

OPTIMIZATION OF *SCHISANDRA HENRYI* EXTRACTION USING RESPONSE SURFACE METHODOLOGY

Hoang Thu Thuy^{1,2}, Ngo Thi Phuong², Ta Thi Thao¹,
Cam Thi Inh², Do Thi Thanh Huyen², Le Minh Ha^{2,*}

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ABSTRACT

Schisandra henryi is a woody climbing species of the genus *Schisandra*, naturally distributed mainly in southwestern China, with recent records of wild populations in the Ngoc Linh mountainous region of Vietnam. The fruits of this species possess medicinal value and are characterized by a chemical profile rich in dibenzocyclooctadiene lignans and phenolic compounds. In this study, an ultrasound-assisted extraction process using 96% ethanol as the solvent was optimized to enhance extraction yield and the recovery efficiency of schisandrin A from *S. henryi* fruits. The effects of solvent-to-material ratio, extraction time, and temperature were simultaneously evaluated using response surface methodology (RSM). The developed RSM models exhibited a high degree of goodness of fit and strong predictive capability. The results indicated that an extraction temperature of 50°C, an ultrasonic extraction time of 64.37min, and a solvent-to-material ratio of 15.22mL/g were the optimal conditions, yielding a schisandrin A content of 0.18% and an extraction yield of 23.28%. Under these optimized conditions, the experimental values were in good agreement with the predicted values, confirming the reliability of the proposed models.

Keywords: *Schisandra henryi*; schisandrin A; extraction; Response Surface Methodology; antioxidation.

¹Department of Chemistry, VNU University of Science, Hanoi, Vietnam

²Institute of Chemistry, Vietnam Academy of Science and Technology (VAST), Vietnam

*Email: leminhha.inpc@gmail.com

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B Thời gian chiết
C Tỷ lệ dung môi – nguyên liệu chiết

ABBREVIATIONS

Abbreviations	Meaning
HPLC-UV	High-Performance Liquid Chromatography – Ultraviolet
MAE	Mean Absolute Error
MAPE	Mean Absolute Percentage Error
R ²	R-squared
RSM	Response surface methodology
RMSE	Root Mean Square Error
PTFE	Polytetrafluoroethylene
SA	Schisandrin A

1. INTRODUCTION

Schisandra henryi (*S. henryi*), also known as Southern *Schisandra* or Ngoc Linh *Schisandra*, is a woody climbing species belonging to the genus *Schisandra*. According to botanical records, *S. henryi* is primarily distributed in southwestern China, particularly in Yunnan Province, where it grows in montane forest ecosystems at medium to high altitudes [1-3]. In recent years, field surveys conducted in Vietnam have reported the presence of a subspecies of *S. henryi* growing wild in the Ngoc Linh mountainous region at elevations of approximately 1,200 - 1,600m above sea level [4]. In traditional Chinese medicine, the fruits of *Schisandra* species have long been used as tonic remedies for strengthening the body, enhancing physical endurance, and supporting overall health [3, 5]. Similar to other species of the genus *Schisandra*, the pharmacological value of *S. henryi* is

SYMBOL

Symbol	Unit	Meaning
%SA	%	Hàm lượng schisandrin A
%Y	%	Hiệu suất chiết xuất
A		Nhiệt độ chiết

closely associated with its characteristic chemical composition, particularly dibenzocyclooctadiene lignans, collectively referred to as Schisandra lignans, along with phenolic and polyphenolic compounds [1, 2].

Among the characteristic lignans of the genus *Schisandra*, schisandrin A (SA) has attracted considerable attention due to its broad spectrum of biological activities and its relatively well-elucidated mechanisms of action. This compound is regarded as one of the major lignans and represents a characteristic bioactive constituent of *S. chinensis* [6, 7]. Previous studies have demonstrated the potential application of this compound in the treatment of inflammatory skin diseases and infections associated with *Propionibacterium acnes* [8]. In addition, SA has been shown to maintain cellular energy metabolism and protect cells against oxidative stress-induced apoptosis [9]. Furthermore, SA exhibits anti-inflammatory activity through the inhibition of reactive oxygen species and the NLRP3 inflammasome, thereby alleviating lung injury in murine models of chronic obstructive pulmonary disease [10]. Other studies have also reported its ability to promote the proliferation and differentiation of neural progenitor cells via the regulation of Cdc42, suggesting promising potential in the fields of neurobiology and tissue regeneration [11].

The content of SA in *Schisandra* raw materials has been reported to vary significantly depending on the geographical origin of the plant material, extraction methods, and applied processing conditions [12]. Therefore, the selection and optimization of extraction parameters are critical for obtaining extracts with high and stable levels of active constituents that meet quality requirements for pharmaceutical and nutraceutical applications. In this context, response surface methodology (RSM) is regarded as an efficient and advanced optimization tool, enabling the simultaneous evaluation of the interactive effects of multiple technological variables on extraction efficiency. Globally, RSM has been widely applied to optimize the extraction conditions of lignans from various *Schisandra* species, particularly *S. chinensis* and *S. sphenanthera* [13-17]. However, to date, no scientific reports have been published on the optimization of extraction conditions for *S. henryi* in Vietnam, a newly recorded species with potential as an alternative domestic source of medicinal raw materials to imported products.

