Optimization and Quality Assessment of Baihu Decoction Granules Using Traditional Concepts and Modern Techniques

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Abstract. Baihu Decoction is a classical traditional Chinese medicine (TCM) formula widely used in the treatment of febrile and inflammatory conditions due to its significant heat-clearing and fluid-generating properties. This study systematically optimized the extraction and granule preparation process of Baihu Decoction by integrating traditional formulation theory with modern pharmaceutical technologies. A multi-step extraction and granulation protocol was developed, combining traditional decoction, concentration, and carboxymethyl chitosan flocculation with modern granulation techniques. Key bioactive constituents, especially from Anemarrhena asphodeloides, were qualitatively and quantitatively analyzed using Thin-Layer Chromatography (TLC) under Total Ion Chromatogram (TIC) conditions and High-Performance Ion Chromatography (HPIC), respectively. The results confirmed the stability and consistency of the granule formulation, demonstrating improved extract concentration and potential for standardized production. While the study effectively improves preparation efficiency and ingredient retention, it is limited by the lack of in vivo pharmacological and clinical efficacy evaluation. Future work should focus on pharmacodynamic studies, toxicity assessment, and industrial-scale process validation to support clinical application and promote the modernization and internationalization of traditional Chinese medicine.

Keywords: Baihu Decoction; Modernization of Traditional Chinese Medicine; Extraction Process Optimization; Chromatographic Analysis; Granule Formulation Technology.

1. Introduction

As a classic Chinese medicine prescription, Baihu Decoction plays an important role in the treatment of various febrile and inflammatory diseases due to its effects of clearing away heat and purging fire, relieving exterior symptoms and dissipating heat [1]. With the advancement of the modernization of traditional Chinese medicine, the traditional decoction method of Baihu Decoction has problems such as low extraction efficiency, easy loss of effective ingredients, and inconvenience in taking, which limits its promotion in modern clinical and industrial applications. Therefore, combining modern extraction technology and preparation technology, systematic research on the extraction and preparation process of Baihu Decoction has become an urgent need to improve its quality control and clinical application value.

In recent years, the research and development of modern preparations of traditional Chinese medicine has become an important direction for promoting the internationalization of traditional Chinese medicine [2]. Although there have been a lot of studies on the pharmacological effects of Baihu Decoction, there is a relative lack of systematic optimization research on its extraction process and particle preparation process. The traditional decoction process is affected by multiple factors such as time, temperature, and solvent, resulting in low and unstable extraction rate of effective ingredients, which is difficult to meet the standardization and quality consistency requirements of modern production. Therefore, this study adopts a combined approach of theoretical analysis and pharmacotechnical design, integrating traditional formulation theory with modern extraction and preparation technologies. By analyzing classical principles and applying contemporary techniques such as optimized decoction, clarification, and granulation, the research aims to enhance the efficacy, stability, and practicality of Baihu Decoction in modern clinical applications. In this study, the preparation process of Baihu Decoction granules will be systematically described, including material selection and detailed procedural steps. In addition, TIC and HPIC methods will be employed to

conduct qualitative identification and quantitative determination of key constituents such as Anemarrhenae Rhizoma, in order to ensure the quality and consistency of the final product.

2. Overview of the Composition and Pharmacological Effects of Baihu Decoction

2.1 Major Herbal Components and Active Constituents of Baihu Decoction

Baihu Decoction, a traditional Chinese medicine formula recorded in Zhang Zhongjing's Treatise on Cold Damage Diseases under the Yangming Disease section. The decoction contains gypsum ($CaSO_4 \cdot 2H_2O$), anemarrhena rhizome, honey-fried licorice root, and non-glutinous rice, each possessing unique medicinal properties that synergistically act on the body to clear heat, nourish yin, tonify qi, and generate fluids [3]. Among them, gypsum serves as the chief herb; it is pungent and sweet in taste, cold in nature, enters the lung and stomach meridians, clears heat from the exterior, promotes heat dispersion, and also dries dampness, promotes tissue regeneration, heals ulcers, and stops bleeding [4]. Anemarrhena rhizome acts as the minister herb; it is bitter and cold, contains flavonoids, saponins, and polysaccharides, nourishes yin and moistens dryness, assists gypsum in clearing heat from the lungs and stomach, and is commonly used to treat lung heat cough, asthma, and constipation. Honey-fried licorice root is the assistant herb; it contains glycyrrhizic acid, glycyrrhetinic acid, and liquiritin, harmonizes the formula and moderates its potency, tonifies qi and spleen, relieves pain, and generates fluids [3]. Combined with non-glutinous rice, it prevents the cold nature of gypsum from harming the spleen and stomach. Non-glutinous rice functions as the envoy herb; although it has no specific chemical formula, it tonifies qi and the stomach, nourishes yin and kidneys, enhances the body's resistance to diseases, and protects the gastrointestinal tract from irritation caused by other herbs [3]. Together, these four herbs produce effects that clear heat, nourish yin, tonify qi, and generate fluids.

