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Pharmacological Effects and Clinical Applications of Shouhui Tongbian Capsules: A Systematic Review

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Abstract: ***Shouhui Tongbian Capsules (SHTB) is a commonly used Chinese patent medicine for treating functional constipation. Recent studies have shown that its effects go beyond relieving constipation, with potential benefits in improving heart failure, reducing obesity, repairing intestinal injury, and slowing atherosclerosis. This review systematically summarizes 25 studies published between 2020 and 2026, covering clinical trials, pharmacological mechanisms, gut microbiota, and chemical composition. The main topics include: (1) clinical efficacy and safety; (2) molecular pathways such as calcium homeostasis, TGF-β/BMP/Smad, and STAT3/c-Myc; (3) gut microbiota regulation as a core mechanism; (4) chemical composition and quality control; and (5) potential uses beyond constipation. Current evidence suggests that SHTB exerts multi-target synergistic effects by restoring gut microbiota balance, protecting the intestinal barrier, and reducing inflammation. Clinical data support its good safety profile with low adverse reaction rates. Future large-scale, multicenter randomized controlled trials are needed to confirm its value in new indications and to further clarify the relationship between its active components and therapeutic targets.***

Keywords: Shouhui Tongbian Capsules, Functional constipation, Gut microbiota, Pharmacological mechanism, Multi-target application.

1. Introduction

Traditional Chinese Medicine (TCM) has been an integral component of healthcare practices in East Asia for millennia, with its global acceptance progressively expanding over recent decades. Among the diverse array of TCM formulations, Shouhui Tongbian Capsules (SHTB) stands as a representative patented Chinese patent medicine, primarily indicated for the management of functional constipation [1, 2]. The formulation is composed of multiple medicinal herbs, including Polygonum multiflorum (Heshouwu), Aloe vera (Luhui), and Rheum palmatum (Dahuang), which act in synergy to exert laxative, anti-inflammatory, and metabolic regulatory effects.

Although SHTB remains predominantly employed for constipation in clinical settings, a growing body of evidence accumulated between 2020 and 2026 has unveiled its considerably broader therapeutic potential. Preclinical investigations have substantiated its efficacy in heart failure with preserved ejection fraction (HFpEF), obesity and associated metabolic disorders, chemotherapy-induced intestinal mucositis, as well as Helicobacter pylori infection. Mechanistic studies have further delineated multiple signaling pathways mediating these pharmacological effects, encompassing calcium homeostasis regulation, gut microbiota remodeling, and anti-inflammatory signaling cascade modulation.

In recent years, the disciplinary landscape of SHTB-related research has undergone substantial expansion, particularly since 2022, extending from analytical chemistry to encompass diverse domains of clinical medicine. Given the accelerated accumulation of knowledge in this field, a systematic synthesis of existing findings is urgently warranted. The present review systematically consolidates the SHTB literature published between 2020 and 2026, with a focus on five key dimensions: clinical evidence pertaining to established and emerging indications, molecular mechanisms of action, the central role of gut microbiota modulation, chemical composition and quality control, as well as prospective directions for future investigation.

2. Clinical Efficacy and Safety

2.1 Functional Constipation

Functional constipation remains the sole indication for SHTB with robust clinical evidence. A multicenter randomized controlled trial involving several hundred patients with functional constipation demonstrated that SHTB significantly improved spontaneous bowel movement frequency, stool consistency, and constipation-related quality of life, with consistent benefits observed across all age groups and constipation subtypes in subgroup analyses [3]. Regarding safety, a pharmacovigilance study encompassing 24, 000 clinical cases reported an adverse reaction rate of 2.16%, predominantly manifesting as mild gastrointestinal discomfort (abdominal distension, loose stools) and occasional allergic reactions, with no serious adverse events attributed to SHTB monotherapy. Collectively, these findings support a favorable risk-benefit profile of SHTB in the management of functional constipation.

2.2 Heart Failure with Preserved Ejection Fraction

Heart failure with preserved ejection fraction (HFpEF) represents a well-recognized therapeutic challenge in cardiovascular medicine, for which effective pharmacological interventions remain scarce. Previous investigations, utilizing both preclinical models and preliminary clinical observations, have pioneered the exploration of SHTB in HFpEF [4]. The

study revealed that SHTB preserves myocardial calcium homeostasis through modulation of ryanodine receptor 2 (RyR2) and sarcoplasmic/endoplasmic reticulum calcium ATPase 2a (SERCA2a), thereby improving cardiac function. These findings offer novel therapeutic avenues for the management of refractory HFpEF.

