

RESEARCH

Open Access



Optimization of the extraction process for Shenshou Taiyi powder based on Box-Behnken experimental design, standard relation, and FAHP-CRITIC methods

Mengcheng Jiang¹, Zhidong Qiu¹, Yuanyuan Diao¹, Yuwen Shi¹, Weipeng Liu¹, Na Li¹ and Ailing Jia^{1*}

Abstract

Background Ancient classic prescription play a crucial role in the preservation and advancement of traditional Chinese medicine (TCM) theories. They represent a significant milestone in the ongoing development and transmission of TCM knowledge and practices and are considered one of the breakthroughs in the development of TCM inheritance. In the process of developing ancient classic prescriptions, many problems may still arise in ensuring quality consistency between traditional methods and modern production processes, among which the extraction process poses major challenges. This paper introduces a practical approach extracting an ancient classic prescription using a modern extraction process. The technique is demonstrated through the study of the extraction process of Shenshou Taiyi powder (STP).

Methods This study focuses on optimising the STP extraction process to ensure consistency in the quality of the product obtained through ancient and modern processes using the standard relation and fuzzy analytic hierarchical process (FAHP) and criteria importance through intercriteria correlation (CRITIC) method integrated weights combined with the Box-Behnken response surface test. Using the contents of rosmarinic acid, isoimperatorin, puerarin, as well as the extract yield and fingerprint similarity as evaluation indexes of STP, the Box-Behnken response surface method was employed to examine the varying extraction parameters, including water addition ratio, extraction duration, and number of extractions. The weighted coefficients for each parameter were calculated by combining the benchmark correlation and FAHP-CRITIC method, deriving a comprehensive score.

Results The optimal extraction process for STP consisted of a two extractions, each using at a tenfold quantity of water, performed for one hour. Process verification across three separate batches yielded a comprehensive score of 94.7, with a relative standard deviation of 0.76%.

Conclusions The application of the Box-Behnken response surface method combined with standard relation and FAHP-CRITIC approach proved to be stable and feasible for optimising the extraction process of STP.

*Correspondence:
Ailing Jia
cczyjal@163.com

Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

Keywords Ancient formulas, Content determination, Optimization of process, Response surface, Fuzzy analytic hierarchy process, CRITIC method

Background

Shenshou Taiyi powder (STP), was first recorded in 'Selected Prescriptions Handed Down for Generations of Physicians' by Wang Qiu in the Song Dynasty and consists of eleven herbs, including dried leaves of *Perilla frutescens* (L.) Britt. (Zisuye in Chinese), dried root of *Angelica dahurica*. (Baizhi in Chinese), dried root of *Pueraria lobata* (Willd.) Ohwi. (Gegen in Chinese), dried roots of *Crepis foetida* L. (Shengma in Chinese), dried root of *Ligusticum chuanxiong* Hort. (Chuanxiong in Chinese), dried root of *Cyperus rotundus* L. (Xiangfu in Chinese), dried root of *Paeonia lactiflora* Pall. (Baishao in Chinese), dried peel of ripe *Citrus reticulata* Blanco. (Chenpi in Chinese), pericarp of unripe fruit of *Citrus reticulata* Blanco. (Qingpi in Chinese), dried root of *Glycyrrhiza uralensis* Fisch. (Gancao in Chinese) and fresh root of *Zingiber officinale* Rosc. (Shengjiang in Chinese) [1].

In the process of developing ancient formulas, it is necessary to consult the ancient prescription books, medical books, and other records as a basis for modern formulas, so as to respect the ancient, and at the same time, retain consistency between ancient and modern formulations, the current production methods, and the application of the actual production process. This ensures the development of processes that integrate the salient aspects of both ancient knowledge and modern techniques [2]. At present, orthogonal experimental design, uniform design experimentation, Box-Behnken response surface methodology, and other methods are commonly used in the modernisation of traditional Chinese medicine extraction processes. The evaluation criterion is typically the maximum extraction efficiency of the components of traditional Chinese medicine; however, modern extraction processes do not always meet the requirement of quality consistency between ancient and modern approaches.

Here, we thus started from the concept of quality by design (QbD) [3] to with the objective of ensuring consistency of product quality between ancient and modern samples. We calculated the standard relation (SR) of different index parameters and determined the weighting coefficients of different evaluation indexes through the subjective-objective combination of fuzzy analytic hierarchy process (FAHP) and criteria importance through intercriteria correlation (CRITIC) method to carry out comprehensive scoring. Then, the modern extraction process parameters were screened to ensure quality consistency of the samples optimised by the modern process and the reference samples prepared through the ancient

extraction process and to lay a foundation for the subsequent development and application of STP.

Methods

Instruments

Five-decimal scales (TG328A, Shanghai Precision Scientific Instrument Co., Shanghai, China); Universal pulveriser (BJ-150, Zhejiang Deqing Baijie Electric Appliance Co., Zhejiang, China); Ultrasonic cleaner (KQ-500B, Kunshan Ultrasonic Instrument Co., Shanghai, China); Rotary Evaporator (RE-52, Shanghai Yarong Biochemistry Instrument Factory, Shanghai, China); Shimadzu High Performance Liquid Chromatograph (LC-15 C, Shimadzu, Kyoto, Japan); Lyophiliser (Epsilon 2–4 LSC plus, Martin Christ Gefriertrocknungsanlagen GmbH, Osterode am Harz, Germany).

Reagents

Rosmarinic acid, isoimperatorin, and puerarin reference standard substances were provided by Shanghai Yuanye Bio-Technology Co. (Batch No.: Y06A9K67402, M19GB148925, S02M9B54875, Shanghai, China); chromatography-grade acetonitrile and methanol were purchased from Thermo Fisher Scientific (Shanghai, China) Co., Ltd; chromatography-grade phosphoric acid was purchased from Tianjin Guangfu Fine Chemical Research Institute (Tianjin, China); analytical-grade anhydrous ethanol and anhydrous methanol were acquired from Guangdong Guanghua Sci-Tech Co., Ltd (Shantou, China); deionised water was used.

Herbs

Zisuye (Batch No.: 20210221-01), Baizhi (Batch No.: 20210508-01), Gegen (Batch No.: 20,210,618), Shengma (Batch No.: 20,210,406), Chuanxiong (Batch No.: 20210508-01), Xiangfu (Batch No.: 20,210,423), Baishao (Batch No.: 202,011,218), Chenpi (Batch No.: 20,210,103), Qingpi (Batch No.: 20,180,911), Gancao (Batch No.: 20,210,121) and Shengjiang (Batch No.: 20180714-04) were provided by Jilin North Medicine Herb Processing Co., Jilin, China.

