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EXPERIMENTAL PAPER

Optimization of microwave-assisted extraction of phenolic compounds from ginger (*Zingiber officinale* Rosc.) using response surface methodology

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Summary

Introduction: Ginger (*Zingiber officinale* Rosc.) is a common spice and precious herbal plant in Vietnam. It contains many bioactive compounds, especially phenolic compounds useful for human health. Hence, the extraction and application of these compounds in medical technology are necessary.

Objective: The goal of this study is to determine the optimal extraction conditions with the assistance of microwave, for instance solvent/material ratio (ml/g), solvent concentration (%, *v/v*) and extraction time, on the extraction yield of ginger rhizome, such as total polyphenol content (TPC) and antioxidant capacity (AC).

Methods: The dried sample was extracted by microwave-assisted extraction (MAE). TPC and AC of received extract were measured by the Folin-Ciocalteu method and phenanthroline assay. The optimization process used response surface methodology (RSM) (Central composite face design, CCF) with major influencing factors including solvent concentration, solvent/material ratio and extraction time.

Results: The results showed that the optimal extraction conditions were the ethanol concentration of 60%, ethanol/material ratio of 48.6/1 (ml/g), extraction time of 1 minute.

Conclusion: The maximum TPC and AC peaked at 27.89±1.99 mg GAE/g dry matter and 12.24±0.04 mmol Fe/g dry matter (DM) at optimal extraction conditions. Besides, some factors strongly affected the extraction yield and interacted together.

Key words: ***antioxidant, extraction, ginger, microwave, phenolic compounds, response surface methodology (RSM)***

Słowa kluczowe: ***antyoksydacja, ekstrakcja, imbir, promieniowanie mikrofalowe, związki fenolowe, response surface methodology RSM (metoda powierzchni odpowiedzi)***

INTRODUCTION

Nowadays, when the population grows, people are more concerned about their health, which leads to continuous development of functional foods as well as the studies on natural compounds from plants, mainly due to the fact that plants produce a significant amount of antioxidants destroying free radicals and preventing oxidative stress. Oxidative stress and free radicals affect metabolism and cellular activity leading to cell destruction [1, 2] and seriously affecting human health. Plants are a potential source of new compounds that have antioxidant activity [3]. There are many different antioxidant compounds in plants such as flavonoids, tannins, phenolics, alkaloids and ascorbic acid which can repair these injuries. In addition, phytochemicals also play an important role in skin wound healing, prevention of infections, cardiovascular and neurological protection, anti-cholesterol action, cancer prevention [1]. Currently, the isolation of bioactive compounds from plants is quite easy with many different methods, especially with use of phenolic compounds. In some previous studies also successful extraction of these compounds was shown, with various materials, for instance tea [4], ginger [5], quercus bark [6], pomegranate peel [7], etc.

Among them, ginger (*Zingiber officinale* Rosc.) is a good source of phytochemicals. It possesses powerful antioxidants, destroys free radicals, thus protecting against certain diseases. In addition, ginger is an inexpensive food, widely used as a spice or traditional medicine in local tribes in Asia, mostly to cure common flu. Besides, it is considered to be a safe herbal medicine and has great potential in functional foods, for instance ginger tea, ginger starch, etc. In addition, supplementing ginger in meals is also considered to be a new way to prevent chronic diseases. It can fight inflammation, protect cells, has anticoagulant and anti-cancer potential [8]. Currently, in many studies it was pointed out that ginger is a very good herbal medicine for effective prevention of nausea and pain [9]. Ginger extracts have anti-inflammatory, anti-cancer, antifungal and other health effects because of the activities of bioactive compounds, especially phenolic compounds [10]. Some studies also showed that ginger contains many precious phenolic compounds, for instance 6-gingerol, 8-gingerol, 10-gingerol, 6-shogaol, 8-shogaol, 10-shogaol, dehydro-6-gingerdione, dehydro-10-gingerdione, 6-paradol [11], (+)-catechin, gallic acid and 3, 4-dihydroxybenzoic acid [12]. Therefore, the use of ginger in pharmaceutical industry or functional food production is feasible.

