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Research Progress on Traditional Chinese Medicine Interventions for Helicobacter Pylori

Yizhuo Gao[1], Tao Yu[2,*]

[1]Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China
[2]Shaanxi Provincial Hospital of Chinese Medicine, Xi'an 710003, Shaanxi, China
Correspondence Author

Abstract: ***Helicobacter pylori (Hp) infection is a major global cause of gastritis, peptic ulcers, and gastric cancer. With rising antibiotic resistance, integrated Chinese and Western medicine approaches for treating Hp infection have gained increasing attention. This systematic review summarizes recent advances in TCM research for Hp infection prevention and treatment, exploring the mechanisms of action, clinical applications, and future directions of single-herb and compound TCM formulations. Studies indicate that TCM exerts effects through multiple pathways, including direct antibacterial activity, immune modulation, gastric mucosal repair, and improvement of intestinal microecology. Active components such as berberine, Coptis chinensis, Scutellaria baicalensis, and Panax notoginseng saponins inhibit Hp growth and reduce inflammatory responses; Compound formulas like Lianpu Decoction, Banxia Xiexin Decoction, and Jiawei Xiangshaliujunzi Decoction demonstrate promising efficacy in enhancing Hp eradication rates, alleviating symptoms, and mitigating antibiotic side effects. Furthermore, TCM syndrome differentiation studies indicate that spleen-stomach damp-heat syndrome is most prevalent in Hp infection, arising from dietary imbalances and the accumulation of damp-heat pathogenic factors.***

Keywords: Hp infection, Traditional Chinese Medicine treatment, Syndrome differentiation, Mechanism, Spleen-stomach damp-heat**.**

1. Introduction

In 1983, Barry J. Marshall and J. Robin Warren isolated and identified Helicobacter pylori (Hp) through groundbreaking research, overturning the traditional notion that "the stomach is a sterile organ" [1]. Hp infection is highly correlated with dyspepsia, gastric inflammatory responses, gastric ulcers, duodenal ulcers, gastric MALT lymphoma, and gastric cancer development [2]. Transmission primarily occurs via oral-oral, fecal-oral, or gastric-oral routes [3], and it is now recognized as an infectious disease [4]. Hp infection is the greatest risk factor for gastric cancer [5]. Although the probability of Hp infection progressing to gastric cancer is less than 5%, nearly all non-cardia gastric cancers are associated with Hp infection [6]. Additional studies indicate that eradicating Hp significantly reduces the recurrence rate of gastric ulcers [7]. Therefore, Hp eradication can effectively lower the incidence of both gastric cancer and gastric ulcers. However, due to resistance mechanisms such as gene mutations [8] and biofilm formation [9], the annual Hp recurrence rate in China reaches 2.2% [10]. In recent years, the combination of traditional Chinese medicine (TCM) and Western medicine for Hp eradication has gained widespread application. This review aims to provide new options for clinical Hp eradication regimens.

2. Hp Infection and Traditional Chinese Medicine Syndrome Differentiation

Within the TCM theoretical framework, Hp infection has not yet been assigned a specific disease name. Based on its clinical manifestations—such as epigastric fullness, belching, loss of appetite, and epigastric pain—it can be classified under the "Spleen-Stomach Disorders" pattern differentiation system.

2.1 Research on the Relationship Between Disease (Hp Infection) and Syndrome

Multiple large-scale clinical studies have revealed significant associations between Hp infection and TCM syndrome patterns. Zhang Yangyang et al. [11] conducted a systematic literature review involving 172,773 patients, identifying a core triad of syndrome patterns: spleen-stomach damp-heat syndrome (32.1%), spleen-stomach deficiency syndrome (24.7%), and liver-stomach disharmony syndrome (13.2%). Notably, this distribution pattern showed high consistency across regional studies: Huang et al. [12] reported that in a cross-sectional survey of 5,544 patients, spleen-stomach damp-heat syndrome (42.21%) and liver-stomach disharmony syndrome (21.48%) together accounted for 63.69%. Xu et al. [13] further confirmed in a chronic gastritis cohort that these two syndromes constituted 61.06% of cases. Notably, Tao Feibao et al. [14] employed dual diagnostic criteria of gastric mucosal histology and C14 breath test, revealing that the proportion of spleen-stomach damp-heat syndrome in the Hp-positive group (68.5%) was significantly higher than that in the negative group (23.1%). A multicenter study by Zhao Gang et al. [15], based on the "Consensus on Integrated Chinese and Western Medicine Diagnosis and Treatment of Chronic Gastritis", demonstrated a dose-response relationship between spleen-stomach damp-heat syndrome and Hp infection. The mechanism may be related to the damp-heat microenvironment promoting the expression of the Hp flagellin gene flaA.