Preparation of STP reference samples

The preparation process of STP reference samples was determined by analysing relevant literature combined with the prescription of the ancient original records. The preparation process was as follows: The herbs were crushed into coarse powder, after which 8.673 g of each herb was weighed and added to 3150 mL water and 21 g Shengjiang (21 slices; each slice weighed approximately

1 g), and the mixture was decocted to 2520 mL. The decoction was filtered through a 200-mesh double-layer nylon filter cloth, and the aqueous decoction was prepared for the STP reference samples. It was pre-frozen at -20°C for 12 h and then placed in a freeze dryer at -80°C for 30 min and freeze-dried for 72 h to obtain lyophilised STP powder as reference samples.

Determination of fingerprints of Chinese materia medica

Chromatographic Conditions. Chromatographic column: Agilent ZORBAX Eclipse Plus C18 (4.6 mm \times 250 mm, 5 μm). Mobile phase: acetonitrile (B)–0.1% phosphoric acid solution (A). Gradient elution for 0 to 15 min: 10% B; for 15 to 30 min: 10–15% B; for 30 to 58 min: 15–21% B; for 58 to 70 min: 21–25% B; for 70 to 80 min: 25–40% B; for 80 to 100 min: 40–55% B; for 100 to 105 min: 55–10% B; for 105 to 120 min: 10% B. Flow rate: 1.0 mL $\cdot\text{min}^{-1}$. Measurement wavelength: 270 nm. Column temperature: 30°C . Injection volume: 10 μL .

Preparation of test solution

A sample of 1 g of STP lyophilised powder was weighed, and 25 mL of 75% methanol was added. The mixture was extracted by ultrasonication for 30 min, cooled, and restored to its original volume using 75% methanol. The solution was then filtered through a 0.22 μm microporous filter membrane, and the filtrate obtained was used as test solution.

Preparation of reference standards solution

Appropriate amounts of rosmarinic acid, isoimperatorin, and puerarin reference standard substances were weighed accurately, and methanol was added to produce reference standard solutions at concentrations of 9.92, 3.96, and 47.2 $\mu\text{g}/\text{mL}$, respectively.

Determination of the content of indicator components

Determination of Rosmarinic Acid Content. A sample of 1 g of STP lyophilised powder was weighed and added to 25 mL 50% ethanol. Ultrasonic extraction was performed for 30 min, after which the mixture was cooled and restored to the original volume using 50% ethanol. The solution was then filtered through a 0.22 μm microporous filter membrane, and the obtained filtrate was the used as the test solution. Chromatographic column: Agilent ZORBAX Eclipse Plus C18 (4.6 mm \times 250 mm, 5 μm). Mobile phase: acetonitrile (B) – 0.1% phosphoric acid solution (A). Isocratic elution for 0 to 120 min: 15% B. Flow rate: 1.0 mL/min. Measurement wavelength: 330 nm. Column temperature: 30°C . Injection volume: 10 μL .

Determination of Isoimperatorin Content A sample of 2 g of lyophilised STP powder was weighed and added to 25 mL anhydrous methanol. Ultrasonic extraction

was performed for 30 min, after which the mixture was cooled and restored to the original volume using anhydrous methanol. The solution was then filtered through a 0.22 μm microporous filter membrane, and the obtained filtrate was used as the test solution. Chromatographic column: Agilent ZORBAX Eclipse Plus C18 (4.6 mm \times 250 mm, 5 μm). Mobile phase: acetonitrile (B) – water (A). Isocratic elution for 0 to 65 min: 42% B. Flow rate: 1.0 mL/min. Measurement wavelength: 300 nm. Column temperature: 30°C . Injection volume: 10 μL .

Determination of Puerarin Content. A sample of 0.1 g of lyophilised STP powder was weighed and added to 50 mL 70% ethanol. Ultrasonic extraction was performed for 30 min, after which the mixture was cooled and restored to the original volume using 70% ethanol. The solution was then filtered through a 0.22 μm microporous filter membrane, and the obtained filtrate was used as the test solution. Chromatographic column: Agilent ZORBAX Eclipse Plus C18 (4.6 mm \times 250 mm, 5 μm). Mobile phase: methanol (B)–water (A). Isocratic elution for 0 to 45 min: 21% B. Flow rate: 1.0 mL/min. Measurement wavelength: 271 nm. Column temperature: 30°C . Injection volume: 10 μL .

Single-factor investigation experiment

Effect of Extraction Time. The prescribed amount of STP herbs were weighed, and a fixed volume of water eight times that of the sample weight was added. Extractions were performed twice for either 0.5, 1, 1.5, or 2 h. The content of rosmarinic acid, isoimperatorin, puerarin, as well as the extract yield were measured to determine the effects of extraction time.

Effect of Water Addition The prescribed amount of STP herbs was weighed. The extraction time was fixed at 1 h, and extraction was performed twice. Either 6, 8, 10, or 12 times the volume of water was added, and the rosmarinic acid, isoimperatorin, puerarin and extract yield was determined to examine the effects of water volume used in the extraction process.

Box-Behnken experimental design

Based on the results of the single-factor investigation experiment, the extraction durations and water volumes resulting in the highest and lowest yields were determined, as well as the high (+1) and low (-1) levels of the number of extractions according to the actual production needs and experience, and a centre point (0) level was set. A Box-Behnken experimental design was carried out, and the prescribed amount of each herb was weighed for the experiments. The rosmarinic acid (Y_1), isoimperatorin (Y_2) and puerarin (Y_3) contents as well as the extract yield (Y_4) were determined. The test solutions of reference sample (S1) of STP and the test solutions of 17 response surface experiments (S2 through S18) were

prepared according to the method under “Preparation of Test Solution” and were determined according to the method under “Chromatographic Conditions”. The reference sample (S1) was used as the reference fingerprint.

Results

Analytical method validation

The test solution was prepared, and negative test solutions without either Zisuye, Baizhi, or Gegen were prepared. The content was determined according to the

content determination method, and the results are shown in Fig. 1. According to the guideline for the validation of analytical methods of the 2020 edition of the *Chinese Pharmacopoeia* (Part IV 9101) [4], linear relation, precision, reproducibility, stability, and sample recovery were examined, and the results are shown in Table 1. The method exhibited good specificity, and all examined indexes were in accordance with the requirements.