2.3 Metabolic Disorders

Obesity and constipation frequently coexist in the same patient population, underscoring the clinical significance of identifying agents that confer dual benefits in weight reduction and bowel regulation. A 2025 study reported that in high-fat diet-induced obese mice, SHTB significantly reduced body weight and adipose tissue mass while improving glucose tolerance [5]. Mechanistic investigations suggest that this effect is closely associated with activation of brown adipose tissue and browning of white adipose tissue, involving enhanced energy expenditure and reprogramming of lipid metabolism. These findings indicate that SHTB may confer dual therapeutic benefits in metabolically compromised populations; however, current evidence is confined to animal models, and further clinical translation remains to be evaluated.

In addition, SHTB has demonstrated promising potential in several adjunctive therapeutic contexts: (1) alleviating 5-fluorouracil-induced mucositis through restoration of intestinal barrier function [6]; (2) exhibiting anti-Helicobacter pylori activity, potentially serving as an adjunct to standard eradication therapy [7]; and (3) promoting regression of intestinal polyps in preclinical models. These diverse applications further underscore the multi-target characteristics of the SHTB formulation.

3. Molecular Mechanisms of Action

3.1 Calcium Homeostasis and Cardiovascular Protection

Calcium homeostasis imbalance constitutes a common pathophysiological basis for multiple diseases, involving intestinal absorption impairment and myocardial diastolic dysfunction, among other pathological processes. Recent studies have demonstrated that SHTB exerts calcium signaling regulatory effects in both intestinal and cardiac tissues. At the intestinal level, multiple experiments have confirmed that SHTB promotes transcellular calcium absorption by upregulating the expression of TRPV6 channels and calbindin-D9k in intestinal epithelial cells. At the cardiac level, it has been reported that SHTB improves cardiac function by restoring RyR2 phosphorylation status and SERCA2a activity, thereby inhibiting the diastolic calcium leak characteristic of HFpEF pathophysiology. These findings suggest that calcium homeostasis modulation may represent a common mechanism underlying the multi-organ protective effects of SHTB [8].

3.2 Intestinal Microenvironment Repair and Metabolic Regulation

Chronic inflammation is a significant driver of constipation-related intestinal mucosal injury and polyp formation. The anti-inflammatory effects of SHTB have been substantiated across multiple studies [9]. Existing evidence indicates that: (1) SHTB suppresses the STAT3/c-Myc signaling axis, thereby reducing colonic inflammatory cytokine production; and (2) SHTB promotes intestinal polyp regression through modulation of the TGF-β/BMP/Smad signaling pathway. Notably, these anti-inflammatory effects may be achieved through two distinct pathways: direct modulation of host inflammatory signaling cascades, and indirect regulation of the immune microenvironment via gut microbiota remodeling.

In synergy with its anti-inflammatory actions, SHTB also plays a significant role in maintaining intestinal barrier integrity. In both chemotherapy-induced mucositis models and constipation-associated barrier dysfunction models, SHTB upregulates the expression of tight junction proteins (occludin, claudin-1, ZO-1) and reduces intestinal permeability. Mechanistically, this effect involves activation of the Nrf2/ARE-mediated antioxidant defense pathway and inhibition of the TLR4/MyD88/NF-κB inflammatory cascade, which synergistically preserve intestinal barrier stability through “attenuating oxidative damage” and “blocking inflammatory signals,” respectively [10].

Beyond these local effects, SHTB also exerts systemic metabolic regulatory actions. Studies have indicated that SHTB enhances energy expenditure, improves insulin sensitivity, and modulates lipid metabolism, effects closely associated with AMPK signaling pathway activation and promotion of brown adipose tissue thermogenesis. Additionally, SHTB influences bile acid metabolism and enterohepatic circulation, contributing to cholesterol-lowering effects. Notably, these metabolic effects may be partially attributable to SHTB-mediated calcium homeostasis regulation (see Section 2.1), as intracellular calcium signaling itself constitutes a critical regulatory node in energy metabolism.

Collectively, SHTB orchestrates systematic intestinal microenvironment repair through three interconnected dimensions: anti-inflammatory action attenuates tissue damage, barrier restoration reinforces the physical defense, and metabolic regulation reinstates energy homeostasis. These three components act synergistically to constitute the local foundation of SHTB’s intestinal function-improving effects.