2.2 Modern Pharmacological Advances in Baihu Decoction Research

Baihu decoction mainly has multiple pharmacological effects such as antipyretic, antiviral and immune enhancement. The core components, gypsum (Shi Gao) and Rhizoma Anemarrhenae (Zhi Mu), both exhibit significant antipyretic effects [5]. Gypsum induces a rapid but short-lived reduction in body temperature, whereas Rhizoma Anemarrhenae provides a slower onset of antipyresis with a more prolonged effect. The combination of the two yields a more effective antipyretic response through complementary mechanisms of action. Studies have found that calcium ions in Baihu decoction have a significant inhibitory effect on the central nervous system, especially the heat-producing center, and can regulate the sodium-calcium ratio in the brain, thereby promoting the disappearance of high fever. In terms of antiviral, Baihu decoction can significantly improve the survival rate of mice infected with epidemic encephalitis B virus and reduce the mortality rate [6]. In addition, Baihu Decoction can enhance the body's immune function, promote the phagocytosis and cell maturation of alveolar macrophages against pathogens such as Staphylococcus aureus, and enhance the nonspecific defense ability of the respiratory tract. This is of great significance for the treatment of acute infections such as lung infections. Baihu decoction combined with other Chinese herbal medicines can be used to treat diseases such as epidemic hepatitis B, rheumatic heart disease, and epidemic hemorrhagic fever.

Baihu Decoction, when combined with specific herbs, addresses distinct pathophysiological patterns: with ginseng, it clears heat while replenishing qi and promoting fluid production, suitable for qi-yin deficiency with excessive heat; with cinnamon twig, it facilitates heat clearance and meridian unblocking, applied in febrile malaria and rheumatic fever; with atractylodes, it targets damp-heat syndromes characterized by predominant heat, chest fullness, and greasy tongue coating, and is also effective for rheumatic manifestations.

3. Extraction Techniques and Optimization Approaches

3.1 Extraction Methods for Traditional Chinese Medicine

The preparation method of Baihu Decoction recorded in "Treatise on Febrile Diseases" adopts the traditional decoction method, that is, gypsum, Anemarrhena, licorice, polished rice and other medicinal materials are added with water in a certain proportion, and then heated and cooked, so that the effective ingredients in the medicinal materials are fully dissolved in the water. The specific operation is usually to soak the medicinal materials with an appropriate amount of water first, then decoct them with a slow or medium fire, and filter the soup after the polished rice is cooked. As the oldest and most commonly used extraction method of traditional Chinese medicine, the decoction method has the advantages of simple operation and low equipment requirements. It is suitable for a variety of medicinal materials of different properties. Whether it is rhizomes, leaves, flowers or fruits, the effective ingredients can be released through decoction. In addition, different medicinal ingredients will interact with each other during the decoction process, promoting the synergy of drug effects or producing new active substances. For example, the heat-clearing and detoxifying effect of gypsum in Baihu Decoction complements the yin-nourishing and moistening effects of Anemarrhena, thereby enhancing the overall heat-clearing and body fluid-producing effect [7].

However, the decoction method also has obvious limitations. First, the heat, decoction time and amount of water added must be strictly controlled. Any mistake in any link may lead to insufficient extraction or destruction of the effective ingredients. Secondly, traditional decoction usually takes a long time, often tens of minutes to several hours, which is not ideal for the efficient extraction required by modern production. Furthermore, some effective ingredients are sensitive to heat, and long-term high-temperature decoction may cause these ingredients to denature, degrade or volatilize, thereby reducing the stability of the efficacy and overall efficacy. In addition, the decoction process may also lead to the loss of some water-insoluble or volatile components, affecting the retention of all ingredients of the drug.

In summary, although the decoction method is a traditional and widely used extraction method, it has shortcomings in terms of efficiency, precision and ingredient protection, and urgently needs to be improved and optimized in combination with modern extraction technology.

