

Research Progress on Traditional Chinese Medicine Treatment Strategies for Gallstone Disease

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Abstract: *Gallstone disease is a common clinical digestive disorder with a steadily rising global incidence in recent years. Traditional Chinese medicine (TCM) offers unique advantages in preventing and treating gallstones. Based on the theory of "liver qi stagnation and gallbladder dysfunction," TCM demonstrates significant efficacy in alleviating clinical symptoms and reducing recurrence rates through syndrome differentiation and treatment. This paper systematically reviews the latest research advances in TCM treatment strategies for cholelithiasis, comprehensively elaborating on theoretical understanding, therapeutic approaches (internal and external treatments), and mechanisms of action. Studies indicate that TCM exerts a significant role in the prevention and treatment of cholelithiasis through multi-pathway, multi-level integrated regulation. Particularly, the promotion and application of integrated Chinese and Western medicine treatment models provide patients with superior diagnostic and therapeutic options. Future efforts should focus on deepening mechanism-of-action research, conducting high-quality clinical trials, and advancing the standardization and internationalization of TCM.*

Keywords: Gallstone disease, Traditional Chinese Medicine treatment, Impaired liver qi regulation, Impaired gallbladder qi descent.

1. Introduction

Gallstone disease refers to the formation of stones within the biliary tract (encompassing the gallbladder and bile ducts). Based on composition differences, stones can be classified into various types, including cholesterol stones, bilirubin stones, calcium salt stones, and mixed stones. The clinical symptoms of this condition are closely related to the location of the stones, whether they cause biliary obstruction, and the presence of secondary infection. Research data indicates that the prevalence of cholelithiasis in the adult population is approximately 10% to 15%, with a marked gender disparity: female patients number about 2.5 times more than males. The peak incidence age range is between 40 and 60 years old. In recent years, with the acceleration of societal aging and changes in dietary habits, its incidence rate has shown a continuous upward trend [1]. Common clinical manifestations include abdominal pain, chills and fever, jaundice, and nausea/vomiting. Gallstone disease is characterized by high recurrence rates, difficulty in stone dissolution, and obstructed stone passage. It not only impacts patients' quality of life but may also lead to severe complications such as suppurative cholangitis, biliary pancreatitis, biliary obstruction, or even gallbladder perforation. Modern medical treatment primarily relies on surgical intervention and medical lithotripsy. While laparoscopic cholecystectomy has become the standard treatment for symptomatic gallstones, postoperative complications and stone recurrence remain concerns. In recent years, traditional Chinese medicine (TCM) has demonstrated unique advantages in preventing and treating gallstones, particularly in symptom control, recurrence reduction, and quality of life improvement.

Ancient Chinese medical texts do not explicitly mention "gallstone disease," yet its symptoms are evident in discussions of "flank pain" and "jaundice." The core pathogenesis is closely linked to dysfunction of the liver and gallbladder. The Ling Shu: Ben Shu states: The liver is paired with the gallbladder; the gallbladder is the organ that stores

essence. It further explains that bile is "the surplus energy of the liver, discharged into the gallbladder, where it accumulates to form essence." This establishes the physiological foundation of the "mutual relationship between liver and gallbladder." Thus, the liver's function of free flow directly affects bile production and excretion. If the liver fails to regulate this flow, bile excretion becomes obstructed. Prolonged stagnation eventually leads to stone formation. From the perspective of the six fu organs' characteristics — "The function of the six fu organs lies in their unimpeded flow" — the vital energy of the gallbladder organ must remain unobstructed. Impaired middle jiao qi function due to dietary indiscretion, internal accumulation of damp-heat, or spleen-stomach deficiency (where earth obstructs wood) can all impede gallbladder qi flow. This leads to bile stagnation and eventual crystallization into stones [2]. The fundamental pathogenesis of cholelithiasis is "inadequate liver qi regulation and impaired gallbladder harmonization and descent." Thus, treatment must prioritize "regulating liver qi and resolving depression, promoting gallbladder function and expelling stones." Liver qi stagnation and bile stasis represent the critical pathological links in stone formation. Based on this theory, this article systematically reviews TCM strategies for treating cholelithiasis and their research progress, aiming to provide a reference for clinical practice and scientific research.

