Heliyon 8 (2022) e11109

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Optimization of ultrasound-assisted extraction of phenolic content & antioxidant activity of hog plum (*Spondias pinnata L. f. kurz*) pulp by response surface methodology

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ARTICLE INFO

Keywords:
Hog plum
Ultrasound-assisted extraction
Optimization
Total phenol content
Antioxidant activity
Response surface methodology

ABSTRACT

Background: The pulp of hog plum (*Spondias pinnata L. f. kurz*) has been documented as a potential source of nutritional, physiological, and pharmacological purposes due to its phenolic content (TPC) and antioxidant activity. However, an optimal extraction condition for hog plum pulp remains elusive. Optimization of extraction process conditions using Ultrasound-assisted extraction (UAE) technique has recently attracted research interest.
Objectives: The present study focused on optimizing the UAE extraction conditions of TPC and antioxidant activities (DPPH and FRAP) from hog plum pulp by using response surface methodology (RSM).
Methods: The RSM with a three-factor-three-level Box-Behnken design (BBD) was used to optimize the extraction conditions. The BBD was used to investigate the effects of three independent variables, X_1: ultrasonic temperature (40–60 °C), X_2: ultrasonic time (30–60 min), and X_3: ethanol concentration (40–80%) on TPC, DPPH and FRAP assays. Fifteen experimental trials have been carried out to optimize the UAE extraction conditions. A second-order polynomial model was used for predicting the responses. Statistically, the model was validated using an analysis of variance (ANOVA).
Results: The ANOVA results revealed that UAE extraction temperature, time, and ethanol concentration had a significant ($p < 0.01$) influence on the TPC, DPPH, and FRAP, suggesting that all extraction parameters included in this investigation were crucial to the optimization process. For TPC, DPPH, and FRAP, the R^2 values were 0.9976, 0.9943, and 0.9989, respectively, indicating that the models developed based on second-order polynomials were satisfactorily accurate for analyzing interactions between parameters (response and independent variables). RSM analysis showed that the optimal extraction parameters which maximized TPC, DPPH, and FRAP were 52.03 °C temperature, 30 min, time, and 79.99% ethanol. Under optimal conditions, experimental values for TPC, DPPH, and FRAP were 370 ± 26 mg GAE/100g DM, 57 ± 7%, and 7650 ± 460 mg AAE/100 g DM, respectively. The experimental values showed a good agreement with the predicted values with residual standard error values below 0.2% under optimum conditions. Pearson's correlation coefficients (r) demonstrate that the TPC showed a weak positive correlation with DPPH (r = 0.3508) and moderate correlation with FRAP (r = 0.3963).
Conclusion: The experimental results agreed with the predicted values, confirming the model's appropriateness and RSM's efficacy in optimizing the UAE extraction conditions. This optimized UAE extraction method may be effective in the industrial extraction process; moreover, further research should be conducted to determine the efficacy of these extracts when applied to food.

1. Introduction

An Anacardiaceae species, hog plum (*Spondias pinnatum L. f. kurz*), is a wild edible fruit found in India, Bangladesh, China, and other South-East Asian nations. Amra, Bala, Jobito, *Jobo blanco* and *Jobo corronchoso* are some of the more common names for hog plum in Bangladesh, Costa Rica, Panama, Colombia, and Venezuela. They are also known as Jocote, Yellow Mombin, Purple Mombin, Red Mombin, Siriguela, and Sineguela

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https://doi.org/10.1016/j.heliyon.2022.e11109
Received 28 December 2021; Received in revised form 27 February 2022; Accepted 11 October 2022
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[1]. There has been a growth in consumption of hog plum fruit pulp as raw or processed food as a result of its taste (which ranges from sour to sour-sweet) and rich in minerals, vitamin A and C, potassium, reducing sugars, copper, as well as its intense antioxidant activity and total phenolic content (TPC) than other fruits [2]. The pulp extracts of hog plum fruit have been shown in numerous studies to have neuro-protective, anti-bacterial and anti-tumour, antiulcerogenic, antipyretic and diuretic properties and are used to alleviate muscle pain and articular. The abundance of phenols and antioxidants, phytonutrients, phytosterols, minerals, carotenoids, and terpenoids in the pulp of hog plum is likely responsible for these qualities [3].