Until now, there have been many methods to extract phenolic compounds from plants, such as microwave-assisted extraction (MAE), utrasound-assisted extraction (UAE), enzyme-assisted extraction (EAE), maceration, etc. Among them, MAE is the process of the use of microwave energy and solvent to extract natural compounds. This method widely used in extraction technique from herbal plant, flower, fruit waste, etc, for instance, *Polygonum multiflorum* Thunb. root [13], blackthorn flowers [14], kinnow peels [15], etc. For MAE method, the suitable temperatures and pressures can extract the desired compounds into a solvent with a faster rate compared to conventional methods. The main advantages of MAE save the extraction time and are less the solvent [16]. There are also many factors that strongly affect TPC and AC, for instance moisture content, particle size, solvent type, material/solvent ratio, device capacity, extraction time, temperature and extraction pressure [17]. Positive or negative role of each factor in extraction process is not always clear and it is quite difficult to predict. Therefore, response surface methodology (RSM) is an effective approach to process development and optimization. It also provides more information out of smaller number of experiments and determines interactions between factors. In addition, this method can precisely predict the results [18].

Until now, there has been no study on optimization of MAE process of polyphenols from ginger by response surface methodology. For this reason, the main objective of the study is to apply the central composite face (CCF) model to optimize the extraction conditions (solvent concentration, solvent/material ratio and extraction time) for ginger extract and maximize total polyphenol content (TPC) and antioxidant capacity (AC) simultaneously.

MATERIAL AND METHODS

Sample preparation

Ginger rhizome *(Zingiber officinale)* were harvested from Nghe An province (Vietnam). Its age was from 6 to 9 months, fresh, intact and with no physical damage, strong aroma, dark yellow inside. Rhizome was cleaned, sliced and dried at 60°C until moisture was lower than 12%. The slices were ground into a fine powder (<0.5 mm) and packed in vacuum. It was stored in the dark at room temperature.

Chemicals and reagents

Gallic acid and Folin-Ciocalteu (FC) were purchased from Sigma-Aldrich (USA). The organic solvents (ethanol, methanol and distilled water) and other chemicals (1,10-phenanthroline, $FeSO_4 \cdot 7H_2O$, $FeCl_3$ and Na_2CO_3) used in this study were of analytical reagent grade.

Extraction process

Dried samples (2 g) were extracted by ethanol as a solvent (40–60%, by volume), solvent to solid ratio of 30–50 ml/g and extraction time of 1–5 min. The extraction process was carried out with using a microwave apparatus (Sanyo, model EM-S2088W, China). The values of operating parameters were set according to the CCF table (tab. 1). The received extracts were filtered through Whatman No. 4 filter paper for removal of the residue and then was prepared for TPC and AC.

Determination of TPC in extracts

The method used is the Folin-Ciocalteu assay. Phenolic compounds in extract react with the reagent containing blue chromogens in alkaline pH conditions and the absorbance was measured at a wavelength of 738 nm in a Genesys 20 spectrophotometer (USA). Measurements were based on the standard curve obtained with gallic acid as a standard reagent [19]. Total polyphenol content (TPC) was calculated as mg of gallic acid equivalents (GAE) per gram of dry matter (mg GAE/g DM).

Determination of AC in extracts

Antioxidant capacity (AC) was determined by the color of the 1,10-phenanthroline solution in methanol. Reactions of Fe (II) and 1,10-phenanthroline complexes had a characteristic orange-red color. The result was based on the standard curve measured at a wavelength of 510 nm [20]. AC was calculated as mmol Fe equivalents per gram of dry matter (mmol Fe/g DM).