2.2 Research from Syndrome to Disease (Hp Infection)

Recent studies have revealed the dynamic association between TCM syndromes in chronic gastritis and Hp infection. A retrospective cohort study by Ma Lijuan et al. [16] involving 287 chronic gastritis patients demonstrated that the Hp positivity rate was as high as 91.89% in patients with spleen-stomach deficiency-cold syndrome, significantly higher than in those with spleen-stomach damp-heat syndrome (86.05%) and stomach yin deficiency syndrome (77.55%), showing a marked syndrome gradient difference. Notably, this study first identified gender-specific distribution

patterns: Hp-positive males predominantly exhibited spleen-stomach damp-heat syndrome, while females showed a higher prevalence of liver-qi stagnation syndrome. This may correlate with differences in male alcohol consumption rates and female psychological stress levels. Analysis of disease duration further revealed progression patterns: among patients with a disease duration exceeding 10 years, spleen-stomach deficiency-cold syndrome accounted for 48.57%, corroborating the TCM pathogenesis theory that "prolonged illness affects the kidneys, and yang deficiency generates cold. "A prospective study by Liu Dongbing et al. [17] on chronic atrophic gastritis showed distinct features: among 108 patients with chronic atrophic gastritis, spleen-stomach deficiency syndrome was the most prevalent pattern, yet spleen-stomach damp-heat syndrome exhibited the highest Hp infection rate and showed a strong positive correlation with serum PGI levels. Hp infection distribution varies significantly across different TCM syndromes in chronic gastritis. Both spleen-stomach damp-heat and spleen-stomach deficiency-cold syndromes exhibit high infection rates. Hp infection occurrence is closely associated with gender, disease duration, and relevant physiological indicators. These findings not only enrich TCM pathogenesis theories for chronic gastritis but also provide crucial evidence for precise clinical syndrome differentiation. Li Peicai et al. [18] conducted a systematic literature review analyzing the distribution of TCM syndromes in Hp infection, incorporating 69 studies covering 14, 398 cases across 14 syndrome types. Results indicated that spleen-stomach damp-heat syndrome was the most prevalent, followed by liver-stomach disharmony and spleen-stomach deficiency syndromes, highlighting the significance of damp-heat pathogenic factors in Hp-related diseases. Traditional Chinese medicine classifies Hp infection as an "external pathogen." Its invasion of the body hinges on spleen-stomach deficiency and insufficient vital energy. The Huangdi Neijing states: "Where pathogens gather, vital energy must be deficient," indicating that external pathogens more readily invade when vital energy is depleted. Hp primarily enters through food and resides in the stomach; if spleen-stomach function is impaired, it can linger, generating dampness and heat. The Suwen · Discussion on Bi Syndrome mentions: "When damp-heat is not expelled, the large tendons become stiff and short, the small tendons become slack and long, and the flesh loses sensation," indicating that damp-heat pathogens disrupt qi circulation, leading to various discomfort symptoms. Modern dietary changes have exacerbated the formation of spleen-stomach damp-heat. The Yellow Emperor's Inner Canon states: "When food intake doubles, the intestines and stomach suffer injury." This means overindulgence in rich, greasy, sweet, and spicy foods promotes dampness and heat, damaging the spleen and stomach. This impairs the spleen's ability to transform and transport nutrients, disrupts the stomach's harmonious descent, and causes qi movement to become imbalanced. If damp-heat stagnates, it may cause epigastric and abdominal distension; if damp-heat descends, it manifests as sticky stools and scanty, dark urine; if dampness obstructs qi movement, it results in heavy limbs; if damp-heat suppresses body fluids, it produces dryness and a bitter, greasy taste in the mouth. The Essential Prescriptions of the Golden Cabinet: Pulse Patterns and Treatment for Vomiting, Hiccuping, and Diarrhea states: When the stomach is deficient and cold, it cannot digest food, hence undigested food and water pass out undigested." This indicates that impaired spleen-stomach transformation can further aggravate damp-heat obstruction, leading to digestive dysfunction. Clinically, patients with spleen-stomach damp-heat syndrome often present with a red tongue, a thick yellow or greasy coating, and a slippery-rapid or soft-rapid pulse. Compared to other syndromes, the diagnostic criteria for spleen-stomach damp-heat are more straightforward.