On the other side, studies show that consuming more antioxidant-rich foods like polyphenols lowers one's risk of developing chronic diseases. Antioxidants can delay or inhibit the oxidation of a substrate that can be oxidized in a chain reaction. In addition, the food and pharmaceutical industries have stepped up the utilization of natural antioxidants like polyphenols. Researchers have been particularly interested in phenolic compounds because of their significant antioxidant properties both *in vitro* and *in vivo*, as well as their capacity to scavenge free radicals, which are responsible for the body's destructive oxidation response [4]. However, because the polarity of phenolic compounds can vary greatly, it is difficult to establish an optimum extraction process. In the past, conventional extraction procedures were used to obtain phenolic compounds from plant sources (i.e., hydro-distillation, squeezing, cold pressing, maceration, and extraction with stirring). However, most of these methods rely on the extraction power of different solvents, heat, and long extraction time. These methods can cause the antioxidant activity and total phenolic content to be lost because of oxidation, hydrolysis, and ionization, making it essential to look for better alternative methods [5, 6, 7].

In order to increase productivity, decrease processing time, and conserve energy, using green extraction processes is an alternative worth considering. Ultrasonic-assisted extraction (UAE), subcritical water, and microwave-assisted treatments are only a few new technologies developed [8]. UAE is becoming more popular as an alternative technology. UAE has been utilized to reduce process temperature, time, and solvent use [9, 10]. Ultrasonic waves induce a process known as cavitation, which results in a rapid series of compression and expansion waves near the surface of a solid matrix. Decompression causes giant air bubbles to grow, eventually collapsing and imploding, releasing the stored energy as waves. The microscopic channels formed by the procedure above create a sponge effect in tissues, allowing the solvent to more easily penetrate and release the compounds of interest [11, 12]. The extraction efficiency of TPC and antioxidant activity can be affected by ultrasonic extraction cycles, ultrasonic duration, ultrasonic temperature, solvent concentration, solvent acidity, and solvent type employed in the UAE [13]. Several authors [14, 15, 16], have investigated the extraction of phenolic compounds from natural sources based on the UAE technique and suggested that the three key factors affecting extract composition are ultrasonic time, ultrasonic temperature, and solvent concentration. The variation is attributable to the different affinities of these compounds for solvent extraction, specifically to the polarity of the molecules constituting the solvent. In recent years, extracting antioxidant compounds from plants and plant-based foods using polar solvents like methanol and ethanol has been common practice [17]. For food ingredients extraction, it is better to use the less toxic solvents and approved by the regulatory agencies. The present study preferred ethanol to methanol because ethanol is less toxic than methanol and other organic solvents [18], possessing the highest affinity for phenolics. According to Neves et al. [19], ethanol extracts of Anacardiaceae species can be potential sources of new biotechnological products, acting as natural antioxidant and antifungal agents. However, UAE has been used to extract phenolic compounds and determine antioxidant activity from mulberry pulp [20], Genipap berry fruit pulp [21], jackfruit pulp [22], peaches fruit pulp [23], and apple pulp [24] among many other plants with nutritional or medicinal effects. Even though there is a lot of research on UAE, the optimization of UAE conditions on hog plum pulp has not been investigated.

For optimizing analytical procedures, response surface methodology (RSM) is frequently used in the food and medicine fields. Recently several researchers used RSM for optimization study and concluded that the RSM would be used in the food sector to explore the effects of various factors and their interactions on response variables [25, 26, 27, 28]. RSM strategy is less time consuming and less labor intensive than others since it requires fewer experimental trials to analyze many parameters and their interactions. Many experiments have utilized the RSM's most frequent designs, such as central composite design (CCD) and Box-Behnken design (BBD) [29]. BBD for the RSM is explicitly developed to fit a second-order model, the primary focus of most RSM investigations. Besides, the BBD only requires three levels of each factor to fit a second-order regression model, whereas CCD requires five levels for each factor. In addition, the BBD frequently necessitates fewer experimental runs. Thus, this study aimed to assess hog plum pulp's chemical composition and physicochemical properties and use RSM to optimize the UAE extraction parameters (ultrasonic time, ultrasonic temperature, and ethanol concentration) to determine TPC and antioxidant activity of hog plum pulp using BBD.