Experimental design

The central composite face design (CCF) comprising 20 experimental runs with 6 experiments at the center was employed. These experiments were performed based on the influencing factors such as solvent concentration, solvent/material ratio and extraction time. All levels of independent variables and CCF design were presented in tables 1 and 2, respectively. The ranges of the parameters were selected based on the prior screening experiments.

Experimental data were expressed by quadratic polynomial models for correlation with independent variables. The general CCF design and the regression equation were calculated by the quadratic polynomial as follows:

$$Y = a_o + a_1X_1 + a_2X_2 + a_3X_3 + a_{11}X_1^2 + a_{22}X_2^2 + a_{33}X_3^2 + a_{12}X_1X_2 + a_{13}X_1X_3 + a_{23}X_2X_3$$

where the investigated responses (Y) named total polyphenol content (TPC, mg GAE/g DM) or antioxidant capacity (AC, mmol Fe/g DM). X_1, X_2 and X_3 were the independent variables.

Statistical data analysis

All the experimental data collected from the extraction process were analyzed using Modde 5.0 software (Umetrics AB company, Sweden) that was set to search the optimal desirability of the investigated response, for instance the maximum TPC and AC. Strength of analysis was assessed by one-way analysis of variance (ANOVA). The optimal extraction conditions were determined by three dimensional (3D) response surfaces and contour plots.

Ethical approval: The conducted research is not related to either human or animal use.

Table 1

Coded level and actual values of independent factors

Independent factors	Symbols	Coded levels		
		−1	0	1
Concentration of ethanol [%]	X_1	40	50	60
Ethanol/material ratio [ml/g]	X_2	30/1	40/1	50/1
Extraction time [min]	X_3	1	3	5

Table 2

Experimental design matrix and predicted results for TPC and AC

Run	Independent variables			Responses			
	X_1	X_2	X_3	Y_1 [TPC, mg GAE/g DM]		Y_2 [AC, mmol Fe/g DM]	
				Exp.	Pred.	Exp.	Pred.
1	40	30	1	14.79	14.47	1.8	1.77
2	60	30	1	26.25	26.44	10.01	9.90
3	40	50	1	16.34	16.19	5.98	5.67
4	60	50	1	28.12	27.79	12.62	12.33
5	40	30	5	17.46	17.73	2.47	2.75
6	60	30	5	27.46	27.55	10.09	10.39
7	40	50	5	15.09	14.84	3	3.10
8	60	50	5	24.03	24.29	9.25	9.26
9	40	40	3	16.65	17.10	3.15	3.11
10	60	40	3	28.02	27.81	10.17	10.26
11	50	30	3	22.53	22.30	8.69	8.25
12	50	50	3	21.06	21.53	9.15	9.64
13	50	40	1	21.21	21.80	10.1	10.84
14	50	40	5	22.03	21.67	10.48	9.80
15	50	40	3	22.48	22.47	9.1	9.53
16	50	40	3	22.1	22.47	9.8	9.53
17	50	40	3	22.94	22.47	9.2	9.53
18	50	40	3	22.43	22.47	9.63	9.53
19	50	40	3	22.69	22.47	9.74	9.53
20	50	40	3	22.64	22.47	9.82	9.53

RESULTS AND DISCUSSION

Optimization of the extraction process

The experimental conditions of polyphenols extraction with MAE and responses for the 20 extraction treatments are shown in table 2. They were expressed according to the CCF design and this model was used to investigate the effect of solvent concentration, solvent/material ratio and extraction time on the TPC and AC of ginger rhizome extract. Table 3 shows that obtained results of RSM in the form of analysis of variance (ANOVA) for the regression model are summarised.

Analysis of variance indicated that the p_{values} of the developed response surface models for the TPC and AC were below 0.05. Besides, p_{values} of the lack of fit tests were higher than 0.05 (p_{value}=0.087 and p_{value}=0.091 for TPC and AC, respectively) (tab. 3). This pointed out that the regression models could be used to predict the responses. In addition, the values of R^2 for TPC and AC were 0.994 and 0.987, respectively. This indicated that the models explained 99.4% and 98.7% of total variation, while the values of R^2_{adj} were quite close to the values of R^2 (R^2_{adj}=0.988 and R^2_{adj}=0.976 for TPC and AC, respectively), indicating that the model fits the experimental data. These results were also similar to those of Thanh-Blicharz *et al.* [21] and Phaiphan [22], who also researched on antioxidant capacity of starch products and banana fruit peels, respectively.