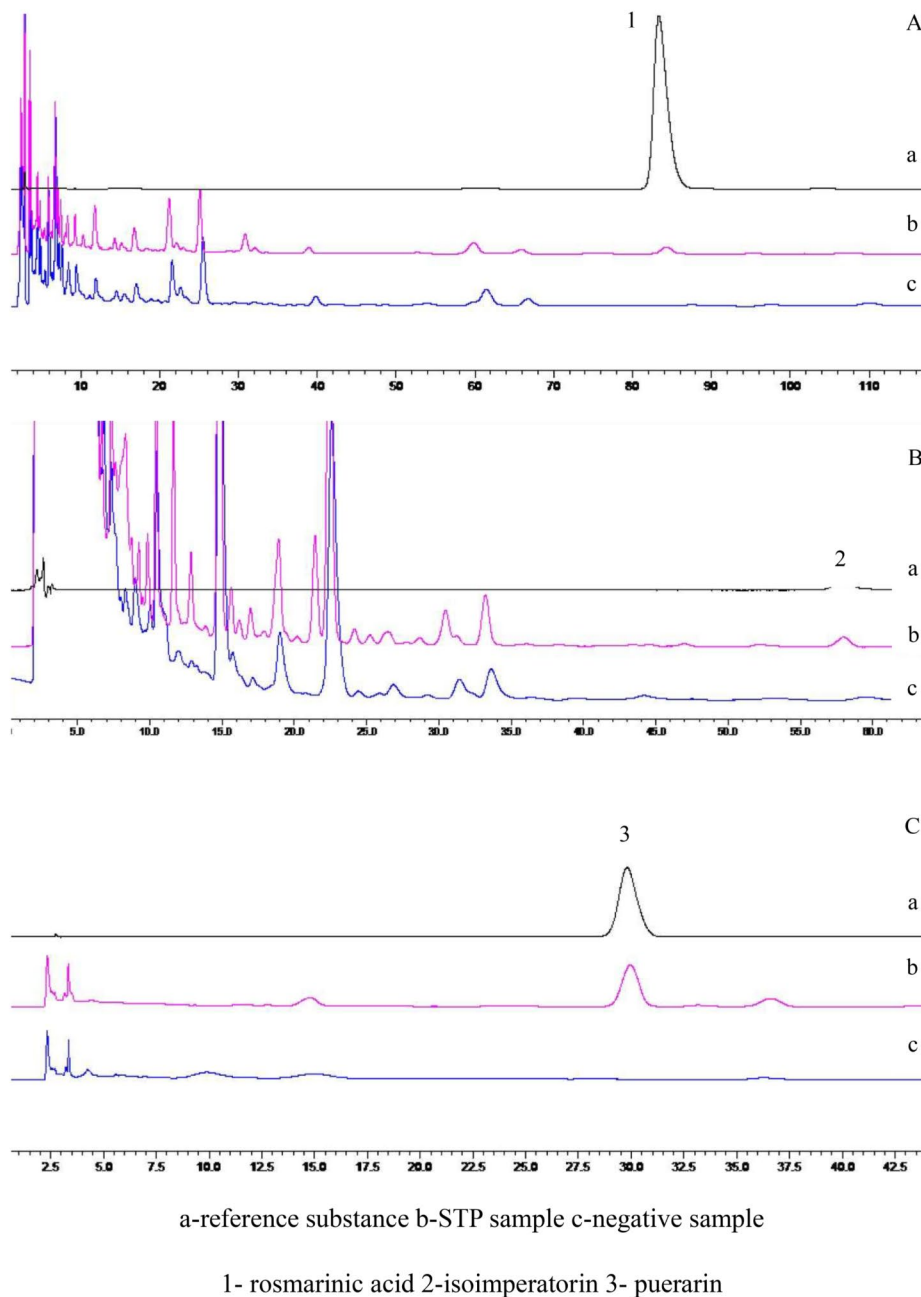


Fig. 1 HPLC of specificity determinations of (A) rosmarinic acid, (B) isoimperatorin, and (C) puerarin

Table 1 Determination of the content of index components in STP

Indicator components	Linear relation	Linear range(µg/mL)	RSD%			Sample recovery(RSD%)
			Precision	Reproducibility	Stability	
Rosmarinic acid	$y = 28397x - 39,557$ ($R^2 = 0.9998$)	4.9–79.3	0.8	1.1	2.5	97.6 (2.4)
Isoimperatorin	$y = 30608x - 14,984$ ($R^2 = 0.9990$)	0.2–23.8	1.0	1.0	1.3	101.2 (2.0)
Puerarin	$y = 41355x + 26,996$ ($R^2 = 0.9996$)	3.8–47.2	0.7	0.6	0.5	100.9 (1.3)

Table 2 Results of extraction time

Extraction time/h	Mass fraction (mg/g)			Extract yield (%)
	Rosmarinic acid	Isoimperatorin	Puerarin	
0.5	1.0101	0.0065	13.6082	20.4
1	1.1950	0.0101	13.9572	23.5
1.5	0.9721	0.0109	14.1734	23.3
2	0.9005	0.0074	14.2169	21.7

Table 3 Results of water addition

Water addition/times of solvent volume	Mass fraction (mg/g)			Extract yield (%)
	Rosmarinic acid	Isoimperatorin	Puerarin	
6	1.3767	0.0097	12.3057	19.8
8	1.2950	0.0101	12.9572	23.5
10	1.2447	0.0105	14.5220	24.4
12	1.1640	0.0100	12.4333	24.1

Single-factor investigation experiment

Effect of Extraction Time. The rosmarinic acid, isoimperatorin, and extract yields showed an increasing and then decreasing trend; the content of puerarin showed an overall increasing trend with increased extraction time; the isoimperatorin, puerarin, and extract yields were the lowest when the extraction time was 0.5 h. The results showed that the optimal extraction times were those exceeding 0.5 h. For comprehensive consideration, the extraction times with highest and lowest effectiveness were chosen to be 2 and 1 h, respectively, as shown in Table 2.

Effect of Water Addition. The content of rosmarinic acid gradually decreased with increased water volume; the content of isoimperatorin was stable; the content of puerarin showed an increasing and then decreasing trend. The rosmarinic acid content was lowest when the water volume was 12 times the sample weight. For comprehensive consideration, the water volumes with the highest and lowest yields were chosen to be 10 times and 6 times, respectively, as shown in Table 3.