2. Materials and methods

2.1. Materials and samples

Fresh hog plum fruits were collected from Bangladesh Agricultural Development Corporation (BADC) Agro Service Center, Kumargaon, Sylhet, during August 2021 (Latitude: 25.6221° N, Longitude: 88.6438°E, and Altitude: 42.0 m). All the solvents and standards used for the antioxidant assays and phenolics content were purchased from Sigma-Aldrich (Sigma-Aldrich, St. Louis, MO, USA).

2.2. Preparation of materials

The husk and seed of the hog plum fruit were manually removed using a sieve to retrieve the pulp. A freeze dryer (Model: LYOQUEST-55, Telstar, Spain) was used to lyophilize the pulp at −50 °C for 24 h under vacuum conditions [30]. The dried samples were then collected and processed into powder using a mixer grinder (Model: MX-AC400, Panasonic, Japan). Following that, the powder was sieved by the lab sieve (Model: BK-TS200, Biobase, China). All the particles that went through an 80-mesh sieve were collected in a Ziplock bag and used as samples for further investigation.

2.3. Ultrasonic assisted extraction (UAE)

The UAE extraction technique was carried out using an ultrasonic bath (Model: Power Sonic 405, Hwashin Technology Co., Korea) with a capacity of 5.7 L, 200 W and 80 kHz. The UAE extraction technique was adapted from Borges et al. [31] with minor modifications, where 0.5 g of hog plum pulp dry powder was taken for each experiment following the Box-Behnken experimental design (Tables 2 and 3) in a three-level three-factor full factorial design with centre points was used. Three independent variables were identified as X_1 (temperature in °C), X_2 (time in min.), X_3 (ethanol concentration in percentage). The samples were thoroughly vortexed both before and after extraction. Whatman filter paper (number 4) was used to filter the samples at the end of each extraction. The samples were stored in an amber flask at 4 °C and capped and sealed for the chemical composition and physical properties, TPC, DPPH (2,2-diphenyl-1-picrylhydrazyl) radical-scavenging activity and FRAP (Ferric reducing antioxidant power) analyses.

2.4. Chemical composition and physicochemical properties

Hog plum pulp was analyzed by the Association of Official Analytical Chemists [32] for its chemical composition and physical qualities as follows: moisture content (920.151), ashes (923.003), fat (922.06),

dietary fibre (924.03; 985.29), and protein (992.15). Carbohydrate contents were obtained through calculation by difference.

2.5. Determination of TPC

In order to determine the phenolic content (TPC) of hog plum pulp, ethanolic extracts were prepared as described by Silva et al. [33]. The Folin–Ciocalteau method was used to determine the TPC [18]. Ethanolic extracts (0.5 mL) were added together with 0.5 mL Folin–Ciocalteau reagent and 1 mL sodium carbonate solution at a concentration of 4%. The solution was incubated at dark ambient for 2 h. The absorbance was determined using the spectrophotometer at 765 nm (Model-UV-1800, Shimadzu Scientific Instruments, Japan). The "mg GAE (gallic acid equivalents)/100 g DM (Dry Matter) of sample" was used to express the results using a gallic acid standard curve ($R^2 = 0.99$).

2.6. Determination of antioxidant activity

The hog plum pulp's antioxidant activity was evaluated by measuring DPPH free radical scavenging activities and ferric reducing antioxidant power (FRAP). DPPH and FRAP were measured according to the method described by Silva et al. [34] and Thaipong et al. [35], respectively. A UV spectrophotometer (Model-UV-1800, Shimadzu Scientific Instruments, Japan) was used to measure the absorbance at 517 nm and 700 nm for DPPH and FRAP, respectively. The DPPH radical scavenging activity was expressed as a percentage of the control. Ascorbic acid was used to prepare the standard curve for FRAP assay, and the results are expressed as mg AAE (Ascorbic Acid Equivalent)/100 g Dry Matter (DM).