3. Research on Traditional Chinese Medicines Against Hp

3.1 Monotherapy Studies Against Hp

Traditional Chinese medicine primarily employs tonic herbs, heat-clearing herbs, and qi-regulating and dampness-resolving herbs as core treatments for Hp infection-related spleen and stomach disorders [19]. Modern research indicates that Chinese herbal medicine not only directly targets Hp but also achieves antibacterial effects and improves gastric mucosal damage through multiple indirect mechanisms. Regarding direct antibacterial effects, TCM disrupts Hp's biofilm structure, reduces its adhesion and motility, and interferes with its respiration and metabolic processes, thereby effectively inhibiting Hp growth and reproduction. Indirectly, TCM achieves anti-Hp effects by modulating host immune responses, suppressing Hp-related inflammatory reactions, and lowering Hp-induced oxidative stress levels [20,21]. Patchouli alcohol enhances Hp clearance by stabilizing lysosomal function and boosting macrophage phagocytosis and degradation of Hp. Concurrently, it suppresses pro-inflammatory factors IL-6 and TNF-α to reduce inflammation, while mitigating Hp damage to host cells through antioxidant effects [22]. Poria cocos polysaccharides demonstrate potent gastric mucosal protective effects in Hp-associated gastritis treatment. Research indicates that Poria polysaccharides mitigate Hp-induced gastric mucosal inflammation and tissue damage by inhibiting NF-κB signaling pathway activation, thereby reducing IL-8 release. Furthermore, they decrease Hp colonization rates on the gastric mucosa, improve gastric tissue structural integrity, and alleviate symptoms of Hp-associated gastritis [23]. The Galangin flavonoid compound also demonstrates potent effects in suppressing Hp-induced inflammatory responses. Studies indicate this compound significantly reduces IL-8 and MyD88 expression levels in Hp-infected mice. By inhibiting PI3K/Akt signaling pathway activation, it curtails inflammatory factor release, thereby mitigating gastric mucosal damage. Additionally, this compound effectively reduces Hp infection rates, offering novel therapeutic insights for Hp-associated gastric diseases [24]. Qu Zhiwei et al. [25] investigated the antibacterial effects of Banxia Xiexin Decoction and its seven constituent herbs (Pinellia, Scutellaria, Ginseng, Coptis, Dried Ginger, Jujube, Licorice) against Hp-resistant strains through in vitro experiments. The minimum inhibitory concentrations (MICs) of these herbs were determined, revealing significant antibacterial activity against resistant Hp by Scutellaria baicalensis, Coptis chinensis, Glycyrrhiza uralensis, and Panax ginseng. Scutellaria baicalensis exhibited the strongest effect, followed by Coptis chinensis, Glycyrrhiza uralensis, and Panax ginseng, while Pinellia ternata, Ziziphus jujuba, and Zingiber officinale showed no notable antibacterial activity in vitro. Further analysis revealed that Scutellaria