Box-Behnken experimental design results

The experimental design results are shown in Fig. 2. An additional file shows this in more detail (see Additional file 1).

Design-Expert software was applied to analyse the experimental results, and a multivariate

quadratic regression equation model was obtained for the comprehensive score (M) and the number of times of water volume (X_1), extraction duration (X_2), and number of extractions (X_3): $M = 142.47 - 28.591 \times X_1 - 23.15 \times X_2 + 64.41 \times X_3 - 1.08 \times X_1 \times X_2 - 3.48 \times X_1 \times X_3 + 0.69 \times X_2 \times X_3 + 2.46 \times X_1^2 + 8.35 \times X_2^2 - 10.12 \times X_3^2$. Analysis of variance was performed on the model equations, and the results are shown in Table 4, the model of the constructed equations was extremely significant ($F_{\text{model}} = 30.34, P < 0.01$); the lack of fit was not significant ($P > 0.05$); the model $R_{\text{adj}}^2 = 0.9750, R_{\text{pred}}^2 = 0.8320$, which indicates that the model of this equation is suitable and reliable, with small experimental error and goodness of fit, and it can be used to analyse and predict the STP extraction process. From the P value, $X_1, X_2, X_3, X_1 \times X_3, X_1^2, X_2^2$, and X_3^2 of the independent variables of the model had a significant effect on the comprehensive score ($P < 0.01, P < 0.05$), and $X_1 \times X_2$ and $X_2 \times X_3$ in the interaction terms had no significant effect on the composite score ($P > 0.05$). From the F value and the response surface plots (Fig. 3), the order of the effect of each factor on the composite score was $X_1 > X_3 > X_2$.

Calculation of the standard relation

The similarity between the reference sample obtained from the ancient decoction process and the samples obtained from the modern decoction process were determined using the standard relation method [5].

Identification of the Subject of the Evaluation and Calculating the relative Deviation (RD_{ij}). The measured values of the reference sample were compared with the measured results values of the 17 experiments of the response surface experiment using the contents of the index components rosmarinic acid (Y_1), isoimperatorin (Y_2), puerarin (Y_3), the extract yield (Y_4), and fingerprint similarity (Y_5) as the evaluation indexes. The RD_{ij} value of P_{ij} with respect to S_j was calculated using Eq. (1), where P_{ij} denotes the measured value under the j th ($j = 1, 2, 3, \dots, n$) metric of the i th ($i = 1, 2, 3, \dots, m$) sample of the Box-Behnken response surface experiment, and S_j denotes the measured value under the j th ($j = 1, 2, 3, \dots, n$) measured value under the index of the reference sample. An additional file shows this in more detail (see Additional file 2).

$$RD_{ij} = |P_{ij} - S_j| / S_j \tag{1}$$

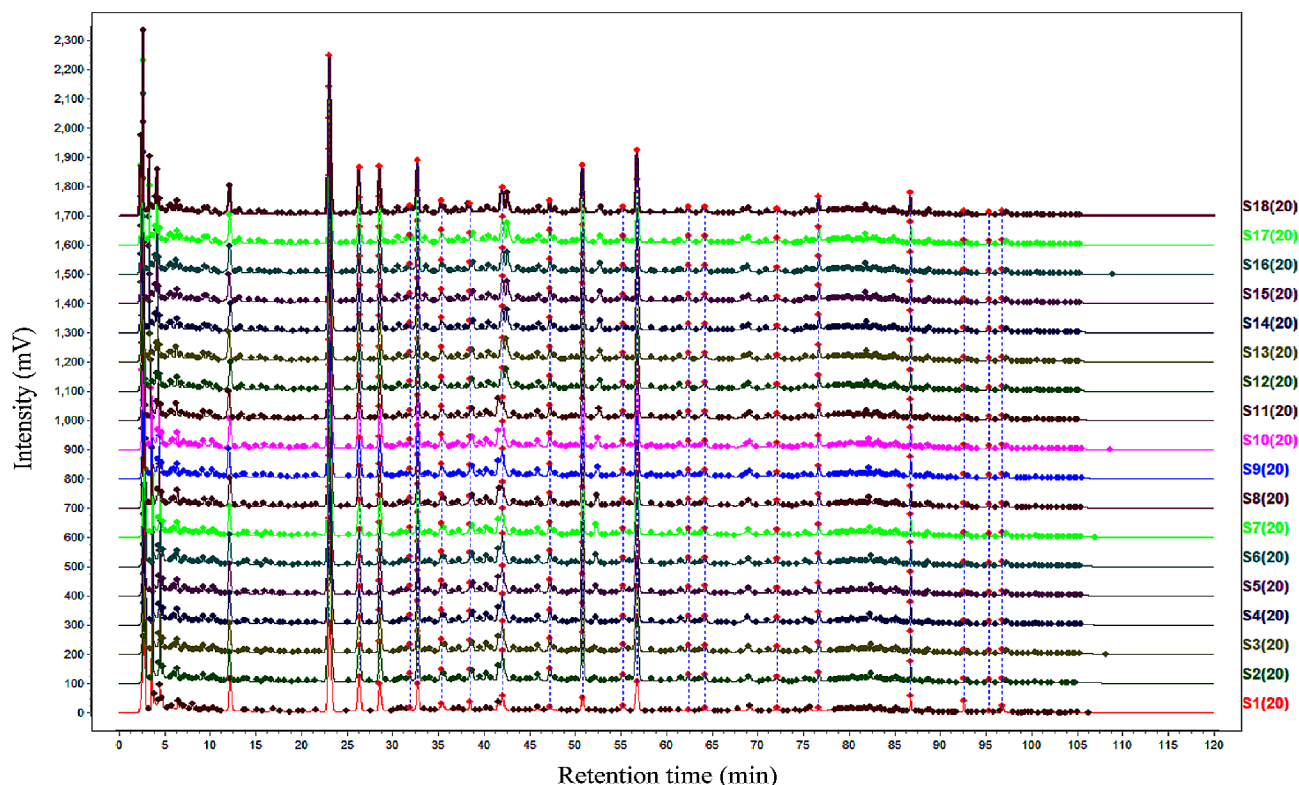


Fig. 2 The HPLC fingerprints of reference sample (S1) and response surface test samples (S2–S18)