2.7. Experimental design and statistical analysis

The present study used a BBD in the form of a three-level three-factor full factorial design for each independent variable (temperature, time, and ethanol concentration) to evaluate the effects of process variables associated with the UAE on the response variables. Three process variables were selected: X_1 (temperature, 40–60 °C), X_2 (time, 30–60 min), and X_3 (ethanol, 40–80%) and a total of 15 runs were performed (Table 3). After obtaining the data, RSM was used to determine the optimal processing settings for each of the three independent variables. The influence of temperature, time, and ethanol concentration on TPC and antioxidant capacity values were investigated using a second-order polynomial equation (Eq. (1)) obtained from RSM:

$$y = a_0 + a_1x_1 + a_2x_2 + a_{11}x_1^2 + a_{22}x_2^2 + a_{12}x_1x_2 \quad (1)$$

Where y is the measured response variables, x_1 and x_2 represent the levels of independent variables. a_o is a constant (predicted response at the centre), a_1, a_2; a_{11}, a_{22}; and a_{12} are the linear, quadratic, and two-factor interaction coefficient of the model, respectively. The Design-Expert® (version 12.0.3) and Minitab® (version 14) statistical software was used for the experimental design and the analysis of variance (ANOVA) to determine the effects of significant interactions in the model ($p < 0.01$).

3. Results and discussion

The present study optimized ultrasonic temperature, ultrasonic time, and ethanol concentration to maximize the TPC, and antioxidant activity (DPPH, FRAP) of extracts from hog plum pulp. The first stage of the present study was to determine the parameters that affect the phenolic compounds extraction in the UAE and fruit pulps' antioxidant activity. In several investigations, single-factor tests were undertaken to examine the effects of processing parameters on UAE extraction. The bulk of this research discussed various factors affecting the extraction process's efficiency, such as ultrasonic time, ultrasonic temperature, solvent concentration, ultrasonic power, and frequency [36, 37, 38]. Additionally, discrepancies in UAE treatment within the same matrix have been recorded, as phenolic content and antioxidant activity can vary according to variety, cultivar zone, and pretreatment of the residue sample, among other parameters [8]. Meanwhile, the UAE extraction of total phenolics and antioxidant capacity may be adversely affected by some factors of sonication, such as the power and frequency of ultrasonic waves. Nevertheless, a review of the literature concerning the UAE of plant materials reveals that most of the authors only specify the ultrasonic power and frequency of their respective systems [39, 40, 41]. The optimum ultrasonic power and frequency used in the present research agreed with the previously reported in the literature for UAE of polyphenols from Quinoa (*Chenopodium quinoa* Willd.) seeds [42], agro-food industrial by-products (onion, olive, tomato and pear) [43], Argentinian autochthonous plant (*Larrea cuneifolia*) [44], bog bilberry (*Vaccinium uliginosum* L.) marc [45], pomegranate peel [46]. Therefore, the present study primarily focused on optimizing three key variables (ultrasonic temperature, ultrasonic time, and ethanol concentration) to gain maximum phenolic content and antioxidant activity from hog plum pulp. For the optimization study, low and high values for each variable (Table 2) were determined based on previous studies on the extraction of phenolic compounds in different plant materials [47, 48, 49, 50, 51].

Due to the fact that heat makes the cell walls permeable, it increases the effectiveness of extraction. However, excessive temperatures can lead to the degradation of antioxidants. Thus, the present study considered a temperature range of 40–60 °C for BBD to allow broad experimental domains. Regarding the ultrasonic extraction time, many researchers have used extraction times varying from a few minutes to several hours. Due to the probability of oxidation and polymerization of phenolics being increased by long extraction times, the extraction time was investigated within the range of 30–60 min in the current study. Furthermore, antioxidants are frequently extracted from mixtures of ethanol and water. In the UAE, using ethanol/water mixture results in a reduction of highly oxidizing species formed by the decomposition of water. Since the stability of ethanol in terms of homolytic cleavage is greater than that of water. Therefore, mixing both solvents suppresses degradation of the extract and optimizes the extraction process [52]. In the present work, the range of 40–80% of ethanol in the mix with water was intended for investigation.

