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Optimization of the Extraction Process for 6-Gingerol-Rich Extract from *Zingiber officinale* Roscoe Residue Using the Response Surface Methodology

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Abstract— Optimizing the extraction of 6-gingerol enriched extract from ginger's (*Zingiber officinale* Roscoe) residue after distillation is essential for enhancement the value of ginger by-products. Typically, ginger residue is either discarded or underutilized, resulting in resource wastage and environmental concerns. Given the significant pharmacological and economic potential of 6-gingerol, a main compound, an efficient extraction process can enhance sustainability, minimize waste, and support the development of ginger exploitation. This study aims to improve resource efficiency and promote a circular economy in ginger processing by refining the extraction process for higher yield and effectiveness.

***Index Terms*— Vietnamese ginger, 6-gingerol enriched extraction, ginger waste, ginger residue.**

1. Introduction

The Zingiber genus belongs to the Zingiberaceae family and comprises approximately 150 different species, with 34 species reported in China, 24 species in India and 17 species in Vietnam. The chemical composition of ginger rhizomes varies depending on the cultivar, climate, soil conditions, cultivation practices, and harvest time. Fresh ginger typically contains over 80% moisture, 2.3% protein, 0.9% fat, 1.2% minerals, 2.4% fiber, and 12.3% carbohydrates, along with trace elements such as iron, calcium, and phosphorus, as well as vitamins like thiamine, riboflavin, niacin, and ascorbic acid. In addition to essential oil components, the pungent taste of ginger is attributed to bioactive compounds such as 6-gingerols, gingerdiol, zingerone, and shogaols, which constitute approximately 8% of the ginger oleoresin. The main compounds in ginger extract are zingerone, 6-gingerol, gingerdiol, zingerone, shogaol [1].

In 2002, Bui Quang Thuat *et al.* conducted a study on the production of oleoresin from ginger of Vietnam, focusing on extraction technology [2]. 95% ethanol and ethyl acetate were used for extraction and purification, respectively, yielding ginger oleoresin with approximately 24% 6-gingerol and 19% essential oil. Wei Liu *et al*. compared five extraction methods for 6-gingerol from ginger, using 1g of ginger for each method [3]. Except for the MAE method, all other techniques used 80% ethanol as the solvent with a solvent-to-material ratio of 25:1 (mL/g). In a 2023 study by Monserrat Gonzalez *et al*., the UAE method was applied to extract 6-gingerols and shogaols [4]. The optimal extraction conditions were identified as 96% ethanol at 60°C for 10 minutes, with an ultrasonic power of 51.8%, a cycle of 0.458 s^{-1}, and a sample-to-solvent ratio of 0.302g:20mL

This study aims to optimize the extraction process of 6-gingerol-rich extract from *Zingiber officinale* Roscoe residue after essential oil removal using response surface methodology.

2. Materials and Methods

A. Ginger Sample

Ginger (*Zingiber officinale*) residues was collected from ginger's company in Hung Yen in January 2023. The residue was dried to 8% of humidity and kept for experiment.

B. Chemicals and Regents

Standard: 6-gingerol (98%, lot PRF8012004) was purchased from Chengdu Biopurify Phytochem, China.

Solvent: Acetonitrile (≥ 99.9%) (HPLC, Fisher, USA), methanol, ethanol, n-hexane, ethyl acetate (HPLC grade, China), were used for experiments

C. Quantification of 6-Gingerol by HPLC

The quantification of 6-gingerol in ginger residue was performed using High-Performance Liquid Chromatography (HPLC). The method was developed based on the Chinese Pharmacopoeia and validated on a Shimadzu HPLC system. The chromatographic conditions were as follows: A Shim-pack GIST C18 column (250 × 4.6 mm; 5 µm) was used for separation. The detection wavelength was set at 282 nm. The mobile phase consisted of acetonitrile and water. The flow rate was maintained at 1 mL/min, and the injection volume was 10 µL.

A precisely weighed 0.25 g of powdered sample was placed

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into a ground-glass-stoppered Erlenmeyer flask. Subsequently, 50 mL of 75% methanol was added, and the total mass was recorded. The mixture was sonicated (100 W, 40 kHz) for 40 minutes, allowed to cool, and reweighed to compensate for solvent loss. The extract was then filtered through a 0.45 µm membrane filter before HPLC analysis. The concentration of 6-gingerol in the sample was calculated using the following formula:

$$\chi = \frac{C\times50\times P}{m\times10^{2}\times(100-w)}$$

Where:
X: 6-Gingerol content in the sample (%)
C: The concentration of 6-gingerol in the analytical solution (µg/mL).
50: The volume of extraction solvent (mL).
P: The purity of the reference standard (0.98 or 98%).
m: The initial mass of the sample (g).
w: The moisture content of the sample (%).