Table 4 Response surface model ANOVA

Source	Sum of Squares	De-gree of freedom	Mean Square	F value	P value
Model	1277.9100	9	141.9900	30.3400	<0.0001**
X ₁	144.5900	1	144.5900	30.9000	0.0009**
X ₂	56.9700	1	56.9700	12.1800	0.0101*
X ₃	64.4100	1	64.4100	13.7600	0.0076**
X ₁ × X ₂	4.6300	1	4.6300	0.9885	0.3532
X ₁ × X ₃	193.2800	1	193.2800	41.3000	0.0004**
X ₂ × X ₃	0.4748	1	0.4748	0.1015	0.7594
X ₁ ²	406.1000	1	406.1000	86.7900	<0.0001**
X ₂ ²	18.3300	1	18.3300	3.9200	0.0883*
X ₃ ²	431.1500	1	431.1500	92.1400	<0.0001**
Residual error	32.7600	7	4.6800		
Lack of fit	11.7100	3	3.9000	0.7414	0.5804
Pure error	21.0500	4	5.2600		
Total variance	1310.6700	16			

*P is significant (P<0.05), **P is extremely significant (P<0.01). ANOVA=analysis of variance

Calculation of the standard Relation. SR_{ij} denotes the standard relation under the jth (j=1, 2, 3, ..., n) metric for the ith (i=1, 2, 3, ..., m) sample of the Box-Behnken response surface experiment. The closer the value of SR_{ij} is to 100%, the closer the samples are to the reference

sample. The SR_{ij} value is calculated by Eq. (2). An additional file shows this in more detail (see Additional file 2).

$$SR_{ij} = 1 - RD_{ij} = 1 - |P_{ij} - S_j| / S_j \quad (2)$$

Calculation of the comprehensive weights

Subjective Weights of Fuzzy Analytic Hierarchy Process (FAHP). FAHP is a subjective empowerment method that combines the analytic hierarchy process (AHP) and fuzzy mathematical theory to construct a fuzzy consistent judgment matrix, which facilitates results that are more in line with the human thinking mode in the case of more evaluation indexes, which are more fuzzy [6, 7]. First, a fuzzy judgment matrix was created. The index parameters of the extraction process were determined based on the theory of traditional Chinese medicine and the principle of ‘Sovereign, Minister, Assistant, and Guide’ in the compound prescription as the quality control means. As the fingerprint similarity provided limited information when comparing the content of indicator components, the final order of the index parameters was determined as rosmarinic acid (Y₁)>isoimperatorin (Y₂)>puerarin (Y₃)>extract yield (Y₄)>fingerprint similarity (Y₅). According to the criteria for constructing the fuzzy judgment matrix (Table 5), the evaluation indicators were compared with each other so that subjective judgments

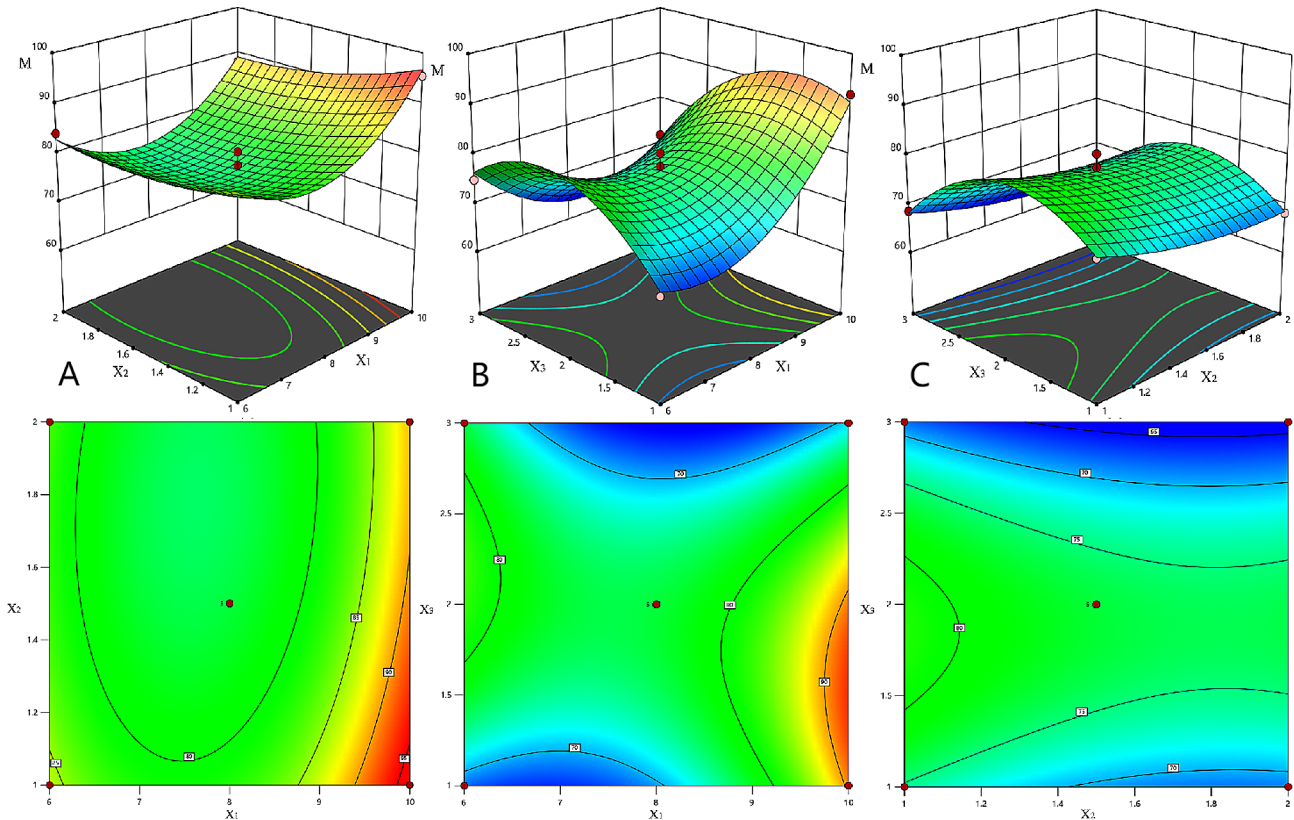


Fig. 3 The effect of number of times of water volume and extraction duration (A), number of times of water volume and number of extractions (B), extraction duration and number of extractions (C) on comprehensive score (M)

