Optimization of the Extraction Process and Establishment of the Preparation Method for Guichen Xuanfei Mixture

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Abstract [**Objectives**] To optimize the extraction and preparation processes of Guichen Xuanfei Mixture and establish a foundation for its industrial-scale production. [**Methods**] Using the dry paste rate as the evaluation index, a single-factor experiment was conducted to examine the effects of soaking time, volume of water added, and extraction duration. Subsequently, orthogonal experiments were employed to optimize the volume of water added, extraction duration, and extraction frequency. Following the determination of the optimal extraction process, process validation tests and pilot-scale production were performed. [**Results**] The optimal extraction process involved soaking the medicinal materials in water for 30 min, followed by two successive boiling steps. During the first extraction, 8 times the volume of water relative to the material was used, and 6 times the volume was applied during the second extraction. Each extraction was conducted for 1 h. The average dry paste rate obtained from the verification test was 24.25%, while the yield rates for the three batches of pilot-scale production were 93.6%, 93.9%, and 93.6%, respectively. [**Conclusions**] The optimized extraction and preparation method is rational, stable, and demonstrates excellent reproducibility, making it well-suited for the industrial-scale production of Guichen Xuanfei Mixture.

Key words Guichen Xuanfei Mixture, Extraction process, Preparation method

1 Introduction

Guichen Xuanfei Mixture comprises 13 traditional Chinese medicinal ingredients, including Ramulus Cinnamomi, Citri Reticulatae Pericarpium, Atractylodis Rhizoma, *etc.* This formulation is a modified and refined version based on the Guizhi Decoction and Erchen Decoction. It is purported to exert multiple therapeutic effects, such as releasing the exterior and dispersing the lung, dispelling cold and eliminating dampness, promoting circulation and cleansing the system, as well as regulating the middle energizer to assist in transportation and transformation[1]. The prescription is based on the *Traditional Chinese Medicine Treatment Plan for Pneumonia Caused by Novel Coronavirus Infection in the Guangxi Zhuang Autonomous Region* (*Trial Version* 2) and represents a clinical experience formula developed by the Guangxi International Zhuang Medical Hospital[2]. Guichen Xuanfei Mixture is a compound formulation derived from traditional Chinese medicine. Its chemical constituents primarily comprise terpenoids[3-4], glycosides[3], flavonoids[4-5], organic acids[3,5], and alkaloids[4-5]. This prescription involves a decoction; however, the resulting liquid is voluminous, possesses an unpleasant taste, and is inconvenient to administer and transport. Additionally, because it must be prepared fresh prior to use, it is susceptible to mold growth and fermentation if stored for extended periods, thereby complicating its preservation. The mixture is a commonly utilized enhanced dosage form of decoction. Owing to the concentration of the liquid medicine volume, it possesses a high concentration and requires a small dosage, which facilitates administration, portability, and storage, thereby increasing patient acceptance. Therefore, this study aimed to develop the Guichen Xuanfei prescription into a mixture to address the aforementioned limitations. To further ensure the quality control of this product and guarantee its clinical efficacy, the extraction process and preparation methods were specifically investigated.

2 Instruments and materials

2.1 Instruments The following instruments were utilized in the study: an electric thermostatic blast drying oven (DHG-9140A, Shanghai Qixin Scientific Instrument Co., Ltd.), a high-speed benchtop centrifuge (TGL-16G, Shanghai Anting Scientific Instrument Factory), an electronic balance (mL204T/02, Mettler Toledo Instruments Shanghai Co., Ltd.), an electric constant temperature water bath (WS-12, Shanghai Qixin Scientific Instrument Co., Ltd.), and an electric heating mantle (98-1-B, Tianjin Taisite Instrument Co., Ltd.).

2.2 Materials Thirteen medicinal materials, including Ramulus Cinnamomi, Atractylodis Rhizoma, Acori Tatarinowii Rhizoma, Pogostemonis Herba, Fructus Crataegi Cuneatae, Citri Reticulatae Pericarpium, Pinelliae Rhizoma Praeparatum, Poriae Sclerotium, Puerariae Lobatae Radix, Radix Scutellariae, Flos Lonicerae Japonicae, Zingiberis Rhizoma Recens, and Radix Glycyrrhizae, were procured from Guangxi Xianzhu Traditional Chinese Medicine Technology Co., Ltd. The aforementioned decoction pieces were authenticated by Mr. Zhong Wen, the chief

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traditional Chinese medicine pharmacist at Guangxi International Zhuang Medicine Hospital, and were found to comply with the *Quality Standards for Zhuang Medicine of the Guangxi Zhuang Autonomous Region* as well as the *Processing Specifications for Traditional Chinese Medicine Decoction Pieces of the Guangxi Zhuang Autonomous Region*. The reference substance, isofraxidin (batch No.: 110837-202009, purity ≥98%), was obtained from the National Institutes for Food and Drug Control of China. Methanol (chromatographic grade; Thermo Fisher Scientific Co., Ltd.; batch No.: 248502), acetonitrile (chromatographic grade; Thermo Fisher Scientific Co., Ltd.; No.: 250160), and phosphoric acid (analytical grade; Sinopharm Chemical Reagent Co., Ltd.; batch No.: T202110324) were used in this study.