Modern Chinese medicine extraction technologies are diverse. Traditional decoction methods are still widely used because of their simple operation and wide range of applications. At the same time, modern extraction technologies such as solvent extraction and nanotechnology extraction also play an important role in the research and development of Chinese medicine. Solvent extraction methods select suitable solvents (water, ethanol, methanol, etc.) to soak and heat the medicinal materials, so that the active ingredients are dissolved and separated. The operation is simple and the application range is wide. It can extract water-soluble and alcohol-soluble components more efficiently. It is suitable for continuous industrial production, with a short production cycle and can improve purity. However, this method has the risk of solvent residues, and the heating process may destroy heat-sensitive components, so safety protection needs to be strengthened. Nanotechnology significantly improves the solubility, bioavailability and stability of the active ingredients by preparing them into nanoparticles, while achieving targeted delivery and sustained release of drugs, enhancing therapeutic effects and reducing side effects [8]. But nanotechnology can also improve extraction purity and promote pharmacodynamics research, but its technology is complex, equipment requirements are high, production costs and safety risks are high, and industrial-scale applications still face challenges.

3.2 Optimization Strategies for Extraction Processes of Traditional Chinese Medicine

Optimization of traditional Chinese medicine extraction process is a key link to ensure the efficacy and quality stability of preparations. In order to maximize the extraction of active ingredients and reduce the loss of active substances, it is necessary to comprehensively consider the synergistic effect of multiple parameters. First, temperature control is crucial. Properly increasing the temperature helps to rupture the cell wall and release the active ingredients, thereby improving the extraction efficiency,

but too high a temperature may cause some heat-sensitive components (such as some flavonoids, polysaccharides, alkaloids, etc.) to degrade, affecting the stability of the efficacy. Secondly, the extraction time needs to be reasonably controlled. Too short a time may lead to insufficient extraction of the components, and too long a time may cause oxidation, hydrolysis or other degradation reactions of the components. The selection and ratio of solvents are also crucial, and should be based on the polarity, water solubility or alcohol solubility of the target components in the medicinal materials. For example, the gypsum component in Baihu Decoction is preferably extracted with water, while plant components such as Anemarrhena may contain some alcohol-soluble compounds, so the ratio of water to solvents such as ethanol needs to be adjusted according to demand.

4. Design of the Preparation Process for Baihu Decoction Granules

By comparing various extraction and separation methods of the effective ingredients of Baihu Decoction, this study chose to use the decoction method as the basis, combined with new technologies, such as increasing the concentration of the effective ingredients by condensation reflux and multiple decoctions, and increasing the purity of the effective ingredients by filtration and concentration with adsorbents to achieve the extraction of the effective ingredients of Baihu Decoction. The following takes the preparation of Baihu Decoction Granules as an example to show the process route.

4.1 Materials and Instruments

The formulation components employed in this study include Gypsum Fibrosum (raw gypsum), Anemarrhenae Rhizoma (Rhizome of Anemarrhena asphodeloides), Glycyrrhizae Radix Praeparata (prepared licorice), Oryzae Semen (non-glutinous rice), distilled water, 0.5% carboxymethyl chitosan (CMC) solution, 88% ethanol, and standard pharmaceutical excipients (designated as excipients A and B).

The experimental process was conducted using a decoction apparatus, centrifuge, vacuum filtration unit, high-speed pulverizer, mechanical stirrer, and granulation equipment.

4.2 Methodology and Extraction Procedure

The preparation of Baihu Decoction Granules followed a multi-step process designed to ensure effective extraction, purification, and granulation of active constituents. The procedure is as follows:

Step 1: Water Extraction. Precisely weighed quantities of Gypsum Fibrosum, Anemarrhenae Rhizoma, Glycyrrhizae Radix Praeparata, and Oryzae Semen were combined in accordance with traditional ratio proportions. The herbs were first immersed in eightfold volume of distilled water for 30 minutes. This was followed by three sequential decoctions, each lasting 30 minutes, using 8×, 6×, and 6× water volumes, respectively. The decoctions were filtered through medical-grade gauze and the combined filtrate was concentrated to a relative density of approximately 1.02 at 60°C.

Step 2: CMC Flocculation and Enrichment. The concentrated extract was treated with 0.5% carboxymethyl chitosan (CMC) solution, added at a volume ratio of 1:5 (extract to CMC solution). The mixture was stirred continuously for 20 minutes at 60°C, followed by static precipitation at room temperature for 12 hours. The resulting precipitate was centrifuged and filtered to obtain a clarified supernatant, which was further concentrated to a dense paste with a relative density of 1.10–1.12.

Step 3: Granulation. Excipients A were blended with the concentrated paste at a mass ratio of 1:0.3 (paste:total excipients). The mixture was subjected to vacuum drying and pulverized into a fine powder. Subsequently, excipients B were incorporated using 88% ethanol to form a soft mass. The wet mass was processed through wet granulation, followed by drying, uniform sizing, and final packaging to yield the finished Baihu Decoction Granules.