D. Experiment Design and Optimization Using Response Surface Methodology (RSM)

The RSM method was utilized to assess the quantity of gingerol in ginger's residue. The optimization involved refining key extraction parameters including ethanol concentration, extraction time, extraction temperature and the ratio of solvent and material [5].

E. Statistical Analysis

One-way analysis of variance (ANOVA) was conducted to identify statistically significant differences, followed by post hoc Tukey test calculations. Results are expressed as means ± standard deviations of triplicates where applicable. Response surface modeling and variance analysis (ANOVA) were performed using Design-Expert version 11 software (StatEase Inc., Minneapolis, USA).

3. Results

A. The Influence of the Extraction Solvent Concentration

According to the previous reported [6-7], 6-gingerol is commonly extracted using various solvents such as methanol, ethanol, and acetone. With the aim of applying this process on a large scale, the use of ethanol will be easier and safer compared to other solvents. Therefore, in this study, ethanol was used as the solvent for the extraction process. The effect of ethanol concentration on the extraction yield of 6-gingerol was studied at ethanol concentrations of 60, 70, 80, 90, and 96%. The results are shown in the following Figure 1.

As the ethanol concentration raised from 60% to 80%, the 6-gingerol content in the extract increased sharply from 5.48% to 11.09%. However, at 90% ethanol, the 6-gingerol content drops to 10.24%, and it further decreases to 8.79% at 96%. This pattern indicates that higher ethanol concentrations reduce solvent polarity to a level that is less compatible with 6-gingerol, thereby diminishing extraction efficiency. Supporting this, Dent *et al.* (2013) found that compound recovery during extraction is influenced by solvent type, polarity, and the solubility of target compounds [8]. Consequently, ethanol concentrations of 80% (baseline), 70% (low), and 90% (high) were selected for the experimental design matrix.

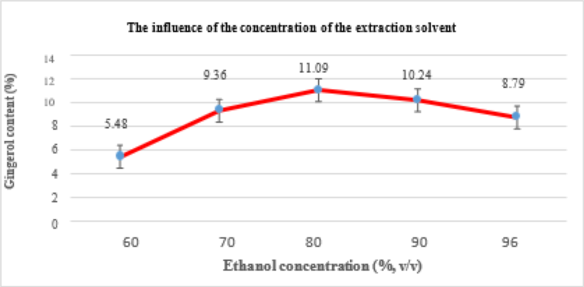


Fig. 1. The effect of ethanol concentration on the yield of 6-gingerol

B. The Influence of the Extraction Temperature

Results on the investigation of extraction at 55°C, 60°C, 65°C, 70°C and 75°C are presented in Figure 2.

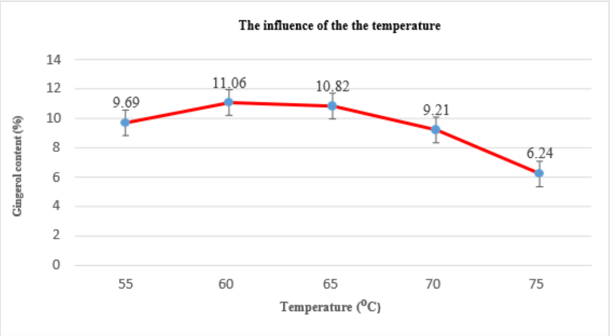


Fig. 2. The effect of temperature on the yield of 6-gingerol

It is evident that as the extraction temperature reaches a certain point, the extraction efficiency of gingerol achieves its peak value due to the reduction in the surface tension of the solvent at higher temperatures, which accelerates the diffusion and mass transfer processes, allowing extraction to occur more quickly. However, excessively high extraction temperatures can lead to chemical reactions such as oxidation, which diminishes gingerol content. Additionally, high temperatures may result in the formation of gel-like compounds that hinder the extraction of gingerol. Therefore, the extraction temperatures of 55°C, 60°C, and 65°C were selected as the baseline level (level 0), low level (-1), and high level (+1), respectively, for the subsequent experimental design.