Table 5 Criteria for FAHP to construct fuzzy judgment matrix

Scale	Definition	Explanation
0.1–0.4	In contrast	Comparing the two indicators, $a_{ij} + a_{ji} = 1$
0.5	Equal	Comparing the two indicators, both are equally important
0.6	Slightly important	Comparing the two indicators, the former is slightly more important than the latter
0.7	Clearly important	Comparing the two indicators, the former is clearly more important than the latter
0.8	Highly important	Comparing the two indicators, the former is considerably more important than the latter
0.9	Extremely important	Comparing of the two indicators, the former is extremely important compared to the latter

and thought processes became quantitative and hierarchical, thus better reflecting the fuzziness of the problem and helping to obtain the fuzzy complementary judgment matrix (Eq. 3). The a_{ij} denotes the fuzzy relationship of the i th element of the lower layer relative to the j th element, and from this matrix, Eq. (4) can be obtained. Mathematical transformation of matrix A according to Eqs. (5) and (6) yields the fuzzy consistency judgment matrix (Eq. 7), which denotes the relative importance of the i th element to the j th element.

$$A = (a_{ij})_{n \times n} = \begin{bmatrix} a_{11} & a_{12} & \dots & a_{1n} \\ a_{21} & a_{22} & \dots & a_{2n} \\ \dots & \dots & \dots & \dots \\ a_{n1} & a_{n2} & \dots & a_{nn} \end{bmatrix} \quad (3)$$

$$a_{ij} + a_{ji} = 1 \quad (4)$$

$$r_i = \sum_{j=1}^n a_{ij}, (i = 1, 2, \dots, n) \quad (5)$$

$$r_{ij} = \frac{r_i - r_j}{2n} + 0.5 \quad (6)$$

$$R = (r_{ij})_{n \times n} \quad (7)$$

The subjective weight coefficients of the evaluation indexes $Y_1, Y_2, Y_3, Y_4,$ and Y_5 were calculated as 0.2650, 0.2350, 0.2000, 0.1750, and 0.1250, respectively, using Eqs. (8) and (9), and then, a consistency test was carried out. Assuming that W (Eq. 10) was the weight vector of the fuzzy consistency judgment matrix R , and W^* (Eq. 11) was its feature matrix. When the consistency index $I(R, W^*) \leq 0.1$, the judgment matrix could be categorised as a fuzzy consistency judgment matrix. The

consistency test was passed by calculating $I=0.0380<0.1$ using Eqs. (12) and (13).

$$w_i = \frac{\sum_{k=1}^n r_{ik} + \frac{n}{2} - 1}{n(n-1)}, (i = 1, 2, \dots, n) \tag{8}$$

$$\sum_{i=1}^n w_i = 1, w > 0, (i = 1, 2, \dots, n) \tag{9}$$

$$W = (w_1, w_2, \dots, w_n)^T \tag{10}$$

$$W^* = (w_{ij})_{n \times n} \tag{11}$$

$$w_{ij} = \frac{w_i}{w_i + w_j}, (\forall i, j = 1, 2, \dots, n) \tag{12}$$

$$I(R, W^*) = \frac{1}{n^2} \sum_{i=1}^n \sum_{j=1}^n |r_{ij} + w_{ij} - 1| \leq a \tag{13}$$

The Objective Weights of CRITIC. Equation (14) was used to calculate the standard deviation α_j , where j indicated the j th indicator and a indicated the a th indicator data; Eq. (15) was used to calculate the correlation coefficient β_j , where m indicated the number of evaluation indicators, and r_{ij} indicated the correlation coefficient between evaluation indicators i and j . Equation (16) and Eq. (17) were used to obtain the final weights (w_j^q). The CRITIC weights of Y_1, Y_2, Y_3, Y_4 and Y_5 were calculated to be 0.2920, 0.3310, 0.1150, 0.2480, and 0.0140, respectively.

$$\alpha_j = \sqrt{\frac{\sum_{a=1}^n (x_{aj} - \bar{x}_j)^2}{n-1}} \tag{14}$$

$$\beta_j = \sum_{i=1}^m (1 - r_{ij}) \tag{15}$$

$$C_j = \alpha_j + \beta_j \tag{16}$$

$$w_j^q = \frac{C_j}{\sum_{j=1}^m C_j} \tag{17}$$

Calculation of the Comprehensive Weights. Based on w_j^o obtained from FAHP and w_j^q obtained from CRITIC, the comprehensive weight coefficients w_j^s of each indicator are

calculated according to formula (18) [8], and the comprehensive weights of Y_1, Y_2, Y_3, Y_4 and Y_5 were calculated to be 0.3470, 0.3480, 0.1030, 0.1940, and 0.0080, respectively.

$$w_j^s = \frac{w_j^o w_j^q}{\sum_{j=1}^n w_j^o w_j^q} \tag{18}$$

Calculation of the comprehensive score

The comprehensive weight coefficients calculated from FAHP-CRITIC showed that Y_1 accounted for 34.7%, Y_2 accounted for 34.8%, Y_3 accounted for 10.3%, Y_4 accounted for 19.4%, and Y_5 accounted for 0.8% in the optimization of STP extraction process. The Box-Behnken response surface experiment comprehensive scores were calculated according to the comprehensive score formula (19), and the results are shown in Table 5. The closer the comprehensive score was to 100, the closer was the quality of the samples produced by the process to that of the reference sample. The highest scores in the Box-Behnken response surface experiment were obtained for the group 15 experiments, so the optimal extraction process consisted of the addition of a volume of water 10 times that of the powder, an extraction time of 1 h, and 2 extractions.

$$M = SR_{i,Y_1} \times 0.347 + SR_{i,Y_2} \times 0.348 + SR_{i,Y_3} \times 0.103 + SR_{i,Y_4} \times 0.194 + SR_{i,Y_5} \times 0.008 \tag{19}$$

Analysis of verification test

The process validation of the STP optimal extraction process obtained by screening through Box-Behnken response surface experiments was carried out in three parallel experiments to determine the content of rosmarinic acid (Y_1), the content of isoimperatorin (Y_2), the content of puerarin (Y_3), the extract yield (Y_4), the fingerprint similarity (Y_5), and to calculate the comprehensive scores, and the results are shown in Table 6. The mean value of the comprehensive score obtained from the three batches of process validation experiments was 94.7, with an RSD value of 0.8%, indicating that the optimal extraction process of this STP was stable and highly reproducible.