4. Gut Microbiota Regulation

4.1 Bidirectional Remodeling of Microbiota Structure

The gut microbiota represents a critical target through which SHTB exerts its therapeutic effects, as corroborated by multiple independent investigations employing 16S rDNA sequencing and metagenomic approaches [11–13]. The impact of SHTB on the intestinal microecology exhibits bidirectional regulatory characteristics: at the level of beneficial bacteria, the abundances of Lactobacillus, Bifidobacterium, and Akkermansia muciniphila are significantly increased; at the level of pro-inflammatory bacteria, the abundances of Escherichia–Shigella and certain Clostridium species are markedly reduced. Furthermore, SHTB restores microbial α-diversity in constipation-

associated dysbiosis models. Collectively, these findings indicate that SHTB not only promotes the colonization of beneficial bacteria but also suppresses the overgrowth of pro-inflammatory taxa, thereby remodeling the microbiota structure through the dual-directional strategy of "augmenting beneficial and diminishing harmful" microbes.

4.2 Validation of Microbiota-Dependent Effects

Whether the alterations in microbiota structure genuinely underlie the therapeutic efficacy of SHTB necessitates causal experimentation. Fecal microbiota transplantation (FMT) experiments have provided direct evidence in this regard: transplantation of SHTB-conditioned microbiota into recipient animals recapitulates key therapeutic benefits. This outcome establishes a causal relationship between SHTB-induced microbiota changes and its pharmacological effects, confirming that the therapeutic efficacy of SHTB is at least partially dependent on gut microbiota remodeling, rather than being merely a concomitant phenomenon following disease improvement.

4.3 Regulatory Networks Revealed by Multi-Omics Integration

To gain an in-depth understanding of the complex interactions among SHTB, the gut microbiota, and the host, multi-omics integration strategies have provided a systemic perspective. Previous studies have combined serum pharmacochemistry with 16S rDNA sequencing to successfully correlate the absorbed active constituents of SHTB with specific microbiota alterations. The same research group integrated microbiome, proteomic, and lipidomic data to construct a comprehensive molecular network of SHTB action [14]. These investigations revealed that the anthraquinone and stilbene glycoside constituents of SHTB are capable of modulating key microbial pathways, including short-chain fatty acid production and secondary bile acid metabolism—metabolites that serve as crucial mediators through which the microbiota influences host health.

4.4 Clinical Significance of Microbiota Modulation

The aforementioned microbiota findings possess clear clinical translational value. The capacity of SHTB to restore intestinal microecological balance provides a mechanistic explanation for its efficacy in constipation treatment and its emerging applications in metabolic and inflammatory diseases. Of particular interest, the polysaccharide and polyphenolic compounds contained in SHTB may exert prebiotic-like effects, selectively promoting the proliferation and colonization of beneficial bacteria. In conjunction with the anti-inflammatory and barrier-repairing actions described in Chapter 2, gut microbiota remodeling, inflammatory suppression, and intestinal barrier protection may form a mutually reinforcing positive feedback loop, collectively constituting the core biological foundation of SHTB's multi-target therapeutic effects.

5. Chemical Composition and Quality Control

5.1 Chemical Composition and Quality Control Markers

With the aid of modern analytical techniques, the chemical composition of SHTB has been systematically elucidated. An UPLC-MS/MS method has been established and validated for the simultaneous quantification of 12 major bioactive constituents in SHTB, including emodin, rhein, chrysophanol, physcion, aloin, and 2, 3, 5, 4'-tetrahydroxystilbene-2-O-β-D-glucopyranoside (TSG). This method demonstrates excellent linearity, high precision, and stable recovery rates, thereby providing reliable technical support for the quality control of SHTB.

Metabolomics-based approaches have further expanded the understanding of the chemical space of SHTB. researchers employed UPLC-MS/MS-based metabolomics to identify 47 prototype components and 89 metabolites in biological samples following SHTB administration, revealing that the pharmacological effects of SHTB originate from the synergistic actions of multiple compound classes, including anthraquinones, stilbenes, flavonoids, and phenolic acids [15].

On this basis, researchers have integrated chemical composition data with bioactivity data to screen for specific markers suitable for quality evaluation. Correlation analyses have demonstrated that emodin, rhein, and TSG exhibit significant correlations with the anti-inflammatory, antioxidant, and prebiotic-like activities of SHTB. These three compounds have been proposed as primary quality control markers for SHTB, providing quantitative criteria for the assessment of formulation quality uniformity [16].

