidal action, but enhances host mucosal immune defence function, improves gastric microenvironment and indirectly inhibits the colonisation of *H. pylori* and conditional pathogenic bacteria [50-52].

Modified Chaihu-Shugan-San

Chaihu-Shugan-San soothes liver and regulates stomach qi, suitable for liverstomach qistagnation subtype *H. pylori*associated functional dyspepsia. It mitigates neuroinflammatory response caused by *H. pylori* infection and improves clinical subjective symptoms [53-55].

Bioactive Herbal Ingredients Against *H. pylori* and Pharmacological Mechanism

Alkaloids

Berberine extracted from *Coptidis Rhizoma*: one of the mostinvestigated anti*H. pylori* natural compounds. It inhibits bacterial urease, damages membrane integrity, suppresses virulence factors such as CagA and VacA. Berberine also modulates gastric and intestinal microbiota, elevates beneficial bacteria abundance and downregulates inflammatory signal transduction. It has been reported to exhibit efficacy against partial antibioticresistant *H. pylori* strains [56-58].

Flavonoids

Baicalin from *Scutellariae Radix*: inhibits *H. pylori* adhesion to gastric epithelial cells, interferes with biofilm maturation, blocks NFκBmediated inflammatory cascade and reduces oxidative stress injury of GES1 gastric epithelial cells. Glycyrrhizic acid from *Glycyrrhizae Radix et Rhizoma* protects gastric mucosal barrier by elevating mucosal prostaglandin levels, cooperating with other components to counteract *H. pylori*induced damage [59,60].

Other active substances

Volatile oil from *Zingiberis Rhizoma*: Inhibits *H. pylori* proliferation and alleviates mucosal inflammatory oedema. Polysaccharides from *Jujubae Fructus* enhance mucosal immune response. Multiple components often generate synergistic effects within compound prescriptions.

The multitarget characteristics distinguish herbal agents from singletarget antibiotics: TCM components not only act directly on pathogens, but also remodel host microenvironment, restrain the overgrowth of conditional pathogenic bacteria such as *Fusobacterium*, *Prevotella* which expand when *H. pylori* gradually decrease in advanced gastric lesions [61,62].

Modern Progress of TCM Intervening Gastric Microecology under *H. pylori* Infection

According to 16S rRNA sequencingbased gastric microbiota researches, as gastritis advances to gastric cancer, gastric microbial community undergoes profound reconstruction: αdiversity rises obviously; *Fusobacteria*, *Firmicutes* and related genera including *Lactobacillus*, *Prevotella*, *Veillonella* are significantly enriched; *Bacillus* beneficial genus declines. *H. pylori* dominate gastric niche at gastritis and intestinal metaplasia phases and lower overall microbial diversity, whereas its predominance disappears in gastric carcinoma tissues. Such microecological disorder further accelerates disease evolution. Traditional Chinese medicine, especially compound formulas, exhibits microecological regulatory effects that go beyond simple bacteriostasis. These effects include suppressing excessive colonization of *H. pylori* without complete eradication, restraining the over proliferation of gastric opportunistic pathogens, facilitating the recovery of beneficial microbes such as *Lactobacillus* and *Bacillus*, and modulating intragastric pH as well as metabolite profiles including short-chain fatty acids [63,64] (Figure 2). Remarkably, integrated Chinesewestern medicine mode combines quadruple therapy with TCM decoctions: TCM mitigates antibioticcaused flora disturbance, lowers adverse reaction incidence and improves eradication rate for partial drugresistant *H. pylori*. Nevertheless, highquality largesample clinical microbiota evidence remains insufficient.