2. Pathogenesis in Traditional Chinese Medicine

Modern medicine holds that the etiology of cholelithiasis is highly complex, associated with factors such as advancing age, gender, and obesity. Traditional Chinese medicine posits that emotional imbalance, irregular dietary habits, and ascending disturbance by roundworms can all contribute to the development of gallstones, with dysfunction in the liver and gallbladder's regulatory functions being the fundamental pathogenesis. Numerous scholars have explored the etiology and pathogenesis of cholelithiasis. Dong Suqin et al [3].

emphasized that liver qi stagnation and liver-gallbladder damp-heat are primary causes. The former arises from emotional imbalance hindering bile drainage, while the latter often results from dietary indiscretion leading to accumulation of damp-heat, which is then cooked into stones. Jiang Aimin et al [4]. concurred, summarizing the fundamental pathogenesis as internal accumulation of damp-heat and qi stagnation, resulting in impaired descending function of the gallbladder. In summary, the core pathogenesis involves impaired liver qi regulation and gallbladder harmonizing descent, with disrupted spleen-stomach transformation and transportation serving as a crucial link.

3. Traditional Chinese Medicine Approaches to Gallstone Disease

3.1 Internal Treatment Method

1) Liver Qi Stagnation is a common syndrome pattern in traditional Chinese medicine, primarily characterized by pathological states resulting from impaired or obstructed liver qi circulation. Typical clinical features include distending pain in the chest and flanks that may radiate to the shoulders and back. Pain intensity fluctuates with emotional changes and is often accompanied by abdominal distension, belching, and frequent sighing. Some patients may experience low-grade fever without high fever, decreased appetite, and a bitter taste in the mouth. The tongue appears pale red with a thin white or thin yellow coating, and the pulse is typically string-like and tight or string-like and thin. In treatment, Professor Shao Ming advocates the Liver-Soothing and Qi-Regulating method, using Sini San as the foundational formula with modifications to treat Liver Qi Stagnation-Type Gallstone Disease [5]. Within the formula, stir-fried Bupleurum and Perilla stem soothe the liver and resolve depression, while stir-fried white peony root nourishes blood and softens the liver. Combined with qi-regulating herbs like Cyperus and Citrus aurantium, and supplemented with blood-activating and pain-relieving agents like Corydalis and Ligusticum, the Angelica sinensis nourishes blood and softens the liver. Combined with qi-regulating herbs like Cyperus rotundus and Citrus aurantium, it is supplemented with blood-activating and pain-relieving agents like Corydalis and Ligusticum. Jiang Peng's [6] controlled trial demonstrated that the modified Four Reversals and Three Golds Decoction group achieved a 90.9% efficacy rate, significantly outperforming the Bile Comfort Capsule control group (72.2%) with lower adverse reaction incidence. Han Kexin et al. [7] also achieved an 83.33% efficacy rate in their clinical study using Liver-Soothing and Gallbladder-Draining Decoction, demonstrating the formula's favorable therapeutic effects.

2) The liver and spleen mutually nourish each other's yin blood and regulate each other's qi mechanisms, exerting reciprocal influence. Liver qi stagnation or impaired liver qi dispersion is a key pathogenic mechanism leading to disharmony between the liver and spleen. When liver qi rebels and invades the stomach and spleen, it directly impairs the transporting and transforming functions of the spleen and stomach. If the patient already has spleen-stomach deficiency, this can more readily create a vicious cycle of wood overacting on earth and earth deficiency allowing wood to

overact, ultimately resulting in impaired bile dispersion. Impeded bile excretion accumulates in the biliary tract, eventually solidifying into stones over time. This pattern manifests clinically with dull or distending pain in the hypochondrium, often accompanied by chest tightness, abdominal distension, fatigue, loss of appetite, and loose stools. The tongue typically appears pale and swollen with a white, greasy or thin white coating, while the pulse is string-like and slippery or deep and fine. Yu Youming [8] adapted the Liver-Soothing and Spleen-Strengthening Stone-Dissolving Decoction to treat this condition, achieving a 75% overall response rate. Follow-up of cured patients showed no recurrence of stones. Ma Xianzhong [9] evaluated the efficacy of Liver-Soothing and Spleen-Strengthening Decoction for liver-qi stagnation with spleen deficiency gallstone syndrome, demonstrating significant clinical benefits. At weeks 4, 8, and 12 of treatment, the total effective rates for symptom and sign improvement in the treatment group reached 85.7%, 90.4%, and 95.2%, respectively. Additionally, the effective rates for stone expulsion and gallbladder volume reduction were 85.7% and 90.5%, respectively. All these indicators significantly outperformed the control group, with statistically significant differences between groups. Tan Rui [10] similarly employed the Liver-Soothing, Spleen-Strengthening, and Qi-Nourishing approach. The treatment group (n=40) received a formula containing chicken gizzard lining, white peony root, curcuma, and white atractylodes, while the control group received bear bile capsules combined with digestive enzyme capsules. Results confirmed significantly superior efficacy in the treatment group, with response rates of 90%, 92.5%, and 97.5% at weeks 2, 4, and 10, respectively, showing significant differences compared to the control group.