Based on the above considerations, this study was conducted to optimize the extraction conditions of *S.*

henryi using RSM, with the aim of maximizing both the extraction yield and SA content, which was quantitatively determined by HPLC-UV analysis. The results of this study are expected to provide a scientific basis for the development of standardized extracts from *S. henryi*, thereby supporting the production of pharmaceutical and health supplement products derived from domestic medicinal plant resources.

2. MATERIALS AND METHODS

2.1. Materials, chemicals, and equipment

S. henryi fruits were harvested in February 2025 in Ngoc Linh Commune, Dak Glei District, Kon Tum Province, Vietnam. The fruits were cleaned to remove pedicels and foreign materials, dried at 50°C then ground using a mill equipped with a 0.355mm sieve to obtain crude *S. henryi* powder. The moisture content of the crude powder was 6.5%.

Ethanol (96%, analytical grade) and methanol (HPLC grade, ≥ 99.9%) were purchased from Merck (Germany). Deionized water was obtained from a Milli-Q purification system (Millipore, USA). Schisandrin A (SA) reference standard (Cat. No. CFN99124, CAS No. 61281-38-7) with a certified purity of ≥ 98.0% was purchased from ChemFaces (Wuhan, China). Elmasonic S80H ultrasonic bath (Elma, Germany), capacity 9.4L, ultrasonic frequency 37kHz, nominal power 750W.

SA stock standard solution (1000ppm) was prepared by accurately weighing 1.0mg of SA and dissolving it in 1.0mL of ethanol, followed by ultrasonication for 5 min to ensure complete dissolution. Working standard solutions of SA at concentrations of 5, 10, 20, 50, and 80ppm were prepared by serial dilution of the stock solution with ethanol.

2.2. Extraction of *Schisandra henryi*

An accurately weighed 1.00g portion of *S. henryi* powder was placed into a 50mL falcon tube. A predetermined volume of ethanol 96% was added, and ultrasound-assisted extraction was performed under the conditions listed in Table 1. The mixture was then centrifuged to obtain the ethanolic extract. The solvent was evaporated to dryness, and the residue was weighed.

The extraction yield of *S. henryi* (%Y) was calculated according to equation (1):

$$\%Y = \frac{m_{\text{residue}}}{m_{\text{raw}}} \times 100 \quad (1)$$

where m_{residue} is the mass of dried extract obtained after solvent evaporation to dryness, and m_{raw} is the initial mass of raw material.

Subsequently, the residue was re-dissolved and made up to 20mL with ethanol, then filtered through a 2 μ m PTFE syringe filter prior to HPLC-UV analysis.

Table 1. Independent variables investigated

Variable	Experimental levels		
	Low (-1)	Center (0)	High (+1)
Temperature ($^{\circ}$ C)	50	65	80
Time (min)	30	60	90
Solvent-to-raw material ratio (mL/g)	10	15	20

2.3. HPLC-UV analysis of schisandrin A

The high-performance liquid chromatography (HPLC) system used for the analysis of schisandrin A consisted of a Shimadzu LC-10AT isocratic pump, a Shimadzu SCL-10A system controller, a Shimadzu SPD-10A UV-Vis detector, and a Shimadzu CTO-10A column oven. Samples were injected manually into the system using a six-port Rheodyne 7725i injection valve equipped with a 20 μ L sample loop. The system was equipped with an Agilent ZORBAX Eclipse XDB-C18 column (4.6 \times 150mm, 5 μ m). The mobile phase consisted of methanol (channel A) and water (channel B) operated under isocratic elution at a methanol-water ratio of 62:38 (v/v) [18]. The injection volume was 10 μ L, the flow rate was set at 1.0mL/min, and the column temperature was maintained at 30 $^{\circ}$ C. UV detection was performed at a wavelength of 254nm for SA quantification [18]. The SA content was calculated as percentages to the mass of the crude raw material.

2.4. Experimental design for extraction optimization

Preliminary single-factor experiments were conducted to evaluate the effects of extraction time (15 - 120min), ultrasonic temperature (room temperature to 90 $^{\circ}$ C), and solvent-to-material ratio (5 - 30mL/g). The temperature in this study was defined based on the set temperature of the ultrasonic device. Based on these results, the ranges selected for optimization of the extraction conditions were an extraction temperature of 50 - 80 $^{\circ}$ C, extraction time of 30 - 90min, and solvent-to-material ratio of 10 - 20mL/g, each investigated at three levels (low, center, and high). The experimental variables were coded according to the equation (2):

$$x_i = \frac{X_i - X_{i,0}}{\Delta X_i} \times 100 \quad (2)$$

where x_i represents the coded value of the variable, X_i is the actual value, $X_{i,0}$ denotes the actual value at the center point of the experimental domain, and ΔX_i is the

step change corresponding to the distance between the center point and the boundary of the investigated range.

3. RESULTS AND DISCUSSION

3.1. Screening and optimization of extraction Conditions

3.1.1. Selection of experimental variable ranges

The calibration curve of SA (Figure 1) was constructed using a series of standard solutions with known concentrations; the corresponding peak area data were processed using Microsoft Excel to establish the regression equation. Under the chromatographic conditions described, SA was detected at a characteristic retention time of approximately 10.25 minutes.