3 Methods and results

3.1 Determination of dry paste rate After collecting the extracting solution, the total volume was recorded, and 25 mL was accurately transferred to an evaporating dish that had been dried to a constant weight. The sample was then dried in a water bath before being placed in an electric constant temperature drying oven set at 105 ℃ for 5 h. Upon removal, the dish was cooled in a desiccator for 30 min and then weighed precisely. The drying process continued at the same temperature for 1 h, followed by cooling and weighing. This procedure was repeated until the difference between two consecutive weight measurements was less than 5 mg. The dry paste rate was subsequently calculated using the following formula:

Dry paste rate (%) = (Dry paste mass × Total volume of medicinal liquid)/(Total mass of medicinal materials × Sampling volume) ×100% (1)

3.2 Water absorption rate test of medicinal materials To prevent variations in the volume of water added due to the absorption by medicinal materials, the initial volume of water added should be increased proportionally based on the water absorption rate. The prescribed daily quantity of medicinal materials was accurately weighed and immersed in water at a volume 10 times their weight (mL/g) for soaking. The soaking process was monitored at 1 h intervals until the materials were fully moistened throughout. Subsequently, any unabsorbed water was removed by filtration. Once no water droplets were observed, the mass of the wet medicinal materials was measured, and the water absorption rate was calculated using the following formula. The results are presented in Table 1.

Water absorption rate (%) = (Mass of wet medicinal materials − Mass of dry medicinal materials)/Mass of dry medicinal materials ×100% (2)

As shown in Table 1, the water absorption rate of the medicinal materials after soaking was 186.65%, which is approximately twice the original mass of the materials. Consequently, when adding water for the first time, the volume of water required should be increased to roughly twice the mass of the medicinal materials.

Table 1 Water absorption rates of medicinal materials

No.	Mass of dry medicinal materials//g	Mass of wet medicinal materials//g	Water absorption rate//%	Average water absorption rate//%
1	161.31	463.54	187.36	186.65
2	162.51	460.19	183.18	
3	162.08	469.06	189.40	

3.3 Single-factor experiments The formulation was prepared using the traditional water extraction method. During the decoction process, several factors, including the volume of water added, extraction duration, soaking time, extraction frequency, and particle size of the crushed medicinal materials, significantly influenced extraction efficiency. Considering practical production conditions, work extraction, and cost control, the volume of water added, extraction duration, and extraction frequency were identified as the primary parameters for evaluation. In accordance with the *Technical Requirements for the Research of TCM and Ethnic Medicine Preparations in Medical Institutions of Guangxi*, these three factors were selected for investigation through single-factor and orthogonal experimental designs. The dry paste rate served as the evaluation index to optimize the extraction process. The single-factor experiments primarily examined the effects of soaking time, volume of water added, and extraction duration on dry paste rate.

3.3.1 Soaking time. A total of 7 doses of the prescribed medicinal materials for a single day were accurately weighed and each was combined with 10 times its volume (mL/g) of water. The mixtures were soaked sequentially for 0, 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 h, respectively. Subsequently, the liquids were subjected to extraction by heating for 1 h, followed by filtration, and the volume of the filtrate was recorded. The dry paste rate under each condition was calculated according to the method described in Section **3.1**. The results are presented in Table 2.

Table 2 Effects of soaking time ($\bar{x}+s$, $n=3$)

No.	Soaking time//h	Dry paste rate//%
1	0	19.62 ± 1.54
2	0.5	22.85 ± 1.78
3	1.0	23.03 ± 2.61
4	1.5	24.07 ± 1.82
5	2.0	23.91 ± 1.84
6	2.5	23.83 ± 1.60
7	3.0	24.10 ± 2.05

According to the experimental results, soaking the herbal materials for 0.5 h was sufficient, as extending the soaking time beyond this period did not lead to a significant increase in the dry paste rate. Therefore, soaking time was not considered a primary factor in optimizing the extraction process. However, given the substantial quantity of raw materials used in actual production, a soaking time of 0.5 h prior to extraction was established to ensure complete water absorption by the medicinal materials.