3.1. Chemical composition and physicochemical properties of hog plum pulp

Table 1 summarizes the chemical composition and physicochemical parameters of hog plum pulp. The moisture content of the hog plum pulp found in the present investigation was 88 ± 4 g/100 g, and the pulp ash concentration was 0.9 ± 0.1 g/100 g. Additionally, proximate analysis of hog plum pulp revealed a low-fat level (0.9 ± 0.1 g/100 g) and higher crude fibre content (2.3 ± 0.5 g/100 g). Also, the hog plum pulp presented a total carbohydrate content of 16 ± 3 g/100 g and a higher protein content level (6.4 ± 0.6 g/100 g). The hog plum pulps' high carbohydrate and fibre content imply that it may be a valuable energy source. The chemical composition of the hog plum pulp found in the current study agrees with the findings of Tiburski et al. [2], Coolborn et al. [53], and Akther et al. [54]. The heterogeneity in the amounts of the

Table 1. Chemical composition and physicochemical properties of the hog plum pulp.

Parameters	Value (g/100 g)
	Mean ± SD, n = 3
Moisture	88 ± 4
Ash	0.9 ± 0.1
Fat	0.9 ± 0.1
Crude Fibre	2.3 ± 0.5
Protein	6.4 ± 0.6
Carbohydrate	16 ± 3

Table 2. Independent variable levels in experimental design for response surface analysis.

Independent variables	Symbols	Coded level		
		−1	0	1
Ultrasonic temperature (°C)	X_1	40	50	60
Ultrasonic time (min.)	X_2	30	45	60
Ethanol (%)	X_3	40	60	80

above-mentioned elements determined for hog plum pulp by these authors could be attributed to the variety of hog plum plants and their geographical location.

3.2. Fitting the model and analysis of variance

Using RSM with BBD, the present study examined the effects of UAE extraction time, temperature, and ethanol concentration on the TPC, DPPH radical scavenging activity, and FRAP of the hog plum pulp. Table 3 summarizes each run's responses (TPC, DPPH radical scavenging activity, and FRAP). According to the experimental results, the values of TPC, DPPH scavenging activity, and FRAP of hog plum pulp ranged between 220 ± 14 and 340 ± 22 mg GAE/100g DM, 41 ± 6 and 57 ± 7%, and 610 ± 15 and 7229 ± 155 mg AAE/100 g DM of the pulp extracts, respectively. Experiment 13 (50 °C, 30 min, 40%) provided the lowest TPC (220 ± 14 mg GAE/100g DM), and the experiment 9 (50 °C, 30 min, 80%) produced the highest TPC (340 ± 22 mg GAE/100g DM). On the other hand, the pulp extract of experiment 10 (60 °C, 45 min, 80%) showed the highest antioxidant activity (46 ± 3% in DPPH, 7229 ± 155 mg AAE/100 g DM in FRAP), and pulp extract of experiment 15 (50 °C, 60 min, 80%) showed the lowest antioxidant activity (55 ± 3% in DPPH, 610 ± 15 mg AAE/100 g DM in FRAP). Multiple regression analysis of the actual data resulted in the following second-order polynomial equations (Quadratic model) for each of the three responses, as illustrated in Eqs. (2), (3), and (4).