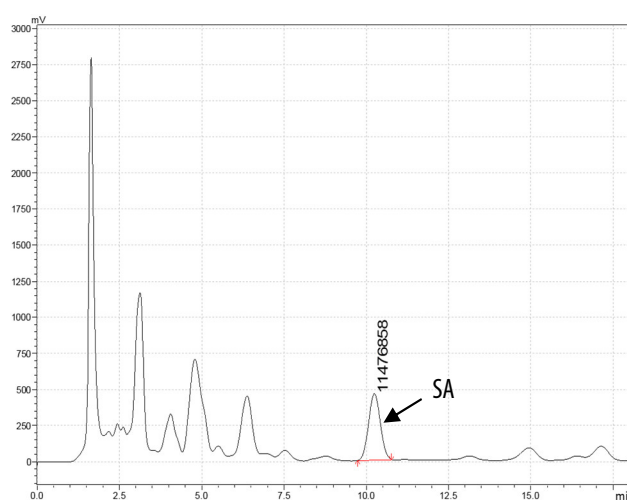


Figure 1. SA peak in the chromatogram of the Schisandra extract sample

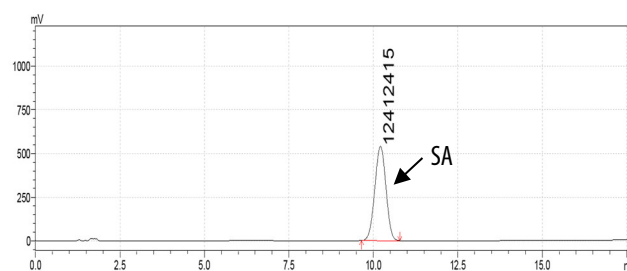


Figure 2. Chromatogram of the SA standard sample

The calibration curve of SA was constructed using Microsoft Excel, as shown in Figure 3. The corresponding regression equation was determined as $y = 159421x - 453447$, with a coefficient of determination (R^2) of 0.9983.

The limit of detection (LOD) and limit of quantification (LOQ) were determined by serial dilution of the standard solution until signal-to-noise (S/N) ratios of approximately 2 - 3 and 9 - 11 were obtained, respectively. The LOD and LOQ values for SA were found

to be 0.41 $\mu\text{g/mL}$ and 1.25 $\mu\text{g/mL}$, respectively. The UV spectrum of the peak in the test sample showed a 99.9% match with that of the SA reference standard, confirming the specificity of the analytical method.

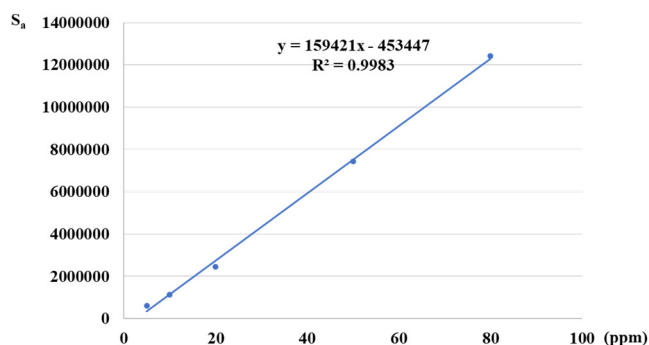


Figure 3. SA calibration curve

To determine the appropriate ranges for constructing the RSM model, single-factor experiments were conducted to investigate the effects of extraction time, temperature, and solvent-to-material ratio. For the investigation of extraction time, the temperature was fixed at 65°C and the solvent-to-material ratio at 15mL/g, while the extraction was performed at different time intervals. The results presented in Figure 4 show that both SA content and extraction yield gradually increased from 15 to 60 min, after which only slight changes were observed with further extension of the extraction time. Therefore, the range of 30 - 90 min was selected for the RSM design.

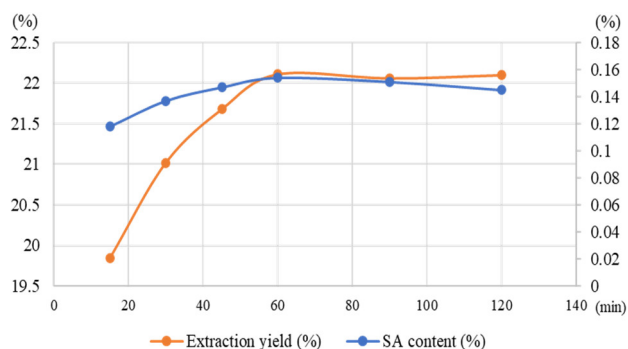


Figure 4. The variation of SA content and extraction yield (right and left vertical axis) over the investigated time range

To investigate the effect of temperature, extractions were carried out at different temperatures while maintaining a constant extraction time of 60 min and a solvent-to-material ratio of 15mL/g. The results shown in Figure 5 indicate that increasing the temperature from room temperature to 65°C markedly increased both SA content and extraction yield; however, at higher temperatures, particularly at 90°C, these values showed a

slight decrease. Consequently, the temperature range of 50 - 80°C was selected for the RSM design.

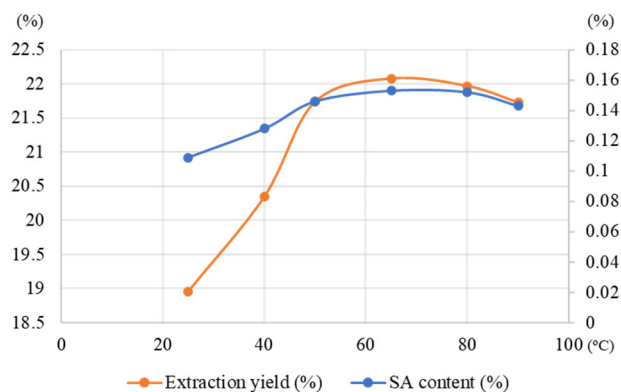


Figure 5. The variation of SA content and extraction yield (right and left vertical axis) over the investigated temperature range

To evaluate the effect of the solvent-to-material ratio, extractions were conducted under fixed conditions of 65°C and 60 min extraction time. The results presented in Figure 6 show that both SA content and extraction yield increased as the solvent-to-material ratio increased from 5 to 15mL/g, while no significant change was observed with further increases in solvent volume. Therefore, the range of 10 - 20mL/g was selected for the RSM design.