5.2 Pharmacokinetic Characteristics

Pharmacokinetic studies have systematically elucidated the in vivo dynamic behavior of the major constituents of SHTB. Anthraquinone components undergo extensive phase II metabolism (glucuronidation and sulfation) after oral administration, with enterohepatic circulation contributing to prolonged systemic exposure. Notably, several constituents of SHTB exhibit low oral bioavailability but can be metabolized by gut microbiota into active metabolites. This finding resonates with the microbiota modulation mechanisms described in Chapter 3, further substantiating the indispensable mediating role of gut microbiota in the pharmacological effects of SHTB.

6. Discussion

6.1 Systematic Integration of Core Mechanisms

Multiple lines of evidence converge to position SHTB as a multi-target therapeutic agent whose actions extend far beyond its traditional laxative effects. Findings from different laboratories employing diverse experimental models collectively provide robust support for the therapeutic potential of SHTB in metabolic, cardiovascular, and inflammatory diseases.

Synthesizing the available evidence, the actions of SHTB can be categorized into three interconnected mechanistic layers: (1) direct modulation of host signaling pathways by absorbed constituents, encompassing calcium homeostasis maintenance, inflammatory signal suppression, and antioxidant defense activation; (2) gut microbiota remodeling, which amplifies

and diversifies therapeutic effects through microbial metabolites; and (3) restoration of intestinal barrier integrity, preventing the translocation of pro-inflammatory bacterial products. These three layers act synergistically to account for the broad therapeutic spectrum and favorable safety profile of SHTB.

6.2 Strengths and Limitations of Current Evidence

The methodological diversity of the existing literature constitutes a major strength, spanning molecular biology, multi-omics integration, and clinical research. Integrated approaches such as microbiome-proteomics-lipidomics and serum pharmacochemistry combined with 16S sequencing reflect methodological sophistication, while large-scale pharmacovigilance data provide robust safety evidence.

Nevertheless, several limitations warrant attention. At the evidence hierarchy level, most mechanistic studies remain preclinical (animal models or in vitro experiments), necessitating clinical validation for translation; emerging indications beyond constipation (HFpEF, obesity, mucositis) still lack human RCT data. At the methodological level, heterogeneity in SHTB batch compositions, study protocols, and outcome measures complicates cross-study comparisons; several studies also exhibit deficiencies in blinding, randomization, or sample size. Regarding safety, long-term safety data beyond 12 weeks of continuous use remain insufficiently characterized.

6.3 Research Gaps and Future Directions

Based on the aforementioned limitations, future research may be advanced along the following priority directions: large-scale, multicenter randomized controlled trials are needed to accumulate clinical evidence for emerging indications such as HFpEF and metabolic syndrome; pharmacokinetic-pharmacodynamic modeling should be employed to determine the optimal dosages for different indications; the specific active constituents responsible for microbiota modulation in SHTB require identification; the interaction risks of SHTB when co-administered with commonly used drugs such as statins and anticoagulants warrant evaluation; the structure-activity relationships of anthraquinone and stilbene glycoside compounds need to be elucidated; and biomarker-driven patient stratification strategies should be explored to promote personalized medication.

7. Conclusion

Shouhui Tongbian Capsules represent a representative example of a traditional Chinese medicine formulation expanding its therapeutic potential beyond its original indication. Research evidence accumulated over the past five years demonstrates that SHTB exerts therapeutic effects through multi-layered mechanisms, encompassing gut microbiota regulation, calcium homeostasis maintenance, inflammatory response suppression, and intestinal barrier protection.

At the clinical level, existing evidence supports the efficacy and favorable safety profile of SHTB in functional constipation. Concurrently, preclinical studies suggest its potential value in HFpEF, obesity, chemotherapy-induced mucositis, and Helicobacter pylori infection. Of particular note, the successful application of multi-omics technologies and integrated pharmacological strategies in SHTB research provides a transferable methodological paradigm for the modernization research of other traditional Chinese medicine formulations.

Looking forward, conducting high-quality randomized controlled trials to validate preclinical findings and further exploring the complex interactions among SHTB components, host signaling pathways, and gut microbiota will be critical directions for advancing this agent toward precision application. In summary, SHTB not only demonstrates the therapeutic value of modern traditional Chinese medicine formulations but also accumulates a valuable evidence base for the integration of traditional Chinese medicine into evidence-based medical practice.

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