$$y_{TPC(mg\ GAE/100g\ DM)} = 252.67 + 14.98 \times X_1 + 1.41 \times X_2 + 29.26 \times X_3 + 10.42 \times X_1X_2 + 6.01 \times X_1X_3 - 32.48 \times X_2X_3 - 6.29 \times X^2_1 + 13.42 \times X^2_2 + 16.77 \times X^2_3 \quad (2)$$

$$y_{DPPH(\%)} = 52.40 + 1.59 \times X_1 + 0.70 \times X_2 + 1.20 \times X_3 + 3.87 \times X_1X_2 - 3.06 \times X_1X_3 + 0.23 \times X_2X_3 - 3.73 \times X^2_1 + 2.25 \times X^2_2 - 1.90 \times X^2_3 \quad (3)$$

$$y_{FRAP(mg\ GAE/100g\ DM)} = 744.435 + 1140.11 \times X_1 - 416.84 \times X_2 - 653.24 \times X_3 - 787.51 \times X_1X_2 + 1763.24 \times X_1X_3 - 2506.11 \times X_2X_3 + 1314.26 \times X^2_1 + 414.32 \times X^2_2 + 2910.78 \times X^2_3 \quad (4)$$

Generally, coefficients with a positive sign in the fitted model imply that the variable can enhance the response. In contrast, a negative sign suggests a variable's ability to lower the response. The equation model for the present study (Eqs. (2), (3), and (4)) indicated that UAE extraction temperature, time, and ethanol concentration positively affected the phenolic content and antioxidant activities (DPPH radical scavenging activity and FRAP). Additionally, UAE extraction time resulted in the lowest coefficient regarding the linear interaction. Moreover, in the case of binary interactions, the interaction between UAE extraction time and the temperature had the highest positive effects on TPC and DPPH radical scavenging activity. On the contrary, in the case of FRAP assay, UAE extraction temperature and ethanol concentration showed the highest positive effects, indicating an antagonistic effect between the three variables.

Furthermore, the quadratic interaction of variables also positively influenced all the responses. Specifically, ethanol concentration demonstrated the most potent positive effects on the TPC and FRAP assay, while UAE extraction time exhibited the most substantial positive influence on DPPH radical scavenging activity. These findings designated that the UAE extraction of hog plum pulp is affected by extraction temperature, time, and ethanol concentration.

Based on an analysis of variance (ANOVA), the coefficient of determination (R^2) for TPC, DPPH radical scavenging activity, and FRAP were 0.9976, 0.9943, and 0.9989, respectively. According to Jumbri et al. [55], high correlation and a strong fit are demonstrated by a regression model with an R^2 value greater than 0.9. The resulting R^2 values revealed that the RSM was capable of adequately representing over 95% of the response variables (TPC, DPPH radical scavenging activity, and FRAP). Moreover, BBD design fits well into the proposed quadratic polynomial models, as indicated by the higher R^2 values for each response. These findings validated the models' reliability in estimating the optimal conditions required to maximize the TPC and antioxidant activity of hog plum pulp.

For all responses, Table 4 shows the results of the regression analysis and ANOVA used in the model fitting design to determine whether the terms were statistically significant. The *F* value of 227.87 (TPC), 97.66 (DPPH), and 494.17 (FRAP) revealed that each model was significant. It was possible that the values were noise-related by 0.01%. Each model

Table 3. Box-Behnken design of three variables with their measured values of responses.

Run	Independent variables			Response variables		
				Antioxidant activity		
	X_1	X_2	X_3	TPC (mg GAE/100 g DM)	DPPH (%)	FRAP (mg AAE/100 g DM)
1	60	60	60	285 ± 41	57 ± 7	2281 ± 163
2	50	45	60	252 ± 27	52 ± 2	680 ± 15
3	60	45	40	240 ± 12	49 ± 4	5123 ± 175
4	40	45	40	223 ± 21	41 ± 6	6235 ± 181
5	40	45	80	273 ± 14	49 ± 2	1288 ± 165
6	40	60	60	235 ± 15	45 ± 3	1710 ± 176
7	50	45	60	253 ± 10	51 ± 2	826 ± 161
8	40	30	60	254 ± 15	52 ± 5	1089 ± 171
9	50	30	80	340 ± 22	52 ± 8	6335 ± 169
10	60	45	80	315 ± 19	46 ± 3	7229 ± 155
11	50	45	60	252 ± 16	52 ± 2	725 ± 11
12	50	60	40	290 ± 11	52 ± 5	6815 ± 159
13	50	30	40	220 ± 14	50 ± 4	2516 ± 178
14	60	30	60	263 ± 25	48 ± 2	4810 ± 151
15	50	60	80	279 ± 18	55 ± 3	610 ± 15

DM: Dry Matter; Data are expressed as mean ± standard deviation of three determinations; TPC: total phenolic content; DPPH: 2,2-diphenyl1-picrylhydrazyl radical scavenging ability; FRAP: Ferric reducing antioxidant power.