Moreover, according to Eriksson *et al.* [23], the values of Q^2 in the model is the goodness of prediction and estimates the predictive power of the model. The values of Q^2 for TPC and AC were 0.95 and 0.919; they should be regarded as good (Q^2>0.5 and R^2-Q^2<0.3). Therefore, the model obtained is quite accurate for predicting the responses.

Table 3 shows that the multivariable linear regression was performed to analyse and predict the constants, coefficients of linear, quadratic and interaction effects of extraction factors. The regression equation was determined below:

$$Y_1 = 22.468 + 5.355X_1 - 0.385X_2 - 0.732X_3^2 - 0.538X_1X_3 - 1.153X_2X_3 \quad (1)$$

$$Y_2 = 9.53+3.574X_1+0.694X_2-0.522X_3-2.841X_1^2+0.789X_3^2-0.888X_2X_3 \quad (2)$$

Table 3

Results of analysis of correlation coefficients

Y_1	Coefficient	Std. Err	*p*	Y_2	Coefficient	Std. Err	*p*
Constant	22.468	0.150	4.33E-18	Constant	9.53	0.166	6.23E-14
X_1	5.355	0.138	3.09E-12	X_1	3.574	0.153	4.58E-10
X_2	-0.385	0.138	0.019	X_2	0.694	0.153	0.001
X_3	-0.064	0.138	0.653	X_3	-0.522	0.153	0.007
X_1*X_1	-0.017	0.263	0.950	X_1*X_1	-2.841	0.291	1.99E-06
X_2*X_2	-0.557	0.263	0.061	X_2*X_2	-0.581	0.291	0.074
X_3*X_3	-0.732	0.263	0.019	X_3*X_3	0.789	0.291	0.022
X_1*X_2	-0.093	0.154	0.562	X_1*X_2	-0.368	0.171	0.057
X_1*X_3	-0.538	0.154	0.006	X_1*X_3	-0.123	0.171	0.489
X_2*X_3	-1.153	0.154	2.14E-05	X_2*X_3	-0.888	0.171	0.0004
	Regression		0.000		Regression		0.000
	Lack of fit		0.087		Lack of fit		0.091
	RSD (CV)=0.437				RSD (CV)=0.483		
N=20	R^2=0.994	Q^2=0.95	R^2_{adj}=0.988	N=20	R^2=0.987	Q^2=0.919	R^2_{adj}=0.976

Based on table 2, the results show that TPC of ginger rhizome extract ranged from 14.79 to 28.12 mg GAE/g DM and AC ranged from 1.9 to 12.62 mmol Fe/g DM. The regression equation (1) and (2) also pointed out that TPC and AC were strongly affected by the independent variables such as solvent/material ratio, solvent concentration and extraction time.

As it was shown in table 3 and the regression equation (1), TPC depends mainly on the solvent concentration (X_1) (the strongest positive effect) and solvent/material ratio (X_2) for the linear term; while it depends only on the extraction time (X_3) for quadratic effect. In addition, there are the interactions between solvent concentration (X_1) and extraction time (X_3); solvent/material ratio (X_2) and extraction time (X_3) (the strongest negative effect). Table 3 shows that some parameters (X_3, X_1^2, X_2^2 and X_1X_2) have p_{values}>0.05. This proved that their effects on TPC and AC are insignificant, therefore, they were eliminated from equation (1). Table 3 and the regression equation (2) also show that AC depends on all independent variables including the solvent concentration (X_1) (the strongest positive effect), solvent/material ratio (X_2) and the extraction time (X_3) for the linear term. Regarding the quadratic effect, the solvent concentration (X_1) and the extraction time (X_3) have negative and positive effects on AC, respectively; whereas there is only interaction between solvent/material ratio (X_2) and extraction time (X_3) (negative effect). In the equation (2), X_2^2, X_1X_2 and X_1X_3 were also eliminated due to p_{values}>0.05. Hence, the TPC and AC were not affected by these parameters. These results are in agreement with those of study of Simíc et al. [24] or Xu *et al.* [25], they proved that extraction conditions (type and concentration of solvents, extraction time and temperature, etc.) had a significant impact on TPC and AC of plant extract.