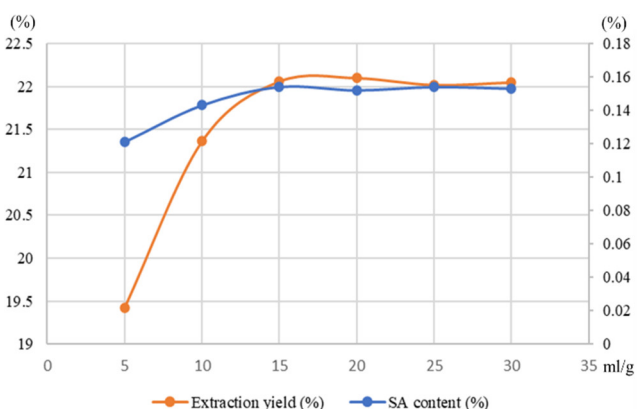


Figure 6. The variation of SA content and extraction yield (right and left vertical axis) over the investigated ratio range

3.1.2. RSM experimental design and experimental responses

RSM based on a Box-Behnken design (BBD) was applied to construct the experimental design using Python 3.12 software. The experimental design consisted of 15 runs, in which the center point was replicated three times to estimate the experimental error. Three independent variables were investigated, including extraction time, extraction temperature, and the solvent-to-material ratio. The results for SA content and the extraction yield are presented in Table 2.

Table 2. Three-factor Box-Behnken design and experimental results for SA content and extraction yield

Run	Temperature (°C)	Time (min)	Solvent-to-material ratio (mL/g)	SA content (%)	Extraction yield (%)
1	65	60	15	0.155	22.54
2	50	60	10	0.150	21.97
3	80	30	15	0.116	20.35
4	65	30	20	0.104	19.31
5	50	30	15	0.146	21.93
6	80	60	20	0.144	21.18
7	65	90	10	0.112	20.18
8	50	90	15	0.158	22.65
9	65	60	15	0.152	21.93
10	80	60	10	0.133	21.12
11	65	30	10	0.084	18.57
12	50	60	20	0.154	21.62
13	80	90	15	0.158	22.43
14	65	60	15	0.153	21.76
15	65	90	20	0.128	20.56

Based on the results of the 15 experimental runs, the coefficients of the regression equations were determined using Python 3.12 software and are presented in Table 3.

Table 3. Regression coefficients and corresponding p-values

Components	Equation for %SA		Equation for %Y	
	Coded coefficient	p-value	Coded coefficient	p-value
Constant	0.1533	< 0.0001	22.0767	< 0.0001
A	-0.0071	0.0455	-0.3863	0.109
B	0.0133	0.00427	0.7075	0.013
C	0.0064	0.149	0.1038	0.704
A ²	0.0147	0.0118	0.7904	0.0474
B ²	-0.0235	0.00161	-1.0271	0.0193
C ²	-0.0228	0.00186	-1.3946	0.0058
AB	0.0075	0.00041	0.3400	0.0455
AC	0.0018	0.755	0.1025	0.795
BC	-0.0010	0.857	-0.0900	0.809

R ²	0.9916	0.9694
RMSE	0.0020	0.2030
MAE	0.0017	0.1728
MAPE	1.370	0.8153
P-value _{lack of fit}	0.1117	0.6926
F-value	20.274	6.7729

%SA: Content of schisandrin A; %Y: Extraction yield; A: Temperature; B: Time; C: Solvent-to-material ratio; R²: R-squared; RMSE: Root Mean Square Error; MAE: Mean Absolute Error; MAPE: Mean Absolute Percentage Error

The reduced second-order multivariate regression equation, obtained by eliminating the coefficients of variables with p-values greater than 0.05, and expressed in terms of coded variables, is given as:

$$\begin{aligned} \%SA &= 0.1533 - 0.0071A + 0.0133B + 0.0147A^2 \\ &\quad - 0.0235B^2 - 0.0228C^2 + 0.0075AB \\ \%Y &= 22.0767 + 0.7075B + 0.7904A^2 - 1.0271B^2 \\ &\quad - 1.3946C^2 + 0.3400AB \end{aligned}$$

Based on the results of 15 experimental runs, second-order multivariate regression models for %SA and %Y were developed and evaluated, demonstrating an excellent goodness of fit. The coefficient of determination (R²) reached 0.9916 for the %SA model and 0.9694 for the %Y model, indicating that the models accounted for the vast majority of the experimental variability. In addition, the RMSE, MAE, and MAPE values were 0.0020, 0.0017, and 1.370%, respectively, for the %SA prediction equation, and 0.2030, 0.1728, and 0.8153 for the %Y prediction equation. All error indices were low and markedly smaller than the range of variation of the experimental responses, confirming the high accuracy and strong predictive capability of the proposed models.