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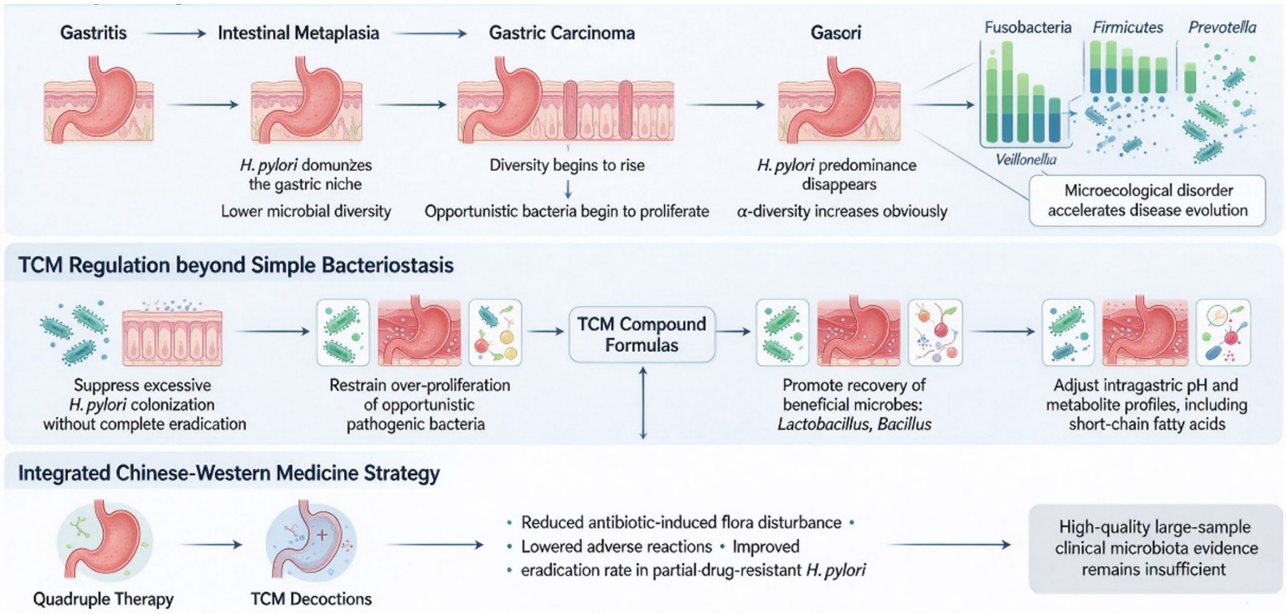


Figure 2: Modern research progress of TCM intervening gastric microecology under *H. pylori* infection.

Limitations and Existing Challenges

Notably, several limitations remain in current related investigations. First, the standardisation of TCM syndrome differentiation is insufficient: TCM pattern classification is short of unified objective biomarkers, and the majority of clinical studies are single-centre trials with small sample sizes. Only a handful of studies have established associations between TCM syndromes and gastric microbiota signatures under *H. pylori* infection. Second, the complex chemical composition of compound prescriptions impedes mechanistic elucidation. These formulas contain hundreds of constituents, making it challenging to dissect the individual contributions of each component to anti-*H. pylori*, anti-inflammatory and microecology-modulating effects, and most mechanistic explorations are still limited to cellular and animal models. Third, herbal active ingredients face unsatisfactory delivery performance. Many bioactive compounds including baicalin and berberine exhibit poor water solubility, susceptibility to gastric acid degradation, low local gastric retention and inadequate bioavailability, thereby constraining them *in vivo* therapeutic efficacy. Meanwhile, emerging nanocarrier and self-assembly strategies are still restricted to laboratory research. Finally, long-term cohort observations are lacking. Existing studies predominantly concentrate on short-term *H. pylori* eradication rates and symptomatic remission, while long-term follow-up data regarding the reversal of precancerous lesions, dynamic shifts of gastric microbiota and gastric cancer preventive effects remain scarce [65,66].

Conclusion

H. pylori-associated gastric disease represents a multifactorial pathological process that integrates pathogenic factors, host inflammatory responses and gastric microecological dysbiosis. Traditional Chinese medicine possesses distinctive advantages in bacteriostasis, mucosal repair and microecological regulation, which can offset the limitations of antibiotic-based quadruple therapy, particularly for drug-resistant *H. pylori* infection and persistent symptoms after eradication. Accordingly, several directions are recommended for future research: to launch multicentre clinical trials for exploring the correlations between TCM syndromes, gastric microbiota and metabolites and developing objective biomarkers for pattern differentiation; to decipher the synergistic mechanisms of TCM compound formulas using multi-omics, network pharmacology and molecular biology approaches; to design innovative herbal delivery systems (e.g., ion-driven self-assembled nanoparticles and mucoadhesive formulations) for improving the local gastric stability and bioavailability of active constituents; and to advance rational integrated Chinese and Western medicine strategies by investigating optimal administration sequences and dosing regimens, alongside long-term cohort studies to assess the capacity of TCM to reverse precancerous gastric mucosal lesions and prevent gastric carcinogenesis.

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Conflict of Interest

The authors have declared that no competing interests exist.

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