Table 4. Analysis of variance (ANOVA) of the quadratic models for total phenolic content and antioxidant activity.

Source	TPC	DPPH	FRAP
X_1	<0.0001	0.0003	<0.0001
X_2	0.2044	0.0107*	0.0004
X_3	<0.0001	0.0011	<0.0001
X_1X_2	0.0006	<0.0001	<0.0001
X_1X_3	0.0070	<0.0001	<0.0001
X_2X_3	<0.0001	0.4036	<0.0001
X_1^2	0.0069	<0.0001	<0.0001
X_2^2	0.0002	0.0003	0.0026
X_3^2	<0.0001	0.0008	<0.0001
R^2	0.9976	0.9943	0.9989
Adjusted R^2	0.9932	0.9842	0.9969
Predicted R^2	0.9631	0.9421	0.9837
F value	227.87	97.66	494.17
Prob > F	<0.0001	<0.0001	<0.0001
C.V. (%)	1.03	0.99	4.44
Lack of fit	0.0882	0.5570	0.1587

Data are significant at $p < 0.01$, $*p < 0.05$; TPC: total phenolic content; DPPH: 2,2-diphenyl1 picrylhydrazyl radical scavenging ability; FRAP: Ferric reducing antioxidant power.

response had a low probability (<0.0001) and a *p*-value of less than 0.01, which indicated that the models were significant. The interaction between the independent variables and the response variables is significant, when the F value is large, and the p-value is low [56]. ANOVA showed a statistically significant correlation between all independent variables and all responses ($p < 0.01$). All responses were significantly affected by UAE extraction temperature (X_1) ($p < 0.01$). Likewise, ethanol concentration (X_3) exhibited significant effects on TPC ($p < 0.01$), DPPH radical scavenging activity ($p = 0.0011$), and FRAP ($p < 0.01$). In contrast, UAE extraction time (X_2) didn't show significant effects on TPC ($p = 0.2044$), while had significant effect on DPPH radical scavenging activity ($p = 0.0107$) as well as FRAP ($p = 0.0004$).

A regression model's Predicted R^2 value reflects how accurately responses values are predicted, while an Adjusted R^2 indicates how well the regression models describe the data when many variables are included. Regardless of statistical significance, a model's R^2 value increases as more variables are added. Thus, it is important to analyze the Adjusted R^2 value while evaluating the model's adequacy, as the value tallied increases only when the variables augment the model beyond what would be obtained by probability. Adjusted R^2 values greater than 0.9 demonstrate the model's adequacy [57]. Additionally, the model's efficacy is demonstrated by a difference of less than 0.2 between Adjusted R^2 and Predicted R^2. In this study, the Adjusted R^2 values were 0.9932, 0.9842, and 0.9969 for TPC, DPPH scavenging activity, and FRAC of hog plum pulp, respectively. Therefore, in the present study, Adjusted R^2 and Predicted R^2 differed by less than 0.2 for all responses (the diagnostics graphs for TPC, DPPH scavenging activity, and FRAC are shown in Figures 6, Figure 7, Figure 8, respectively, in the Supplementary Material).

Further verification of the model's validity was conducted using the Lack of Fit analysis, which indicated that the model accurately fit the actual data with an insignificant *p*-value greater than 0.05. In the present study, *p*-values for TPC, DPPH radical scavenging activity, and FRAP demonstrated a Lack of Fit of 0.0882, 0.5570, and 0.1587, respectively. The findings revealed that the quadratic polynomial models were able to predict relevant responses with accuracy and precision. Furthermore, the low coefficient of the variation value for TPC (C.V. = 1.03%), DPPH radical scavenging activity (C.V. = 0.99%), and FRAP (C.V. = 4.44%) demonstrated that the models had a preferable accuracy. Therefore, all the models could provide reliable experimental data.