Table 6 Results of response surface validation experiment

No.	Mass fraction (mg/g)			Y_4 (%)	Y_5	Comprehensive score
	Y_1	Y_2	Y_3			
1	1.3231	0.0107	14.6278	25.8	0.9960	93.9
2	1.3304	0.0101	14.4465	24.7	0.9940	94.9
3	1.3247	0.0104	14.2997	26.0	0.9940	95.3
Mean value	1.3261	0.0104	14.3731	25.5	0.9950	94.7
RSD (%)	0.3	2.9	0.7	2.7	0.1	0.8

Discussion

STP is a boiled powder formula. Due to limitations in equipment, energy consumption, efficiency, and other factors encountered during the actual production process, it is not feasible to fully replicate the traditional extraction process of boiled powder when developing innovative drugs. Therefore, this study refers to the requirements of the relevant technical guidelines for the development of ancient classic prescriptions, and based on the preliminary examination of the key information of the prescription, the reference samples were prepared according to the traditional process. These samples were compared with those prepared using the modern extraction process, and the standard relation was calculated to establish an interface between the ancient and modern processes in terms of quality.

Rosmarinic acid is a bioactive phenolic compound [9], which is one of the main active components in dried leaves of *Perilla frutescens* (L.) Britt. Further, rosmarinic acid has high antioxidant capacity [10–12], which is why it is a promising nutraceutical compound in the food industry. It exhibits antibacterial, antiviral, and anti-inflammatory [13–15] pharmacological activities, and it has considerable therapeutic potential in the treatment of cancer, diabetes, and neurodegenerative diseases [16–18]. Isoimperatorin has considerable potential for use in the treatment of lung diseases [19, 20]. Puerarin [21] is the major bioactive ingredient isolated from the root of the *Pueraria lobata* (Willd.) Ohwi, and it has neuroprotective, antioxidant, anticancer, and anti-inflammatory pharmacological activities [22–25]. When selecting the indicator components, the active ingredients in the sovereign medicinal should be selected first as the indicator parameters, while considering the stability of the components. The content of puerarin in the minister medicinal Gegen is high and stable, thus the process is based on the content of rosmarinic acid in the sovereign medicinal Zisuye and the content of isoimperatorin in Baizhi, as well as the content of puerarin in Gegen. However, using only the content of a few index components or extract yield as an evaluation index does not reflect the overall quality differences between samples. The fingerprint of Chinese materia medica reflects the contours and qualitative qualities of small-molecule components, and the method of controlling their quality through fingerprint similarity combined with quantitative analysis of the index components has been commonly used in the development of ancient formulas [26]. Therefore, in the present study, the fingerprint similarity between response surface test samples and reference samples was added as an index to evaluate consistency between ancient and modern extraction processes so that the optimised process would be more scientific and reliable.

FAHP is a subjective empowerment method based on AHP and fuzzy mathematical theory to solve the problem

of consistency of hierarchical analysis [27–29]. The CRITIC method is an objective empowerment method using the objective attributes of data for scientific evaluation, which is a better method than the entropy weight and coefficient of variation methods [30]. In the study of extraction process optimization, single use of a certain assignment method ignores both the objective change law embodied in the data and the degree of subjective decision-making on different evaluation indexes. Therefore, the present study adopted the FAHP-CRITIC subjective-objective combination of empowerment methods to produce more reliable and accurate evaluation results.

Box-Behnken experimental design, standard relation, and FAHP-CRITIC Methods applied in the optimization of extraction processes are promising, especially in the study of ancient formulas with unique significance. The method can obtain stable and reliable extraction process parameters and provide data support for industrial production. The method can be applied to industrial production in the future. The process is adjusted and optimized according to the amplification results to obtain the most suitable process conditions for large-scale production and adapt it to the production demand so that products with high quality consistency with reference samples can be produced.

Conclusion

In this study, a quality control system was established using rosmarinic acid, isoimperatorin, puerarin, extract yield, and fingerprint similarity as evaluation indexes of the extraction process. The optimal extraction process of STP was optimised by comparing the quality control standards of the reference samples, and the results of the validation experiments showed that the extraction process of STP was stable, reliable, and highly reproducible. Therefore, it is feasible to optimise the modern extraction process of ancient formulas using the standard relation combined with FAHP-CRITIC subjective and objective comprehensive weights, which provides an evaluation method ensuring consistency in the quality of samples produced using ancient and modern processes in current industrial production, as well as a theoretical basis for the study of modern extraction processes of other ancient formulas.

Abbreviations

AHP	Analytic hierarchy process
CRITIC	Criteria importance through intercriteria correlation
FAHP	Fuzzy analytic hierarchical process analysis
QbD	Quality by design
RSD	Relative standard deviation
SR	Standard relation
STP	Shenshou Taiyi Powder
TCM	Traditional Chinese medicine

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12906-024-04554-7>.

Supplementary Material 1

Supplementary Material 2

Acknowledgements

Not applicable.

Author contributions

MJ designed the study with ZQ and AJ together. Experimental work and data collection were conducted by MJ, YD, YS, and WL. MJ and NL analyzed and interpreted the data. MJ drafted the manuscript. All authors read and approved the final version of the manuscript.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Jilin Provincial Development and Reform Commission (grant number: 2021C002), the Jilin Provincial Administration of Traditional Chinese Medicine (grant number: Ji Chinese Medicine Development [2021] No. 11).