3.3.2 Volume of water added. A total of 6 doses of the prescribed medicinal materials for a single day were prepared and

each was combined with 6, 8, 10, 12, 14, and 16 times its volume (mL/g) of water, respectively. Following a soaking period of 0.5 h, the mixtures were heated for extraction for 1 h, then filtered, and the volume of the filtrate was recorded. The dry paste rate under each condition was calculated according to the method described in Section **3.1**. The results are presented in Table 3.

Table 3 Effects of volume of water added ($\bar{x}+s$, $n=3$)

No.	Volume of water added//times	Dry paste rate//%
1	6	22.52 ± 1.63
2	8	22.93 ± 1.72
3	10	23.12 ± 2.30
4	12	23.17 ± 2.21
5	14	23.32 ± 1.86
6	16	22.99 ± 2.24

The experimental results demonstrated that variations in the volume of water added significantly influenced the dry paste rate. When the volume of water added reached 10 times, the increasing trend of the dry paste rate began to plateau. Considering the practical conditions of large-scale production, the volume of water added was selected as the key factor for optimizing the extraction process, with levels set at 6, 8, and 10 times, respectively.

3.3.3 Extraction duration. A total of 6 doses of the prescribed medicinal materials for a single day were prepared and each was combined with 10 times its volume (mL/g) of water. Following a soaking period of 0.5 h, the mixtures were subjected to heating and extraction for durations of 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 h, respectively. The resulting solutions were filtered, and the volume of each filtrate was recorded. The dry paste rate under each extraction condition was calculated according to the procedure in Section **3.1**. The corresponding results are presented in Table 4.

Table 4 Effects of extraction duration

No.	Extraction duration//h	Dry paste rate//%
1	0.5	17.10 ± 2.02
2	1.0	22.89 ± 1.85
3	1.5	23.46 ± 1.43
4	2.0	23.51 ± 1.02
5	2.5	23.53 ± 2.24
6	3.0	23.37 ± 2.05

Experimental data indicated that extending the extraction duration had a notably significant effect on dry paste rate. When the extraction duration reached 1.5 h, the rate of increase in the dry paste rate began to decelerate. Considering the practical conditions of large-scale production, the extraction duration was selected as a key factor for optimizing the extraction process, with levels set at 0.5, 1.0, and 1.5 h, respectively.

3.4 Factor level design Based on single-factor experiments, as well as considerations of production conditions and the properties of the extract, the primary factors influencing the extraction process were identified as the volume of water added, extraction duration, extraction frequency, and soaking time. Taking all factors into account, three variables, namely, the volume of water added (A), extraction duration (B), and extraction frequency (C), were selected as the experimental factors for the orthogonal design. Using the dry paste rate as the evaluation index, the extraction process of Guichen Xuanfei Mixture was optimized employing the $L_9(3^4)$ orthogonal test. The factor level settings are presented in Table 5.

Table 5 Orthogonal test factor levels for the extraction process of Guichen Xuanfei Mixture

Level	Factor		
	Volume of water added (A)//times	Extraction duration (B)//h	Extraction frequency (C)//times
1	6	0.5	1
2	8	1	2
3	10	1.5	3

3.5 Orthogonal design The arrangements and results of the orthogonal experiments are presented in Table 6, while the analysis of variance is detailed in Table 7.

Table 6 Arrangements and results of the orthogonal experiments

Level		Volume of water added (A)	Extraction duration (B)	Extraction frequency (C)	Blank control (D)	Dry paste rate//%
1		1	1	1	1	16.82
2		1	2	2	2	22.53
3		1	3	3	3	24.29
4		2	1	2	3	23.27
5		2	2	3	1	24.60
6		2	3	1	2	20.17
7		3	1	3	2	24.15
8		3	2	1	3	19.84
9		3	3	2	1	23.92
Dry paste rate	K_1	21.213	21.413	18.943	21.780	
	K_2	22.680	22.323	23.240	22.283	
	K_3	22.637	22.793	24.347	22.467	
	R	1.467	1.380	5.404	0.687	

Table 7 Analysis of variance for dry paste rate

Source of variance	Sum of squared deviations	Degree of freedom	Variance	F	P
Volume of water added (A)	4.179	2	2.089 5	5.513	>0.05
Extraction duration (B)	2.953	2	1.476 5	3.896	>0.05
Extraction frequency (C)	48.882	2	24.441 0	64.488	<0.05
Error (D)	0.760	2	0.380 0		

The analysis of variance indicated that the effects of the volume of water added (A) and the extraction duration (B) on the extraction process were not statistically significant ($P > 0.05$), whereas the extraction frequency (C) exhibited a significant effect. The relative influence of each factor on the extraction outcome was ranked as follows: C > A > B, with extraction frequency having the greatest impact, followed by the volume of water added, and extraction duration exerting the least influence. Regarding the levels within each factor, level A_2 was optimal among factor A ($A_2 > A_3 > A_1$), level B_3 was optimal among factor B ($B_3 > B_2 > B_1$), and level C_3 was optimal among factor C ($C_3 > C_2 > C_1$). Based on this analysis, the preliminary determination of the optimal extraction process combination was $A_2B_3C_3$.