3) Exogenous damp-heat or irregular eating habits, such as excessive consumption of rich and greasy foods, disrupt the spleen and stomach's ability to transform and transport nutrients. This leads to the internal accumulation of dampness and turbidity, which over time transforms into heat. The accumulation of damp-heat in the liver and gallbladder obstructs bile secretion, causing prolonged stagnation that eventually forms gallstones. Clinical manifestations are characterized by distending pain in the right upper abdomen or epigastrium. The pain may present as persistent dull ache or paroxysmal colic, worsening after consuming greasy foods. It is often accompanied by alternating chills and fever, jaundice of the skin and sclera, abdominal distension with poor appetite, aversion to greasy foods, nausea, and vomiting. Additional symptoms include dark urine and sticky, incomplete bowel movements, indicative of internal damp-heat accumulation. Typical tongue manifestations include a red tongue body with a thick, greasy yellow coating, while pulse patterns are characterized by string-like and slippery or soft and rapid pulses. Adhering to the therapeutic principle of clearing heat and draining dampness, Xie Jingri [11] proposed treating this pattern with the Gallbladder Disease Formula No. 1. The formula comprises 15 g Bupleurum, 35 g Herba Lysimachiae, 30 g Lycopodium, 15 g Atractylodes, and 15 g Rheum. This treatment demonstrated remarkable efficacy with a high response rate of 90%. Professor Chen Diping emphasized that the core pathogenesis of cholelithiasis lies in damp-heat obstruction and impaired liver-gallbladder qi flow. Thus, clinical treatment should primarily focus on clearing

liver-gallbladder damp-heat, often employing the Artemisia and Scutellaria Decoction for Gallbladder Cleansing [12]. This formula employs *Artemisia annua*, *Scutellaria baicalensis*, and *Bambusa vulgaris* as principal herbs to clear stagnant fire from the gallbladder. It is supplemented with *Citrus aurantium* and *Erchen* Decoction to harmonize the stomach and resolve phlegm. *Bi Yu* Powder is added as an auxiliary to direct the ministerial fire downward and promote lower jiao drainage. *Poria cocos* serves as the messenger to expel damp-heat to the bladder. Corroborating this, Wang Shijun [13] conducted a randomized controlled trial involving 76 patients with liver-gallbladder damp-heat gallstone disease. Participants were equally divided into a treatment group (using the Gallbladder Stone-Expelling Formula) and a control group (using Dian Kang Capsules). Results demonstrated a high overall efficacy rate of 92.11% in the treatment group, showing significantly superior therapeutic effects compared to the control group.

4) Qi stagnation with blood stasis refers to a condition where liver qi stagnation and liver blood stasis coexist and mutually entangle to cause disease. In this pattern, stones are both pathological products and pathogenic factors that obstruct qi and blood circulation, leading to qi stagnation and recurrent formation of new stones. Characteristic manifestations include: - Stabbing pain in the hypochondrium that worsens with pressure, localized and often worse at night - Palpable masses may be present - Dull complexion - Women may experience irregular menstruation - Purple-dark tongue with ecchymoses or petechiae - Deep and uneven pulse or deep and wiry pulse Ding Zhangsen et al[14].applied the Gu Xia Pai Shi Zhu Yu Tang decoction based on the therapeutic principle of regulating qi and expelling stasis to treat qi stagnation and blood stasis pattern gallstone disease, achieving an overall efficacy rate of 95.11%. Hu Xuchun et al. [15] employed a large-scale clinical observation study using Sijin Stone-Expelling Decoction to treat gallstone disease with qi stagnation and blood stasis. The formula comprised Chinese herbs including moneywort, sea sandwort, chicken gizzard, oyster shell, frankincense, bone-setting herb, curcuma, plantain seed (wrapped), and licorice. After one treatment course, the overall efficacy rate reached 94.64%. Song Xiaodi et al. [16] treated 38 patients with modified Shixiao Powder. After three treatment courses, 35 cases were cured, 2 showed marked improvement, and 1 was ineffective, yielding an efficacy rate of 97%. Medicinal herbs such as Curcuma, Frankincense, Myrrh, Acorus, Curcuma, Manis, Pheretima, Pentaglottis, and Phragmites can promote blood circulation, resolve blood stasis, and disperse nodules, making them excellent remedies for treating this condition.