C. The Influence of the Extraction Time

Extraction was investigated for 20, 30, 40, 50, and 60 minutes. Initially, it can be observed that increasing the extraction time allows soluble compounds to diffuse better into the solvent due to enhanced mass transfer. However, after a certain threshold, an equilibrium state is established, and further increasing the extraction time may not lead to any significant changes in extraction yield [9]. Conversely, extending the extraction time can result in high-temperature exposure, potentially causing unwanted chemical reactions or alterations in sensitive organic compounds. This explains the observed reduction in 6-gingerol content in the extract with prolonged extraction time. Based on the obtained results (Fig. 3), extraction times of 50 minutes, 40 minutes, and 60 minutes were selected as the baseline level (level 0), low level (-1), and high level (+1), respectively, for the subsequent experimental design matrix.

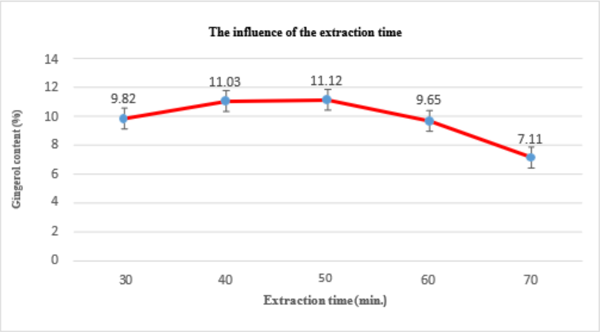


Fig. 3. The effect of extraction time on the yield of 6-gingerol

D. *The Influence of the Extraction Solvent Ratio*

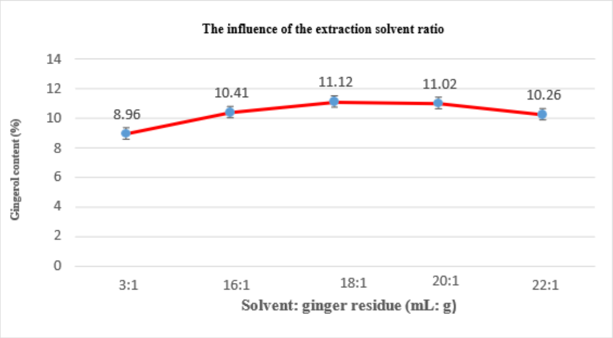


Fig. 4. The effect of the ratio solvent: ginger residue on the yield of 6-gingerol

As the volume of the solvent increases, the surface contact between the material and the solvent improves, allowing compounds to dissolve more rapidly and easily. However, when the solvent volume reaches a sufficiently large quantity, further increases in solvent volume do not enhance the extraction efficiency, as an equilibrium state has already been established. Based on the obtained results (Fig. 4) and to ensure economic viability, solvent to material ratios of 16:1, 18:1, and 20:1 were selected as the baseline (level 0), low level (-1), and high level (+1) for subsequent experiments in the experimental design matrix.

E. *Optimization of the Ginger Residue Extraction Process Using Response Surface Methodology (RSM)*

The experimental design and planning matrix are presented in Table 1 and Table 2, respectively.

The significance of the models and coefficients is conducted through analysis of variance (ANOVA). The analysis of variance indicated that the model was consistent with the experimental data. This was evidenced by the model's F-statistic (Fisher's test) value of 36.90. The model was also statistically significant with a high level of confidence, as the p-value is less than 5% ($p < 0.0001$). The model's fit to the experimental data was further verified using the coefficient of determination (R^2). The closer the R^2 value is to 1, the closer the experimental values are to the model's predicted values. The model's R^2 was 0.9773 (97.73%), while the adjusted R^2 (Adj-R^2) was 0.9508 (95.08%). Additionally, the model's Adeq-Precision (signal-to-noise ratio) was 19.424. According to Guan and Yao (2008) and Zabeti et al. (2009), a model is considered highly compatible with experimental data when both R^2 and Adj-R^2 exceed 0.8, and an Adeq-Precision value greater than 4 is required [10,] [11]. Furthermore, the model's "Lack of Fit" test had a p-value > 0.05, indicating that the lack of fit is not significant. This confirms that the developed model had a high level of agreement with the experimental data. The model's compatibility can also be assessed through predicted and actual value plots, as well as residuals versus runs models, which are illustrated in Figure 5. A strong correlation between experimental and theoretical results is observed when the experimental data points align along a straight diagonal line in the first graph, and the residuals are randomly distributed within the range (-4, 4) in the (b) graph.