baicalensis and Coptis chinensis exerted antibacterial effects by inhibiting Hp urease activity, disrupting Hp biofilm structure, and interfering with flagellar motility. Regarding animal studies, Wang Jianping et al. [26] employed an Hp-infected mouse model to evaluate the anti-Hp activity of various single herbal medicines. Mice were randomly divided into seven groups and treated with saline, Coptis, Scutellaria, Rheum, Corydalis, Lycium, or amoxicillin decoctions. Results showed Hp eradication rates of 76%, 64%, and 68% for Coptis, Scutellaria, and Rheum, respectively. Their antibacterial efficacy was comparable to amoxicillin (80%) and significantly superior to Corydalis and Lycoris (28% and 36%, respectively), suggesting these herbs may be potent anti-Hp agents. Further mechanistic studies revealed that Coptis and Scutellaria downregulated Hp-induced inflammatory mediators IL-8 and TNF-α while inhibiting NF-κB signaling activation, thereby reducing gastric mucosal inflammation caused by Hp infection. Additionally, dandelion, notoginsenosides, astragaloside IV, and baicalin also demonstrated beneficial effects in preventing and treating Hp infection. Ren Zhu et al. [27] found that dandelion decoction inhibited Hp growth at concentrations of 25–50 g/L and exhibited significant bactericidal activity at 50–100 g/L. The anti-Hp activity of dandelion may be related to its regulation of signaling pathways such as FoxO, ErbB, and PI3K-AKT. Modulation of these pathways can influence oxidative stress levels and host immune responses, thereby enhancing Hp clearance capacity. Shi Xueying et al. [28] investigated the cytotoxic effects of notoginsenosides, astragalosides, and baicalins on Hp-infected gastric epithelial cells. Results indicated that these compounds induce apoptosis in Hp-infected cells by activating the mitochondrial apoptosis pathway, upregulating caspase-3 and Bax expression, and inhibiting Bcl-2 activity, thereby enhancing cellular clearance capacity. Jiang Cheng et al. [29] demonstrated that Coptis chinensis exhibited the strongest antibacterial activity among 15 herbal medicines. It effectively reduced Hp pathogenicity by interfering with flagellar motility, inhibiting urease activity, and downregulating virulence factor expression. Berberine, the primary active component of Coptis chinensis, exhibits significant anti-Hp effects. Its main mechanisms include inhibiting Hp N-acetyltransferase activity and disrupting Hp metabolic processes, thereby restricting its growth and proliferation. Additionally, berberine modulates Hp cell membrane permeability, disrupting metabolic equilibrium to impair survival and ultimately induce cell death. Beyond direct antibacterial effects, berberine exhibits immunomodulatory properties. Studies indicate it regulates inflammatory responses via the IL-4/STAT6 signaling pathway, suppressing inflammatory cytokine release to mitigate Hp-induced gastric mucosal damage and enhance host immunity [30,31]. Clinical studies further confirm that replacing bismuth compounds and/or antibiotics in quadruple therapy with berberine hydrochloride achieves comparable eradication rates to traditional quadruple regimens while exhibiting lower adverse reaction incidence [32-34]. Moreover, active components in Paeonia lactiflora extract — including paeoniflorin, benzoic acid, and methyl gallate — exhibit potent growth inhibition and bactericidal activity against amoxicillin-, metronidazole-, and tetracycline-resistant Hp strains in vitro. These components reduce Hp pathogenicity by inhibiting urease activity, disrupting cell membrane structure, and suppressing key metabolic pathways. This discovery offers a novel alternative therapeutic strategy for drug-resistant Hp infections [35].

3.2 Research on Traditional Chinese Medicine Formulas Against Hp

Traditional Chinese Medicine (TCM) classifies Hp as a "pathogenic factor." As stated in the Huangdi Neijing: "When righteous energy resides within, pathogenic factors cannot invade." Therefore, TCM treatment for Hp-related diseases centers on fortifying the body's defenses and expelling pathogens, emphasizing clearing heat, transforming dampness, strengthening the spleen, and harmonizing the stomach to improve the internal environment and enhance disease resistance. In treatment strategies, TCM predominantly employs syndrome differentiation and treatment. According to the "Second Chinese Consensus on Integrated Traditional and Western Medicine Treatment of Helicobacter pylori-Related 'Disease-Syndrome'," specific formulas are selected based on different syndromes. For example: - For spleen-stomach damp-heat syndrome, Lianpu Decoction is often used to clear heat, transform dampness, regulate qi, and harmonize the middle jiao. - For spleen-stomach deficiency (cold) syndrome, Xiangshaliujunzi Decoction is frequently employed to strengthen the spleen, tonify qi, harmonize the stomach, and settle the middle jiao. For mixed cold-heat patterns, Banxia Xiexin Tang may be employed to disperse with pungent herbs and descend with bitter herbs, harmonizing the stomach and eliminating fullness [36]. Additionally, modern research is frequently integrated clinically to apply individualized decoction treatments, enhancing Hp eradication rates while reducing antibiotic side effects. Huang Chaoqun [37] studied 70 patients with initial Hp eradication failure, randomly assigning them to treatment and control groups. The control group received a 14-day quadruple rescue regimen. The treatment group added the modified Lianpu Decoction (Coptis rhizome, Magnolia bark, Pinellia rhizome, Acorus rhizome, light fermented soybean, reed root, fried Gardenia fruit, fried Atractylodes rhizome, calcined oyster shell, licorice) for 14 days, followed by 14 days of the herbal decoction alone. Results indicated that adding the modified Lianpu Decoction increased Hp eradication rate by 4.34%, while enhancing the abundance of beneficial bacteria such as Bacteroidetes and Firmicutes, improving gut microbiota, and alleviating gastrointestinal discomfort symptoms. Gao Yan et al. [38] studied 83 patients with Hp-associated gastritis. After randomization, the control group received triple therapy, while the treatment group added Modified Xiang Sha Liu Jun Zi Tang (Codonopsis, Atractylodes, Poria, Glycyrrhiza, Citrus peel, Pinellia, Aquilaria, Amomum, Taraxacum, Coptis) with individualized modifications based on specific symptoms. After treatment, the Hp eradication rate in the treatment group reached 90. 48%, significantly higher than the 73.17% in the control group. This indicates that Modified Xiang Sha Liu Jun Zi Tang can effectively enhance Hp eradication rates, strengthen gastric mucosal barrier function, and alleviate gastritis symptoms. Yu Zhongshu et al. [39] found that adding Banxia Xiexin Tang (Ginger Pinellia, Dried Ginger, Scutellaria, Codonopsis, Coptis, Jujube) to triple therapy increased Hp eradication by 22.22% and reduced recurrence by 11.11%. This result further confirms that Banxia Xiexin Tang can alleviate gastric mucosal inflammation caused by Hp