Based on the received results, TPC and AC depend on all extraction factors in this study including solvent/material ratio, solvent concentration and extraction time.

Response surface plots

Figures 1 and 2 show the effects of solvent concentration (X_1), solvent/material ratio (X_2) and extraction time (X_3) on TPC and AC. Typically, the response surface plot illustrated the correlation between response and factors. Each plot showed that the two factors affected TPC and AC, while the third factor was not changed. The TPC increased gradually from 15.8 to 27.5 mg GAE/g DM and AC also increased sharply from 1.8 to 12.8 mmol Fe/g DM, when solvent concentration increased from 40 to 60% and the solvent/material ratio rose from 30/1 to 50/1 (ml/g) (fig. 1 and 2). This pointed out that the higher solvent concentration and solvent/material ratio improved TPC and AC value. In addition, the optimal extraction time was 1 minute. The increase in solvent concentration leads to changes in polarity and phenolic compounds were easily dissolved into the solvent. Besides, the solvent/material ratio increases with the increase in the diffusion rate, it results in the improved extraction yield. In this case, extending extraction time has an undesired effect because the bioactive compounds are easily degraded at high temperatures for a long time.

The extraction time of this study was quite different from that of the study of Garofulic *et al.* [26], they extracted phenolic compounds from sour cherry Marasca by MAE for 10 min using RSM. In addition, the solvent/material ratio and solvent concentration also were significantly different to those of study of Hayat *et*