Considering both the economic cost and practical feasibility of large-scale production, and with reference to the traditional decoction method, the extraction process was ultimately established as $A_2B_2C_2$. Specifically, each medicinal material was weighed according to the prescribed amount, soaked in water for 30 min, and then subjected to two extraction cycles. In the first cycle, 8 times the volume of water was added and the mixture was extracted for 1 h; in the second cycle, 6 times the volume of water was added and extraction was performed for 1 h.

3.6 Verification of extraction process Verification tests were conducted following the aforementioned preferred extraction process. Each medicinal material was weighed according to the specified amount, combined with water, and soaked for 30 min. Initially, water was added at 8 times the volume of the material, followed by an addition of 6 times the volume for the second extraction. Each extraction was performed for 1 h, and the two decoctions were subsequently combined. The dry paste rate was determined through triplicate parallel operations. The results are presented in Table 8.

Table 8 Verification test results of the extraction process of Guichen Xuanfei Mixture %

No.	Dry paste rate	Average dry paste rate
1	24.25	24.25
2	24.39	
3	24.10	

The verification test results demonstrated that the average dry paste rate of the mixture prepared using the optimized process was 24.25%, with consistent outcomes, indicating that this process is both reasonable and feasible.

3.7 Three batches of pilot-scale production Based on process research aimed at optimizing the operational conditions, three batches of pilot production were conducted at a scale 280 times greater than the standard formulation volume. The results of these trial productions are presented in Table 9.

Table 9 Pilot production results of three batches of Guichen Xuanfei Mixture

Batch No.	Mass of medicinal materials//kg	Mass of auxiliary materials//g	Total volume of concentrated liquid//kg	Relative density of concentrated liquid	Total volume of supernatant//kg	Theoretical yield//bottle	Actual yield//bottle	Yield rate//%
230501	45.08	136	47.55	1.06	29.58	280	262	93.6
230502	45.08	136	46.40	1.08	29.12	280	263	93.9
230503	45.08	136	46.41	1.08	29.27	280	262	93.6

The results of the pilot production demonstrated that the yield of all three batches of pilot production samples exceeded 90%, and the identification and inspection criteria were satisfactorily met. The production process was generally stable, indicating that the aforementioned preparation process is both reasonable and feasible, and largely fulfills the requirements for large-scale production.

4 Conclusions

The preparation process of Guichen Xuanfei Mixture was as follows: the standard prescribed amounts of medicinal materials were added with water and soaked for 30 min before undergoing two rounds of boiling. During the first extraction, 8 times the volume of water relative to the material was used, and 6 times the volume was applied during the second extraction. Each extraction was conducted for 1 h. The resulting decoctions were combined, filtered, and the filtrate was concentrated to a liquid with a relative density of 1.05 – 1.15 at 60 ℃. The concentrate was then stored in a cool environment and allowed to stand overnight. Subsequently, the supernatant was collected and filtered. Stevia (1 g) and sodium benzoate (3 g) were added, followed by the addition of purified water to reach a final volume of 1 000 mL. The mixture was stirred thoroughly, filled, and thus the final product was obtained. These findings indicate that the Guichen Xuanfei Mixture prepared according to this process exhibits stable formulation quality.

References

[1] QING B, WEI JC, LAN BQ, *et al*. Pharmacodynamic experimental research on antipyretic, analgesic, anti-inflammatory, antitussive and expectorant effects of Guichen Xuanfei Mixture[J]. Chinese Journal of Ethnomedicine and Ethnopharmacy, 2025, 34(7): 44 – 50. (in Chinese).

[2] QIU MY, QING B, ZHONG W, *et al*. Advances in research of epidemic lung preventive mixture[J]. Medicinal Plant, 2023, 14(4): 106 – 108.

[3] LI X, ZHAO JH, WU WX, *et al*. Research progress on chemical constituents and pharmacological effects of Ramulus Cinnamomi[J]. Acta Chinese Medicine and Pharmacology, 2023, 51(5): 111 – 114. (in Chinese).

[4] HUANG XY, LI YX, DONG H, *et al*. Analysis of chemical components of Citri Reticulatae Pericarpium based on UPLC-Q-TOF-MS[J]. China Condiment, 2024, 49(4): 166 – 172. (in Chinese).

[5] MEI TT, YAN J, CHEN J. Overview of active ingredients and pharmacological effects of *Acorus tatarinowii*[J]. Information on Traditional Chinese Medicine, 2022, 39(4): 77 – 80, 89. (in Chinese).