According to the F-critical table, with the degrees of freedom for the model equal to 9 (since the three-factor RSM model contains nine regression terms) and the degrees of freedom for the residual error equal to 5, the critical F value (F_{crit}) is 4.99. The calculated F values are 20.274 for the %SA model and 6.7729 for the %Y model. Since both F values are greater than F_{crit}, this indicates that the developed second-order regression models are statistically significant, meaning that the independent variables included in the models have a significant effect on the studied responses. This result demonstrates that the models are capable of explaining a substantial proportion of the variability in the experimental data and can therefore be reliably used for response prediction,

response surface analysis, and optimization of the experimental conditions.

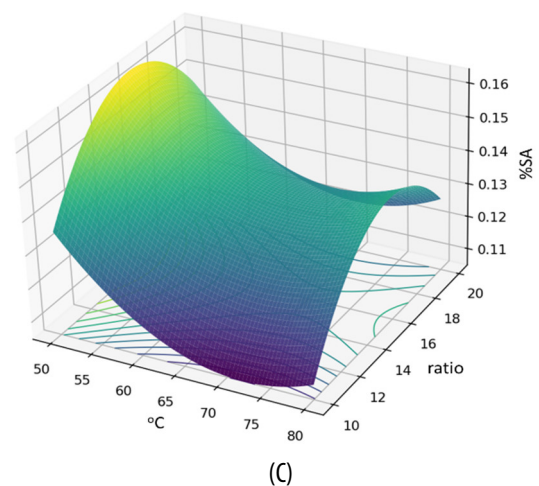
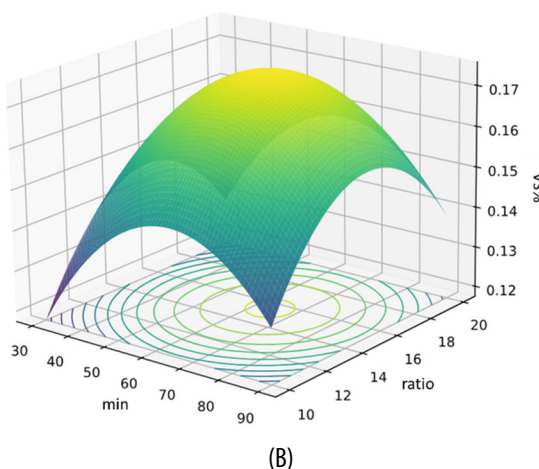
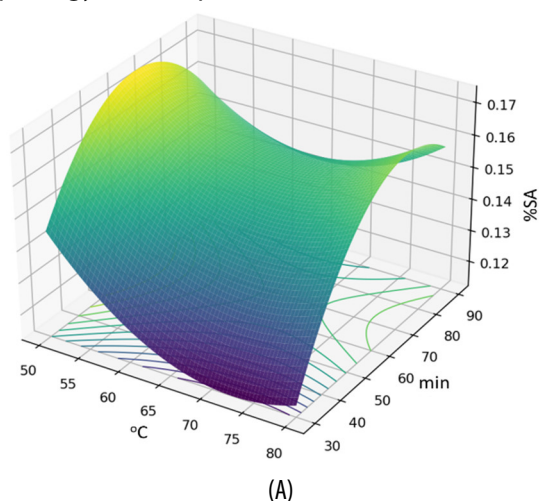
For %SA, the linear coefficient of extraction temperature (A) was negative (-0.0071), suggesting that, when considered individually, an increase in temperature tends to reduce SA content. In contrast, the positive linear coefficient of extraction time ($B = 0.0133$) reflects the favorable effect of prolonged extraction on the dissolution and diffusion of SA into the solvent. The quadratic terms revealed pronounced nonlinear effects of the investigated factors: the coefficient of A^2 was positive (0.0147), whereas those of B^2 (-0.0235) and C^2 (-0.0228) were negative. This indicates that SA content reaches a maximum within an optimal range of temperature, time, and ethanol-to-material ratio, and subsequently decreases when these factors exceed appropriate thresholds. Moreover, the positive interaction coefficient between temperature and time ($AB = 0.0075$) suggests a synergistic effect, whereby the simultaneous adjustment of these two variables enhances SA content more effectively than varying each factor independently.

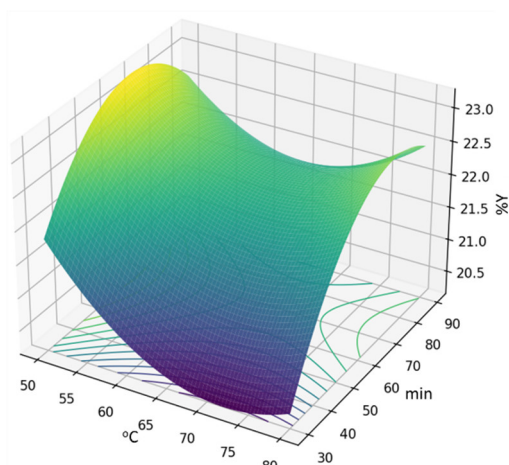
Regarding extraction yield (%Y), the regression equation indicated that extraction time (B) was the dominant linear factor, with a relatively large positive coefficient (0.7075), demonstrating that increasing extraction time markedly enhances the amount of extract obtained. Meanwhile, the quadratic coefficients of temperature ($A^2 = 0.7904$), time ($B^2 = -1.0271$), and especially the ethanol-to-material ratio ($C^2 = -1.3946$) were all substantial, reflecting a strong dependence of extraction yield on nonlinear effects and the existence of an optimal operating region, particularly with respect to the solvent-to-material ratio. The positive interaction coefficient between temperature and time ($AB = 0.3400$) further indicates a synergistic influence of these factors, contributing to improved extraction yield when they are jointly optimized within an appropriate range.