Data availability

The original contributions presented in the study are included in the article, and further inquiries can be directed to the corresponding authors.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹College of Pharmacy, Changchun University of Chinese Medicine, Changchun 130117, Jilin, China

Received: 21 September 2023 / Accepted: 17 June 2024

Published online: 02 July 2024

References

- Wang Q. Selected prescriptions handed down for generations of physicians. *Shanghai Science and Technology*; 2003. pp. 135–6.
- Zhan ZL, Chen WS, Zhao RS, et al. Discussion on principle and detailed rules of textual research on key information of traditional Chinese medicine in classical prescriptions. *Mod Chin Med*. 2020;22(8):1155–61.
- Xu B, Shi XY, Wu ZS, et al. Quality by design approaches for pharmaceutical development and manufacturing of Chinese medicine. *Zhongguo Zhong Yao Za Zhi*. 2017;42(6):1015–24.
- Chinese Pharmacopoeia Commission. *Pharmacopoeia of the people's Republic of China* (volume 1). Chemical Industry; 2020. pp. 1418–29.
- Dai S, Li S, Zhang AJ, et al. Comprehensive evaluation of ancient and modern extraction process of classic prescription xiaoxuming decoction based on standard relation and analytic hierarchy process combined with entropy method. *Chin Trad Herb Drugs*. 2022;53(3):726–34.
- Liu W, Zheng Q, Pang L, Dou W, Meng X. Study of roof water inrush forecasting based on EM-FAHP two-factor model. *Math Biosci Eng*. 2021;18(5):4987–5005.
- Wang Y, Yang Y. Analyzing the green innovation practices based on sustainability performance indicators: a Chinese manufacturing industry case. *Environ Sci Pollut Res Int*. 2021;28(1):1181–203.
- Fan XY, Yang KL, Li HH, et al. Optimization of extraction process for classical prescription Banxia Xiexin Decoction based on Box-Behnken design-response surface, standard relation and analytic hierarchy process combined with entropy method. *Chin Trad Herb Drugs*. 2022;53(21):6716–25.
- Noor S, Mohammad T, Rub MA, et al. Biomedical features and therapeutic potential of rosmarinic acid. *Arch Pharm Res*. 2022;45(4):205–28.
- Ghorbani A, Sadeghnia HR, Afshari AR, Hosseini A. Rosmarinic acid protects adipose tissue-derived mesenchymal stem cells in nutrient-deficient conditions. *Prev Nutr Food Sci*. 2019;24(4):449–55.
- Sadeghi A, Bastin AR, Ghahremani H, Doustimotlagh AH. The effects of rosmarinic acid on oxidative stress parameters and inflammatory cytokines in lipopolysaccharide-induced peripheral blood mononuclear cells. *Mol Biol Rep*. 2020;47(5):3557–66.
- Komeili-Movahhed T, Bassirian M, Changizi Z, et al. SIRT1/NFκB pathway mediates anti-inflammatory and anti apoptotic effects of rosmarinic acid on a mouse model of nonalcoholic steatohepatitis (NASH). *J Recept Signal Transduct Res*. 2021;31:1–10.
- Sutkowska J, Hupert N, Gawron K, et al. The stimulating effect of rosmarinic acid and extracts from rosemary and lemon balm on collagen type I biosynthesis in osteogenesis imperfecta type I skin fibroblasts. *Pharmaceutics*. 2021;13(7):938.
- Panchal R, Ghosh S, Mehla R, et al. Antiviral activity of rosmarinic acid against four serotypes of dengue virus. *Curr Microbiol*. 2022;79(7):203.
- Ijaz S, Iqbal J, Abbasi BA, et al. Rosmarinic acid and its derivatives: current insights on anticancer potential and other biomedical applications. *Biomed Pharmacother*. 2023;162:114687.
- Jin BR, Chung KS, Hwang S, et al. Rosmarinic acid represses colitis-associated colon cancer: a pivotal involvement of the TLR4-mediated NF-κB-STAT3 axis. *Neoplasia*. 2021;23(6):561–73.
- Samsu N, Soeharto S, Rifai M, Rudijanto A. Rosmarinic acid monotherapy is better than the combination of rosmarinic acid and telmisartan in preventing podocyte detachment and inhibiting the progression of diabetic nephropathy in rats. *Biologics*. 2019;13:179–90.
- Fachel FNS, Michels LR, Azambuja JH, et al. Chitosan-coated rosmarinic acid nanoemulsion nasal administration protects against LPS-induced memory deficit, neuroinflammation, and oxidative stress in Wistar rats. *Neurochem Int*. 2020;141:104875.
- Guo H, Ding H, Tang X, et al. Quercetin induces pro-apoptotic autophagy via SIRT1/AMPK signaling pathway in human lung cancer cell lines A549 and H1299 in vitro. *Thorac Cancer*. 2021;12(9):1415–22.
- Elumalai P, Ezhilarasan D, Raghunandhakumar S. Quercetin inhibits the epithelial to mesenchymal transition through suppressing Akt mediated nuclear translocation of β-catenin in lung cancer cell line. *Nutr Cancer*. 2022;74(5):1894–906.
- Zhou YX, Zhang H, Peng C. Puerarin: a review of pharmacological effects. *Phytother Res*. 2014;28(7):961–75.
- Chung MJ, Sung NJ, Park CS, et al. Antioxidative and hypocholesterolemic activities of water-soluble puerarin glycosides in HepG2 cells and in C57 BL/6 J mice. *Eur J Pharmacol*. 2008;578(2–3):159–70.
- Zhang S, Ji G, Liu J. Reversal of chemical-induced liver fibrosis in Wistar rats by puerarin. *J Nutr Biochem*. 2006;17(7):485–91.
- Zhu Z, Xu Y, Zou H, et al. Effects of puerarin on pulmonary vascular remodeling and protein kinase C-α in chronic cigarette smoke exposure smoke-exposed rats. *J Huazhong Univ Sci Technolog Med Sci*. 2008;28(1):27–32.
- Hu JJ, Zhang DD, Chen JJ, Chen CS, Li YP. Effect of pretreatment with puerarin on activation of LPS-induced RAW264. 7 cells. *Zhongguo Zhong Yao Za Zhi*. 2012;37(20):3112–6.
- Zhang Q, Han XX, Mao CQ, et al. Opportunities and challenges in development of compound preparations of traditional Chinese medicine: problems and countermeasures in research of ancient classical prescriptions. *Zhongguo Zhong Yao Za Zhi*. 2019;44(19):4300–8.
- Chalak MH, Bahramiazar G, Rasaee J, et al. Occupational health risk assessment at healthcare institutions: developing a semi-quantitative risk method. *Int J Risk Saf Med*. 2021;32(4):265–78.
- Yadav R, Lee HH. Ranking and selection of dental restorative composite materials using FAHP-FTOPSIS technique: an application of multi criteria decision making technique. *J Mech Behav Biomed Mater*. 2022;132:105298.
- Rathore B, Gupta R. A fuzzy based hybrid decision-making framework to examine the safety risk factors of healthcare workers during COVID-19 outbreak. *J Decis Syst*. 2022;31(1–2):68–101.
- Su J, Su K, Wang S. Evaluation of digital economy development level based on multi-attribute decision theory. *PLoS ONE*. 2022;17(10):e0270859.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.