5) Liver Yin Deficiency Syndrome often results from congenital constitutional insufficiency or prolonged accumulation of pathogenic toxins damaging yin. It manifests as a pathological state characterized by deficiency of liver yin essence, inadequate nourishment of meridians, and disruption of qi dynamics. This pattern is commonly observed in patients with chronic or severe gallstone disease. Professor Zhu Peiting, a nationally renowned veteran TCM practitioner [17], specifically noted that this pattern represents a key syndrome type during the quiescent phase of gallstone disease. Its pathogenesis involves pathogenic turbidity depleting essence and blood, leading to persistent liver yin damage. Clinically,

patients present with yin deficiency manifestations such as dull pain in the hypochondrium, five-heart heat (palms, soles, and chest), dry eyes, and bitter taste in the mouth, accompanied by physical signs including emaciation, soreness in the waist and knees, a red tongue with little coating, and a fine, rapid pulse. Based on the therapeutic principle of nourishing and soothing the liver, Professor Zhu Peiting formulated the Liver-Nourishing and Gallbladder - Promoting Decoction. Within this formula, *Codonopsis pilosula* and *Astragalus membranaceus* boost qi and generate yin, while *Rehmannia glutinosa* and *Paeonia lactiflora* nourish the liver and kidneys. These are supplemented by *Codonopsis pilosula* and *Ophiopogon japonicus* to enhance yin nourishment. *Cyperus rotundus* and *Citrus medica* var. *hystric* regulate liver qi, while *Artemisia capillaris* and *Rheum palmatum* clear heat and promote gallbladder function. Finally, fermented malt and jujube harmonize the spleen and stomach. This formula addresses both the root and branch of the condition, demonstrating remarkable clinical efficacy.

6) Gallbladder Qi Stagnation with Phlegm Disturbance is a pathological state caused by internal disturbance of phlegm-heat and impaired gallbladder qi regulation, often closely associated with emotional imbalance. Prolonged emotional distress can lead to qi stagnation transforming into fire, where heat scorches body fluids to generate phlegm, ultimately resulting in mutual entanglement of phlegm and heat that disrupts the functions of the heart and gallbladder. Phlegm-heat obstructs qi movement, forming the gallbladder qi stagnation syndrome while also causing abnormal bile secretion, which may subsequently trigger gallstone disease. Typical manifestations include distending pain in the right hypochondrium, accompanied by insomnia with frequent dreams, dizziness and irritability, palpitations with bitter taste in the mouth, nausea, and vomiting. The tongue typically presents a pale red body with a slippery or greasy yellow coating, while the pulse is predominantly string-like and slippery. Professor Xu Ren'an [18] identified internal phlegm-dampness and phlegm-turbidity accumulation as the key pathogenesis, advocating a treatment principle of resolving phlegm, eliminating turbidity, promoting gallbladder function, and expelling stones, which demonstrated significant clinical efficacy. Wang Shaoming [19] applied Huo Pu Xia Ling Tang to treat this pattern. The formula combines *Poria* and *White Broad Bean* to strengthen the spleen and transform dampness, *Pinellia* to dry dampness and resolve phlegm, with *Agastache* and *Magnolia* to promote qi circulation and transform dampness. Supported by warming, transforming, and clearing agents, it achieved favorable outcomes. Liu Bencheng's [20] clinical study demonstrated that Wendan Decoction achieved a 75% cure rate in 52 patients with gallstone disease of the gallbladder depression and phlegm disturbance pattern, including 39 complete recoveries and 13 cases with symptom improvement.