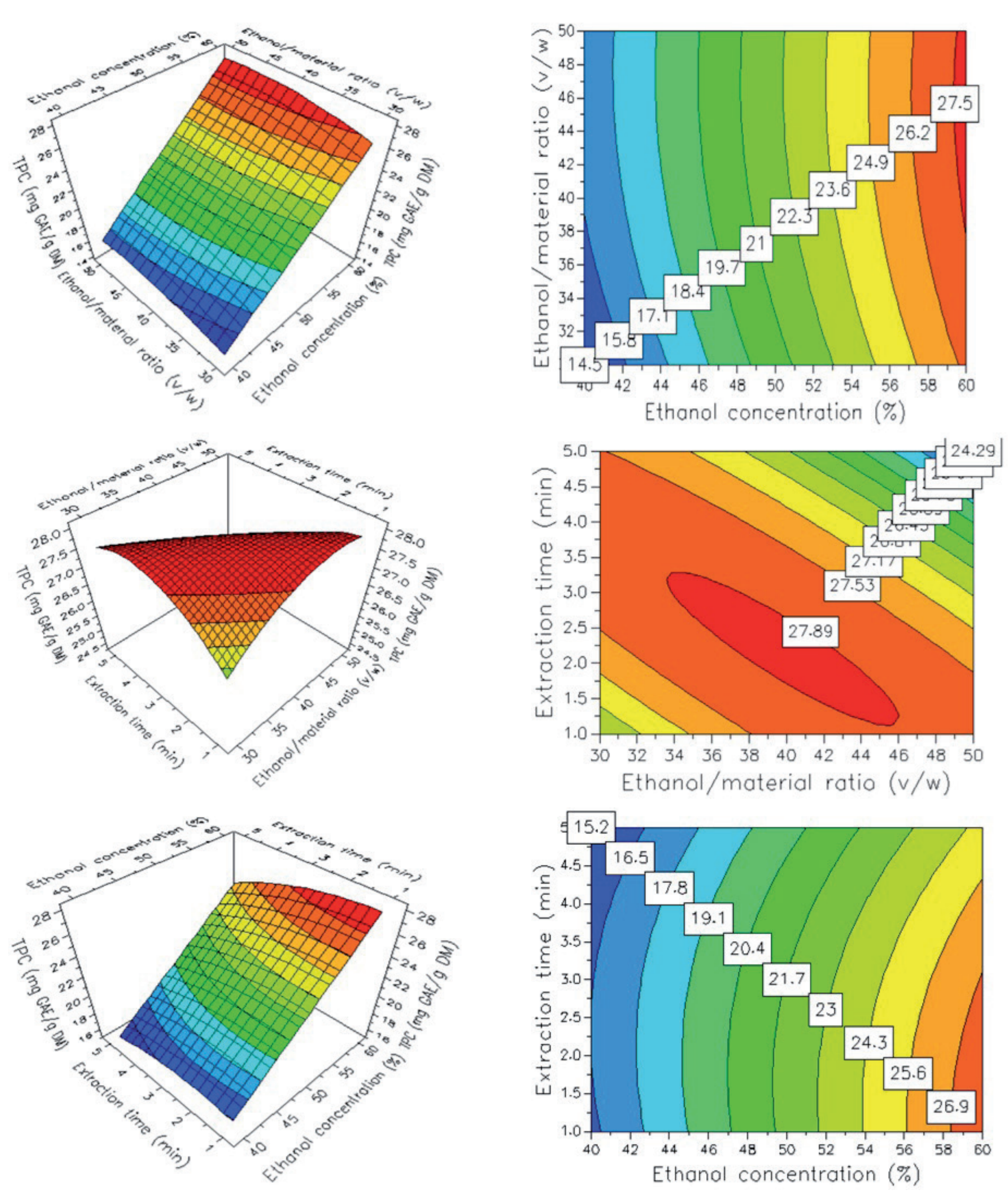

Figure 1
Response surface (left) and contour (right) plots showing the effects of factors on TPC at the optimal conditions