Note:

Excipients A and B were mixed in a mass ratio of 2:1.

The total excipient composition contained dextrin and soluble starch in a 3:2 ratio, ensuring optimal granule formation and stability.

All preparation steps conformed to the technical specifications outlined in the Chinese Pharmacopoeia.

5. Results and Analysis of Compound Characterization

The quality standard testing methods for Baihu Decoction granules are based on their characteristic components. These include qualitative identification of Anemarrhenae Rhizoma (Zhimu) and prepared licorice (Zhi Gancao) using Thin-Layer Chromatography coupled with Total Ion Chromatogram (TLC-TIC), as well as quantitative determination of their content through High-Performance Ion Chromatography (HPIC). The following description focuses on the identification of Anemarrhenae Rhizoma as an example [9].

Qualitative identification employed Thin-Layer Chromatography (TLC) under Total Ion Chromatogram (TIC) conditions. Granule samples were ultrasonically extracted with methanol, and the chromatographic profiles showed distinct spots corresponding to the reference standards mangiferin and neomangiferin, confirming the presence of Zhimu components. For quantitative analysis, High-Performance Ion Chromatography (HPIC) was used to determine the content of Timosaponin BII, a major saponin in Zhimu. Samples were extracted using 30% acetone under ultrasonic conditions. The TLC method with silica gel and vanillin-sulfuric acid staining was applied as a supplementary qualitative confirmation, showing consistent chromatographic bands with the Timosaponin BII standard.

These analyses verify that the Baihu Decoction Granules retain the principal bioactive compounds of Anemarrhenae Rhizoma. The combined TLC-TIC and HPIC approach offers a robust method for quality evaluation of classical Chinese medicine preparations in modern pharmaceutical development.

6. Conclusion

This study systematically investigated the preparation process and quality control of traditional Baihu Decoction granules. This paper combines the traditional decoction method with modern extraction and formulation technology to optimize the multi-step extraction process, which greatly improves the concentration and stability of the finished active ingredients. In addition, the study also used TLC and HPIC approach for qualitative and quantitative analysis, confirming the retention and consistency of the key active ingredients extracted from Anemarrhena asphodeloides. These results show that the granular dosage form developed by the institute can ensure quality, efficacy and reproducibility, providing a feasible method for the modernization and standardization of traditional Chinese medicine preparations.

However, this study also has limitations. Current research mainly focuses on the improvement of technology and process, while comprehensive pharmacological evaluation and clinical efficacy evaluation are still insufficient. Future research should focus on making up for these shortcomings through in vivo pharmacodynamic and toxicological studies to verify the efficacy and safety of the granules. In addition, the optimization of large-scale industrial production processes and stability studies under different storage conditions are also crucial parts.

References

[1] Khan, M. S. S., & Dashti, M. G. (2023). Optimizing extraction techniques for maximized bioactive compound yield in medicinal herbs. Australian Herbal Insight, 6(1), 1-10.

[2] Ping, Y., Li, Y., Lü, S., Sun, Y., Zhang, W., Wu, J., ... & Li, Y. (2020). A study of nanometre aggregates formation mechanism and antipyretic effect in Bai-Hu-Tang, an ancient Chinese herbal decoction. Biomedicine & pharmacotherapy, 124, 109826.

[3] Zhang, B., Cheng, T., & Liu, Q. (2009). Pharmacological effects and modern clinical research on Baihu Decoction. Chinese Patent Medicine, 31(8), 1272–1275.

[4] Wang, Y., Zhang, Z., Peng, H., Zeng, H., & Wu, X. (2025). Exploring the Scientific Connotation of Gypsum in Baihu Decoction Compatibility with Heat-clearing Effect Based on Phase Composition. Chinese medicine and natural products, 5(01), e35-e46.

[5] Shi, J. (2010). Study on the antipyretic effect of Baihu Decoction. Shanxi Medical Education, (1), 32–34.

[6] Tian, S., Xie, J., Cai, X., Shang, Q., Li, D., Han, L., et al. (2024). Advances and key issues in modern research on antiviral granules. Chinese Patent Medicine, 46(7), 2284–2292.

[7] Zhou, H. (2012). Analysis of the decoction method of Baihu Decoction: "Rice cooked, decoction completed." Modern Distance Education of Chinese Traditional Medicine, 10(3), 56.

[8] Pingyang. (2022). Preparation process of nanoscale Baihu Decoction (Patent No. CN202210931440.3).

[9] Li, F. X. (2018). Research on the preparation process and quality standards of Baihu Decoction granules (Master's thesis, Shandong University of Traditional Chinese Medicine).