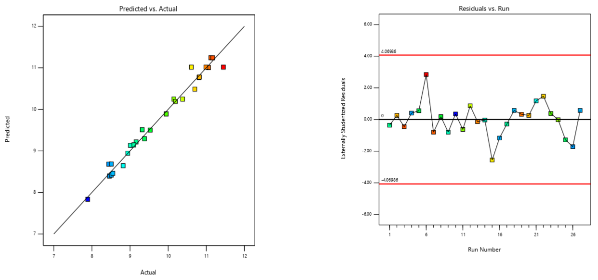
Table 1
Experimental level

Actual variable	**Variable code**	**Variation range**	**Research range**		
			-1	**0**	**+1**
Z1: Ethanol concentration (%)	A	10	70	80	90
Z2: Extraction temperature (°C)	B	5	55	60	65
Z3: Extraction time (min)	C	10	40	50	60
Z4: Solvent/material ratio	D	1:2	16:1	18:1	20:1

Table 2
Experimental planning matrix for the 6-gingerol extraction

No	**Coded variable**				**Y %**	
	A	**B**	**C**	**D**	**Experiment**	**Design**
1	-1	-1	0	0	7.89	7.83
2	+1	-1	0	0	9.38	9.29
3	-1	+1	0	0	9.53	9.50
4	+1	+1	0	0	9.95	9.89
5	0	0	-1	-1	10.70	10.49
6	0	0	+1	-1	8.46	8.40
7	0	0	-1	+1	11.06	11.01
8	0	0	+1	+1	10.15	10.25
9	-1	0	0	-1	9.01	9.13
10	+1	0	0	-1	8.44	8.68
11	-1	0	0	+1	8.94	8.96
12	+1	0	0	+1	11.12	11.24
13	0	-1	-1	0	9.32	9.51
14	0	+1	-1	0	11.17	11.24
15	0	-1	+1	0	8.51	8.68
16	0	+1	+1	0	9.16	9.22
17	-1	0	-1	0	9.10	9.15
18	+1	0	-1	0	10.81	10.77
19	-1	0	+1	0	8.51	8.42
20	+1	0	+1	0	8.82	8.64
21	0	-1	0	-1	8.55	8.46
22	0	+1	0	-1	10.19	10.19
23	0	-1	0	+1	10.38	10.25
24	0	+1	0	+1	10.82	10.78
25	0	0	0	0	10.99	11.02
26	0	0	0	0	11.45	11.08
27	0	0	0	0	10.61	11.02

Additionally, the analysis of the predicted versus actual value plots and the residual distribution further supports the model's strong compatibility with the experimental results (Figure 5).



(a) (b)

Fig. 5. Experimental and predicted value plot (a), random distribution (b) of the objective function Y

Based on the analysis results, the objective function of the model was determined by the second-order regression equation:

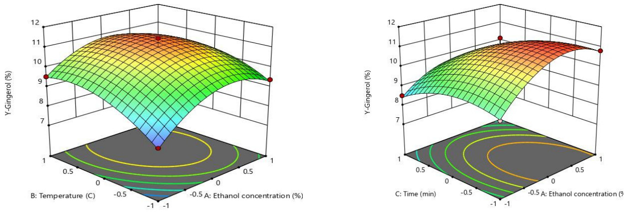
$$Y = 11.02 + 0.46A + 0.56B - 0.71C + 0.59D - 0.26AB - 0.35AC + 0.68AD - 0.3BC - 0.3BD + 0.33CD - 1.15A^2 - 0.73B^2 - 0.62C^2 - 0.36D^2 \quad (1)$$

The greatest impact on Y comes from the linear effects (A, B, C, D), followed by the interaction effects (AB, AC, AD, BC, BD, CD), and the least impact comes from the quadratic effects (A^2, B^2, C^2, D^2). Among them, A, B, and D have a positive effect, while C has a negative effect. The influence order is: C > D > B > A.

The interaction effects AD and CD positively impact Y, whereas AB, AC, BC, BD, and the quadratic effects have a negative impact.

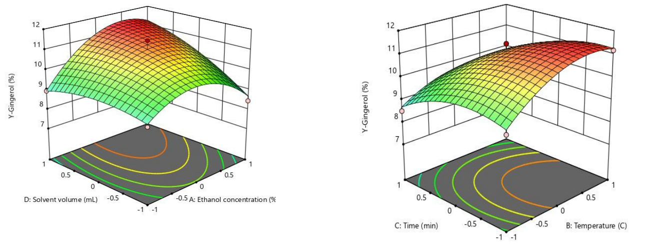
The response surface in Figure 6 illustrates the interaction between technological factors, where the optimal region (dark red) has the highest Y values. This analysis aligns with previous univariate results, identifying the optimal conditions:

Ethanol concentration was the best in the range of 0.5 – 1
Extraction temperature was the best in the range of 0 – 0.5
Extraction time was the best in the range of -1 – 0.5
Solvent volume was the best in the range of 0.5 – 1