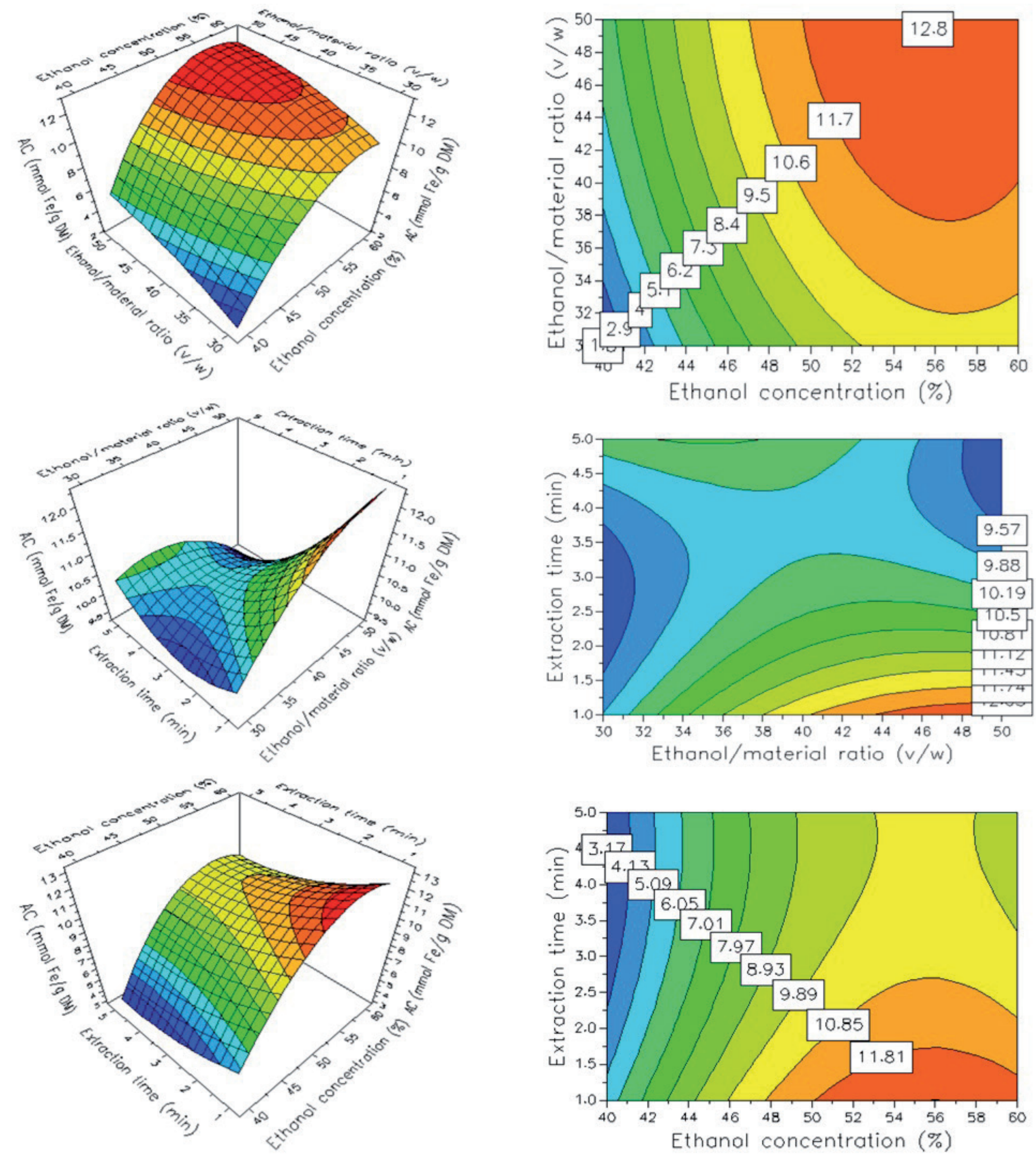

Figure 2

Response surface (left) and contour (right) plots showing the effects of factors on AC at the optimal conditions

al. [15], these authors optimized the extraction process of phenolic compounds from citrus mandarin peels by MAE (liquid/solid ratio of 16/1 and methanol concentration of 66%). Various materials, type of solvent and extraction methods cause all these differences.

Validation of optimal conditions

Based on the results of the RSM, the optimized extraction parameters for collecting TPC and AC from ginger rhizome were solvent concentration, solvent/material ratio and extraction time which were

Table 4

Results of optimal parameters

Factors	X_1 (%)	X_2 [ml/g]	X_3 [min]	Y_1 [mg GAE/g DM]	Y_2 [mmol Fe/g DM]
Predicted values	60	48.6	1	27.84	12.31
Experimental values				27.89±1.99	12.24±0.04

60%, 48.6 ml/g and 1 min, respectively. The TPC and AC were estimated to be 27.84 mg GAE/g DM and 12.31 mmol Fe/g DM, respectively; whereas the optimal TPC and AC value obtained were 27.89 mg GAE/g DM and 12.24 mmol Fe/g DM, respectively (tab. 4). All tested result was performed under optimal conditions and the experimental values were not significantly different from the predicted values. This proves that the suggested model could be used to predict the response value.

CONCLUSIONS

In conclusion, phenolic compounds were successfully extracted from the ginger rhizome and MAE was optimized for the extraction of phenolic compounds. All independent factors at three levels of CCF design in this study were optimized the extraction condition. From the results obtained, solvent concentration, solvent/material ratio and extraction time were the most important factors and they strongly affected the TPC and AC. These models obtained are useful and reliable for a large-scale extraction of phenolic compounds from the dried ginger rhizome.

Conflict of interest: Authors declare no conflict of interest.

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