3.2. Effect of extraction conditions on schisandrin A content and extraction yield

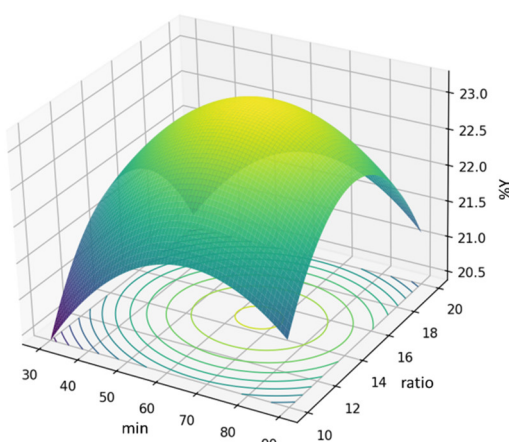
Based on the response surfaces generated using Python 3.12, both SA content and extraction yield were found to be significantly and nonlinearly influenced by all three investigated factors, namely extraction temperature, extraction time, and solvent-to-material ratio. In general, SA content and extraction yield exhibited similar variation trends in response to changes in the extraction conditions. When temperature and

extraction time were considered simultaneously (Figures 7A and 7D), both responses increased progressively as the temperature rose from low to intermediate levels. However, at higher temperatures, a slight decline in SA content and extraction yield was observed, suggesting possible thermal degradation or reduced stability of the target compounds under prolonged thermal exposure. This behavior is clearly reflected by the concave surface morphology and the presence of closed contour lines.

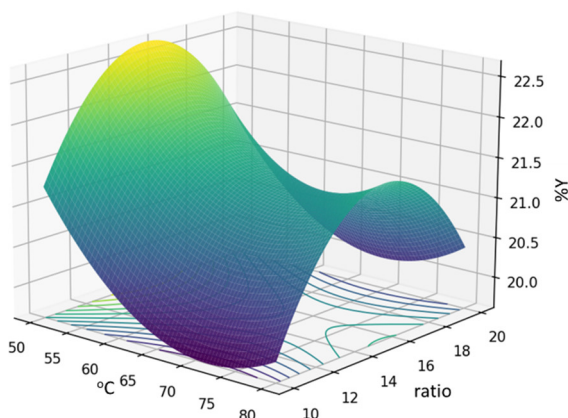




(D)



(E)



(G)

Figure 7. Effects of temperature, extraction time, and solvent-to-material ratio on %SA (A-C) and %Y (D-G)

For the combined effects of extraction time and solvent-to-material ratio (Figures 7B and 7E), maximum values of SA content and extraction yield were achieved at intermediate solvent ratios, whereas excessively low or high solvent-to-material ratios led to a reduction in both responses. Similarly, the response surfaces describing the

interaction between temperature and solvent-to-material ratio (Figures 7C and 7G) revealed a distinct optimal region, in which a moderate solvent-to-material ratio coupled with relatively low temperatures within the investigated range enhanced the diffusion and dissolution of SA as well as other extractable constituents.

Overall, the response surface analysis indicates the presence of pronounced second-order interactions among the studied factors and confirms that the optimal extraction conditions for SA content and extraction yield are not located at the extreme levels of individual variables, but rather at a balanced combination of temperature, extraction time, and solvent-to-material ratio.

3.3. Model optimization results

Based on the regression analysis, the developed quadratic models were further expressed in terms of actual variables to facilitate prediction and determination of the optimal extraction conditions.

$$\begin{aligned} \%SA &= 0.1972 - 0.0103X + 0.0026Y + 0.0275Z \\ &+ 6.53703 \times 10^{-5}X^2 - 2.6157 \times 10^{-5}Y^2 - 0.0009Z^2 \\ &+ 1.6667 \times 10^{-5}XY \end{aligned}$$

$$\begin{aligned} \%Y &= 23.9460 - 0.5483X + 0.1204Y + 1.6414Z \\ &+ 0.0035X^2 - 0.0011Y^2 - 0.0558Z^2 + 0.0008XY \end{aligned}$$

where X is the actual extraction temperature (°C), Y is the actual extraction time (min), and Z is the actual solvent-to-material ratio (mL/g).

On the basis of the regression models that were developed and validated, an optimization process was carried out to identify the optimal extraction conditions using both single-factor and multi-factor approaches. The corresponding optimization results are summarized in Table 4.

Table 4. Single-factor and multi-factor optimization conditions

Variable	Optimization for %SA		Optimization for %Y		Combined optimization	
	Actual value	Coded value	Actual value	Coded value	Actual value	Coded value
Temperature (°C)	50	-1	50	-1	50	-1
Time (min)	63.75	0.125	65.37	0.179	64.37	0.146
Solvent-to-material ratio (mL/g)	15.44	0.088	14.97	-0.005	15.22	0.044
Optimal value	%SA	0.17574	0.17542		0.17566	
	%Y	23.27151	23.28631		23.28180	

Under single-objective optimization, both %SA and %Y reached their maximum values at the lowest temperature within the investigated range (50°C, coded level - 1), indicating that SA tends to be thermolabile and susceptible to degradation as the extraction temperature increases. Although previous studies have not explicitly reported the thermal degradation of SA during extraction, it has been demonstrated that lignans such as schizandrin A, schisandrol A, and schisandrol B exhibit a decreasing trend in content with increasing drying temperature [19]. The optimal extraction times for %SA (63.75 min) and %Y (65.37 min) were both close to the central point of the experimental design, while the optimal solvent-to-material ratio was approximately 15mL/g.