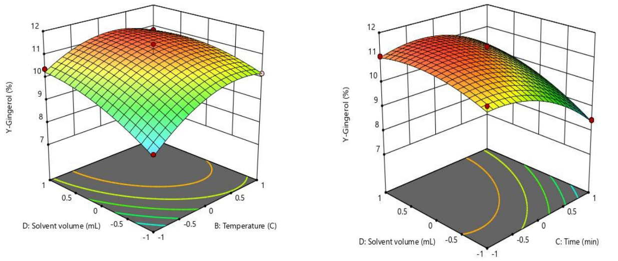
Response surface of Y-6-gingerol content as a function of ethanol concentration and temperature

Response surface of Y-6-gingerol content as a function of ethanol concentration and extraction time



Response surface of Y-6-gingerol content as a function of ethanol concentration and solvent ratio

Response surface of Y-6-gingerol content as a function of extraction time and temperature



Response surface of Y-6-gingerol content as a function of temperature and solvent ratio

Response surface of Y-6-gingerol content as a function of solvent ratio and extraction time

Fig. 6. The response surface from the interaction effects of technological factors on the objective function Y

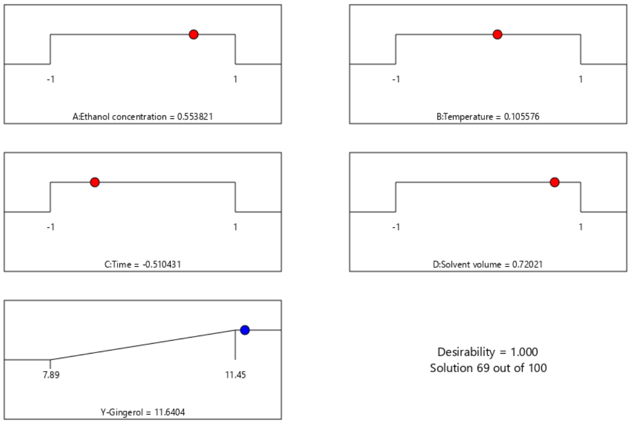


Fig. 7. Optimal conditions and values of objective functions

Table 3
Optimization of technological factors

Coded variable				Real variable (rounded)			
A	**B**	**C**	**D**	**Ethanol concentration (%)**	**Extraction temperature (°C)**	**Extraction time (min)**	**Solvent ratio**
0.553	0.105	-0.51	0.72	85.53	60.05	45.1	19.4:1

Table 4
Experimental results of the objective functions under optimal conditions

Technological parameter				Y function	
Ethanol concentration (%)	**Temperature (°C)**	**Extraction time (min)**	**Solvent: material**	**Experimental (%)**	**Theoretical (%)**
86	60	45	19:1	11.46 ± 0,42	11.64

The extraction process is optimized to maximize the objective function Y (6-gingerol content) using the desirability function method in Design Expert 13.0.0, with the variables shown in Table 3.

The optimization results (Figures 7) indicated that under the technological conditions, the predicted Y value reaches 11.64% (Table 4).

The experiment was repeated three times with the technological parameter set under optimal conditions, which include: ethanol concentration of 86%, extraction temperature of 60°C, extraction time of 45 minutes, and solvent ratio to material of 19: 1. The test results are presented in Table 4.

Table 4. Experimental results of the objective functions under optimal conditions.

The results in Table 4 showed that the experimental results at optimal conditions are very close to the predicted values of the objective function (with an error of less than 5%). This once again confirms that the optimal computational model aligns well with the experimental data. Additionally, the extraction efficiency of 6-gingerol at optimal conditions reaches 90.26%.

4. Conclusion

This study optimized the extraction process of 6-gingerol-rich extract from the residue of *Zingiber officinale* Roscoe. By employing response surface methodology (RSM), optimal extraction conditions were identified, including an ethanol concentration of 85%, an extraction temperature of 61°C, an extraction time of 12 minutes, and a solvent-to-material ratio of 5.7:1. The experimental results demonstrated a high extraction efficiency of 6-gingerol, achieving 90.26% under these optimal conditions, which closely aligned with the predicted values from the model. This research not only enhances the value of ginger by-products but also contributes to sustainable practices in ginger processing, promoting a circular economy. The findings underscore the potential of refining extraction techniques to maximize resource utilization and minimize waste, thereby supporting both economic and environmental sustainability in the ginger industry. Future studies may explore the application of these optimized conditions on a larger scale and investigate the bioactive properties of the extracted compounds for potential health benefits.

Acknowledgments

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