infection, enhance gastrointestinal function, and reduce the risk of Hp recurrence. Zhao Nan et al. [40] studied 93 patients with drug-resistant Hp infection. After randomization, the control group received quadruple Western medication therapy, while the observation group added Detoxifying and H. pylori-eliminating Decoction (Poria cocos, Litchi seed, Atractylodes macrocephala, Acorus tatarinowii, Wormwood, Coptis, Scutellaria, Fried Licorice, Salvia, Angelica, Ligusticum, White Peony, Sanguisorba, and Herba Eupatorium). After excluding dropouts, the Hp eradication rate in the observation group reached 86.67%, exceeding the control group by 17.78%. The study indicates that Detoxifying Wu You Decoction not only enhances Hp eradication rates but also alleviates Hp infection-related gastrointestinal symptoms with good safety. Xu Minyi et al. [41] conducted a clinical observation comparing Hp eradication rates between standard quadruple therapy and quadruple therapy combined with Modified Liver-Soothing and Stomach-Harmonizing Decoction (Coptis, Yinchen, Forsythia, Paeonia alba, Glycyrrhiza, Hordenum, Fried Citrus peel, Prepared Pinellia, Taraxacum, Scutellaria). Results showed the combined TCM-Western medicine group had a 20% higher overall efficacy rate than the Western medicine-only group, demonstrating significant advantages in improving Hp-related gastritis symptoms and promoting gastric mucosal repair. Wang Jing et al. [42] studied 96 Hp-positive gastric ulcer patients, randomly assigned to a control group (quadruple therapy) and a treatment group (quadruple therapy combined with Qi Bei Xiao Yong Tang). Post-treatment analysis revealed a 22. 92% higher Hp eradication rate in the treatment group compared to the control group, indicating that Qi Bei Xiao Yong Tang significantly enhances Hp eradication rates. Mechanistic studies demonstrated that this formula repairs gastric mucosal structure and reduces the recurrence risk of Hp-associated gastric ulcers by inhibiting oxidative stress responses, downregulating NF-κB gene expression, and decreasing inflammatory factor secretion.

4. Discussion

In recent years, with increasing antibiotic resistance, integrated Chinese and Western medicine approaches for treating Hp infection have garnered widespread attention. Traditional Chinese medicine offers multi-targeted and multi-level advantages in Hp infection prevention and treatment. Regarding direct antibacterial effects, berberine inhibits Hp's N-acetyltransferase (NAT) activity, disrupting its energy metabolism and thereby limiting growth. Herbs such as Scutellaria baicalensis, Coptis chinensis, and Taraxacum officinale can disrupt Hp cell membranes, inhibit urease activity, and enhance Hp clearance rates. Regarding immunomodulation, saponins from Panax notoginseng and baicalin can reduce the release of inflammatory cytokines IL-8 and TNF-α, regulate the NF-κB signaling pathway, and repair gastric mucosal damage. Compound Chinese herbal formulas adhere to the principle of "strengthening the body's defenses while expelling pathogens." They not only focus on clearing heat, resolving dampness, and strengthening the spleen and stomach but also emphasize enhancing the body's inherent disease resistance. This approach aligns with modern medical Hp eradication strategies to some extent, offering a more comprehensive clinical treatment perspective. Compared to antibiotic monotherapy, TCM demonstrates advantages in Hp infection treatment, including fewer adverse reactions, superior antimicrobial efficacy, and better patient compliance, suggesting potential for developing novel anti-Hp drugs. Despite its positive role in Hp infection management, TCM currently faces limitations. TCM lacks large-scale, high-quality randomized controlled clinical trials for Hp eradication. Existing studies are predominantly small-sample observational research with insufficiently rigorous experimental design, undermining their credibility. Furthermore, the complex composition of TCM formulations and significant variations in herbal ingredients between batches compromise treatment consistency. Additionally, while certain herbal medicines demonstrate promising anti-Hp effects, their precise mechanisms of action remain unclear and require further investigation.

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