Under multi-objective optimization, the obtained extraction conditions showed slight adjustments compared to the single-objective optimization, with an extraction time of 64.37 min, a solvent-to-material ratio of 15.22mL/g, while the temperature remained at 50°C. Under these conditions, the %SA and %Y values reached 0.17566% and 23.28180%, respectively. Compared with the single-objective optimal values, both %SA and %Y obtained from the combined optimization were slightly lower than their respective maximum values (0.17574% for %SA and 23.28631% for %Y), but higher than the values calculated under the single-factor optimization conditions of the other response. However, the differences were minimal and practically negligible when transitioning from single-objective to multi-objective optimization.

Extraction was carried out under the conditions optimized by the RSM approach using a Box-Behnken design, namely at 50°C for 64.37 min with a solvent-to-material ratio of 15.22mL/g. All experiments were performed in five replicates, and the results are reported as mean values. The deviations from the theoretically predicted optimal values (%SA = 0.18% and %Y = 23.28%) were evaluated using the *t*-test. The repeated experiments indicated that %SA and %Y varied within a narrow range, with %SA from 0.17% to 0.18% and %Y ranging from 23.15% to 23.46%. The variability among replicates was minimal, with RSD values below 2%, demonstrating that the extraction process was highly stable and exhibited good repeatability.

In comparison with the optimal values predicted by the model, the experimental %SA and %Y showed no statistically significant difference from the predicted

values at the 95% confidence level ($p > 0.05$). These findings confirm the reliability of the Box-Behnken model and the practical feasibility of the proposed optimal conditions, and further indicate that the multi-objective optimum achieved an effective balance between bioactive compound content and extraction yield under experimental conditions.

Although the Vietnamese Pharmacopoeia does not include a monograph for *S. henryi*, the obtained results are consistent with the quality requirement specified for *S. chinensis*, which stipulates an extraction yield of not less than 19.0%, calculated on a dried raw material basis, when extracted with 96% ethanol [20]. Previous studies have reported that the SA (in some cases referred to as deoxyschizandrin) content in *Schisandra* species ranges from 0.082% to 0.663%, depending on the species and geographical origin of the plant material [21-24]. The SA content determined for *S. henryi* in the present study falls within an intermediate range, reflecting interspecific variability in the accumulation of bioactive constituents among *Schisandra* species.

4. CONCLUSIONS

This study successfully applied response surface methodology to optimize the extraction process of *Schisandra henryi* (Southern *Schisandra*), an indigenous medicinal plant of Vietnam, with the aim of enhancing both extraction yield and schizandrin A recovery. The results demonstrated that ultrasound-assisted extraction using ethanol 96% as the solvent at 50°C for 64.37 min and a solvent-to-material ratio of 15.22mL/g constituted the optimal conditions, yielding the highest extraction efficiency and schizandrin A content. Establishing these optimal extraction parameters not only contributes to the standardization of the process for obtaining bioactive constituents from *Schisandra henryi* but also provides a scientific basis for the sustainable exploitation and development of this native medicinal resource. In the context of the potential use of *Schisandra henryi* as an alternative to Northern *Schisandra* (*Schisandra chinensis*) in certain medicinal and nutraceutical applications, the findings of this study enhance the utilization value, economic potential, and commercial feasibility of extracts derived from Southern *Schisandra*, while also offering guidance for future research and scale-up applications.