3.2 External Treatment Methods

3.2.1 Acupuncture treatment

Primary Points: *Yanglingquan*, *Gallbladder Point*, *Qiu Xu*, *Gallbladder Shu*, *Zusanli*, *Qimen*, *Riyue*, *Zhigou*

Additional Points:

- Liver Qi Stagnation Pattern: Add Hegu, Taichong
- Blood Stasis Pattern: Add Diao Shu, Xuehai, Diji, Ashi Point
- Liver-Gallbladder Damp-Heat Pattern: Add Zhongwan, Sanyinjiao
- Liver Yin Deficiency Pattern: Add Gan Shu, Shen Shu

Treatment regimen: One session per day, with needles retained for 20–40 minutes. Each course consists of 7 days [21].

3.2.2 Auricular Therapy

The Yellow Emperor's Inner Canon states: "The ear is where the meridians converge." Moreover, the course of the Foot Shaoyang Gallbladder Meridian is closely related to the ear. Selecting auricular points such as Pancreas-Gallbladder-Liver and Shenmen for treatment can promote bile secretion and gallbladder contraction [22]. Based on different stages of cholelithiasis, auricular acupuncture employs differentiated protocols: 1) During remission, targeting prevention of acute attacks: Stimulate Liver, Gallbladder, Spleen, and Triple Energizer points once daily. 2) For patients post-minimally invasive gallbladder-preserving stone removal surgery, to prevent stone recurrence, the acupoint selection expands to seven points: Liver, Gallbladder, Bile Duct, Spleen, Stomach, Duodenum, and Triple Energizer. Press daily for the first three months, then switch to every other day. Each session involves pressing for 3–5 minutes half an hour after dinner, alternating between both ears. After completing 15 treatment cycles, pause for 5 days. The entire treatment course lasts for 2 years [23].

4. Recent Advances in Research on the Modern Mechanisms of Traditional Chinese Medicine in the Treatment of Gallstones

4.1 Regulate Bile Composition and Metabolism

Its mechanism of action lies in stimulating increased bile acid secretion, thereby reducing the saturation level of cholesterol in bile.

4.2 Improve Gallbladder and Sphincter of Oddi Function

By enhancing gallbladder contractility, thereby promoting bile emptying; relaxing or coordinating the movement of the sphincter of Oddi.

4.3 Anti-inflammatory, Analgesic, and Protective Effects

Inhibits the release of inflammatory mediators (such as TNF- α and IL-6), alleviating inflammation of the biliary mucosa; thereby relieving pain.

4.4 Dissolving and Expelling Stones

Promotes stone dissolution by altering the bile environment and increases bile flow to flush out small stones.

5. Conclusion and Outlook

Traditional Chinese Medicine (TCM) offers unique advantages and distinctive therapeutic effects in preventing and treating gallstones based on the theory of "liver failure to regulate and gallbladder failure to descend and harmonize." Through therapeutic methods such as soothing the liver and relieving depression, promoting bile flow, and expelling stones, TCM can regulate bile metabolism at multiple stages, improve gallbladder function, suppress inflammatory responses, and facilitate stone expulsion. TCM offers multidimensional advantages in gallstone management: First, its holistic regulatory mechanisms focus not only on the stone lesions but also systematically restore physiological balance across the liver, gallbladder, spleen, and stomach. Second, guided by the principle of syndrome differentiation and treatment, it enables personalized protocols tailored to distinct patterns, significantly enhancing therapeutic precision. On the preventive front, it effectively disrupts the pathological basis of stone formation by improving the body's microenvironment. Furthermore, its natural medicinal properties ensure minimal side effects and high safety during treatment, making it particularly suitable for long-term maintenance therapy.

To systematically reveal the scientific basis of TCM in preventing and treating cholelithiasis, it is recommended to integrate modern techniques such as molecular biology, network pharmacology, and metabolomics to thoroughly analyze its multi-target regulatory mechanisms. By conducting large-scale, multicenter randomized controlled clinical trials, a high-level evidence-based medicine system should be established. Concurrently, the distinctive TCM theory of preventing disease before it occurs should be fully leveraged, with a focus on strengthening research into early intervention strategies for cholelithiasis to effectively reduce disease incidence. With the advancement of modern TCM research and strengthened international collaboration, TCM will undoubtedly play an increasingly vital role in the prevention and treatment of gallstones, offering more effective and safer therapeutic options for patients worldwide.

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