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REFERENCES

- [1]. Jaferník K., Ekiert H., Szopa A., "Schisandra henryi - A rare species with high medicinal potential," *Molecules*, 28(11), 4333, 2023.
- [2]. Szopa A., Barnaś M., Ekiert H., "Phytochemical studies and biological activity of three Chinese Schisandra species (*Schisandra sphenanthera*, *Schisandra henryi* and *Schisandra rubriflora*): current findings and future applications," *Phytochemistry Reviews*, 18, 109-128, 2019.
- [3]. Jaferník K., Szopa A., Barnaś M., Dziurka M., Ekiert H., "Schisandra henryi C.B. Clarke in vitro cultures: a promising tool for the production of lignans and phenolic compounds," *Plant Cell, Tissue and Organ Culture*, 143, 45-60, 2020.
- [4]. Nguyen X. T., Tran T. L., Cao N. G., Ly N. S., "A new subspecies of *Schisandra henryi* Clarke (Schisandraceae) from Tay Nguyen, Vietnam," *Taiwania*, 65(4), 521-528, 2020.
- [5]. Jaferník K., Kubica P., Dziurka M., Kulinowski Ł., Korona-Główniak I., Elansary H.O., Waligórski P., Skalicka-Woźniak K., Szopa A., "Comparative assessment of lignan profiling and biological activities of *Schisandra henryi* leaf and in vitro PlantForm bioreactor-grown culture extracts," *Pharmaceuticals*, 17(4), 442, 2024.
- [6]. Hou W., Gao W., Wang D., Liu Q., Zheng S., Wang Y., "The Protecting Effect of Deoxyschisandrin and Schisandrin B on HaCaT Cells against UVB-Induced Damage," *PLoS ONE*, 10(5), 2015. doi:10.1371/journal.pone.0127177
- [7]. Fu M., Sun Zh., Zong M., He X. P., Zuo H. C., Xie Z. P., "Deoxyschisandrin modulates synchronized Ca²⁺ oscillations and spontaneous synaptic transmission of cultured hippocampal neurons," *Acta Pharmacol Sin*, 29(8), 891-898, 2008. <https://doi.org/10.1111/j.1745-7254.2008.00821.x>
- [8]. Guo M., An F., Yu H., Wei X., Hong M., Lu Y., "Comparative effects of schisandrin A, B, and C on Propionibacterium acnes-induced, NLRP3 inflammasome activation-mediated IL-1 β secretion and pyroptosis," *Biomedicine & Pharmacotherapy*, 96, 129-136, 2017.
- [9]. Choi YH, "Schisandrin A prevents oxidative stress-induced DNA damage and apoptosis by attenuating ROS generation in C2C12 cells," *Biomedicine & Pharmacotherapy*, 106, 902-909, 2018.
- [10]. Zeng J., Liao S., Liang Z., Li C., Luo Y., Wang K., Zhang D., Lan L., Hu S., Li W., Lin R., Jie Z., Hu Y., Dai S., Zhang Z., "Schisandrin A regulates the Nrf2 signaling pathway and inhibits NLRP3 inflammasome activation to interfere with pyroptosis in a mouse model of COPD," *European Journal of Medical Research*, 28(217), 1-15, 2023.
- [11]. Zong W., Gouda M., Cai E., Wang R., Xu W., Wu Y., Muneke P.E.S., Lorenzo J.M., "The antioxidant phytochemical schisandrin A promotes neural cell proliferation and differentiation after ischemic brain injury," *Molecules*, 26(24), 7466, 2021.
- [12]. Lee HJ, Kim CY, "Simultaneous determination of nine lignans using pressurized liquid extraction and HPLC-DAD in the fruits of *Schisandra chinensis*," *Food Chemistry*, 120(4), 1224-1228, 2010.
- [13]. Cheng Z, Song H, Yang Y, Zhou H, Liu Y, Liu Z, "Smashing tissue extraction of five lignans from the fruit of *Schisandra chinensis*," *Journal of Chromatographic Science*, 2015, 1-11, 2015.
- [14]. Wang Y, Zhu J, Du X, Li Y, "Simultaneous extraction and determination of lignans from *Schisandra chinensis* (Turcz.) Baill. via diol-based matrix solid-phase dispersion with high-performance liquid chromatography," *Molecules*, 28(18), 6448, 2023.
- [15]. Zhang YB, Wang LH, Zhang DY, Zhou LL, Guo YX, "Ultrasound-assisted extraction and purification of schisandrin B from *Schisandra chinensis* (Turcz.) Baill seeds: optimization by response surface methodology," *Ultrasonics Sonochemistry*, 21(2), 461-466, 2014.
- [16]. Guo Y.X., Han J., Zhang D.Y., Wang L.H., Zhou L.L., "Aqueous two-phase system coupled with ultrasound for the extraction of lignans from seeds of *Schisandra chinensis* (Turcz.) Baill," *Ultrasonics Sonochemistry*, 20(1), 125-132, 2013.
- [17]. Zhao Q., Li J., Shang Q., Jiang J., Pu H., Fang X., Qin X., Zhou J., Wang N., Wang X., Gu W., "Optimization of the extraction process and biological activities of triterpenoids of *Schisandra sphenanthera* from different medicinal parts and growth stages," *Molecules*, 29(10), 2199, 2024.
- [18]. Zhang G., *Quality control method for Schisandra chinensis in Yixinshu traditional Chinese medicine preparation* [patent]. CN 101596274 A. 2009 Dec 9. <https://patents.google.com/patent/CN101596274A/zh>
- [19]. Sheng YH, Wang R, Wang YK, Li MM, Liu FX, Huang X, Chen CB, "Evaluation of multicomponent changes of *Schisandra chinensis* fruits with different drying process by UPLC-QQQ-MS-based targeted metabolomics analysis," *J Chem.*, 2022:2616122, 2022. doi:10.1155/2022/2616122
- [20]. Ministry of Health, *Vietnamese Pharmacopoeia*, Volume II, 5th edition. Medical Publishing House, Hanoi, pp. 1273-1274, 2017.
- [21]. Deng X, Chen X, Cheng W, Shen Z, Bi K, "Simultaneous LC-MS quantification of 15 lignans in *Schisandra chinensis* (Turcz.) Baill. Fruit," *Chromatographia*, 67:559-566, 2008.
- [22]. Hu J, Mao C, Gong X, Lu T, Chen H, Huang Z, Cai B, "Simultaneous determination of eleven characteristic lignans in *Schisandra chinensis* by high-performance liquid chromatography," *Pharmacognosy Magazine*, 9(34), 155-161, 2013.
- [23]. Wei H, Sun L, Tai Z, Gao S, Xu W, Chen W, "A simple and sensitive HPLC method for the simultaneous determination of eight bioactive components and fingerprint analysis of *Schisandra sphenanthera*," *Analytica Chimica Acta*, 662, 97-104, 2010.
- [24]. Lu TL, Hu JY, Mao CQ, Wu Y, Yin FZ, Cai BC, "Quality analysis of raw and processed *Schisandra chinensis* fructus by simultaneous determination of eleven bioactive lignans using RP-HPLC method," *Journal of Food and Drug Analysis*, 20(4), 846-854, 2012.