3.3. Response surface analysis of TPC

The response surface plot was used to visualize the main effects and interaction effects of the variables used in TPC extraction from the hog plum pulp. The contour plot takes the two variables concurrently while keeping the other variables constant. In Figure 1, a standardized Pareto chart and main effects plot were used to demonstrate the relative importance of the variables and their interactions using statistical significance ($p = 0.05$). According to Figure 1(b), (d), and (f), the result exhibited the effect of the independent variables UAE extraction temperature (X_1), time (X_2), and ethanol concentration (X_3) and their interactions on TPC, DPPH radical scavenging activity, and FRAP assay, respectively. The present study recorded for the TPC that UAE extraction temperature and ethanol concentration were statistically significant with 95% confidence, and the positive effects of variables and their interactions were ranked as follows: ethanol concentration (X_3) > temperature (X_1) > ethanol concentration × ethanol concentration (X_3^2) > time × time (X_2^2) > temperature × time (X_1X_2) > temperature × ethanol concentration (X_1X_3). Also, the temperature had the highest significant positive effect on DPPH radical scavenging activity, followed by ethanol concentration > time. Similarly, in the case of FRAP assay, temperature showed a significant positive impact, while ethanol concentration and time negatively affected the FRAP antioxidant activity of hog plum pulp.

The contour plots in Figure 2(a)–(f) depict the UAE extraction temperature, time, and ethanol concentration, with the yield of TPC as the response. Each time, the effect of two variables on the response was evaluated, while the other variable remained constant. Figure 2(a) and (b) visualized TPC production in the presence of two variables: UAE extraction temperature and extraction time. The yields of TPC grew gradually as the extraction temperature was increased from 40 to 60 °C. However, the trend was reversed as the extraction time increased from 30 to 60 min. The yields of TPC increased with the ascending of UAE extraction temperature and ethanol concentration, as illustrated in Figure 2(b) and (c). Meanwhile, Figure 2(e) and (f) demonstrates the reciprocal effects of extraction time and ethanol concentration on TPC yields. TPC yields arose with increasing ethanol concentration from 40% to 80%.

In the present study, three different temperatures (40, 50, and 60 °C, respectively) were used to examine the effect of temperature on the extraction efficiency based on TPC. The extraction temperature is critical in extracting phenolic content since it affects the physical and chemical properties of a product. As illustrated in the main effects plot (Figure 1(a)), increasing the UAE extraction temperature increases the TPC extraction yield. Numerous studies have been conducted to determine the effect of increasing the temperature on the effectiveness of phenolic content extraction [58, 59, 60]. The findings of the present study are in agreement with the findings of Espada-Bellido et al. [20], Madrona et al. [21], Hossain and Hossain [61], Hossain et al. [22], and Altemimi et al. [23], who reported a higher temperature for phenolic content extraction from mulberry pulp (64 °C), Genipap berry fruit pulp (71 °C), Burmese grape fruit pulp (69.01 °C), jackfruit pulp (50 °C), and peaches fruit pulp (41.60 °C), respectively. Several authors observed increasing TPC yields as temperature increased, and they explained the reason as a result of softening of cell tissues and weakening of the connection between polyphenols and polysaccharides or proteins [62]. Besides, Li et al. [63] mentioned in their study that temperature increase promotes the solubility of solutes in the solvent and decreases the viscosity and surface tension of the solvent. By increasing the extraction temperature, mass transfer is increased to an appropriate level, resulting in a rise in the total quantity of phenolic compounds. Indeed, increasing the temperature results in both a reduction in the extraction time and an increase in the extraction rate. On the other hand, phenolic compounds may get desaturated over a specific temperature. This temperature range is different in various studies [64, 65]. In the present study, the concurrent increase in temperature leads to an increase in the TPC. On the contrary, it's important to consider that the TPC might be harmed by

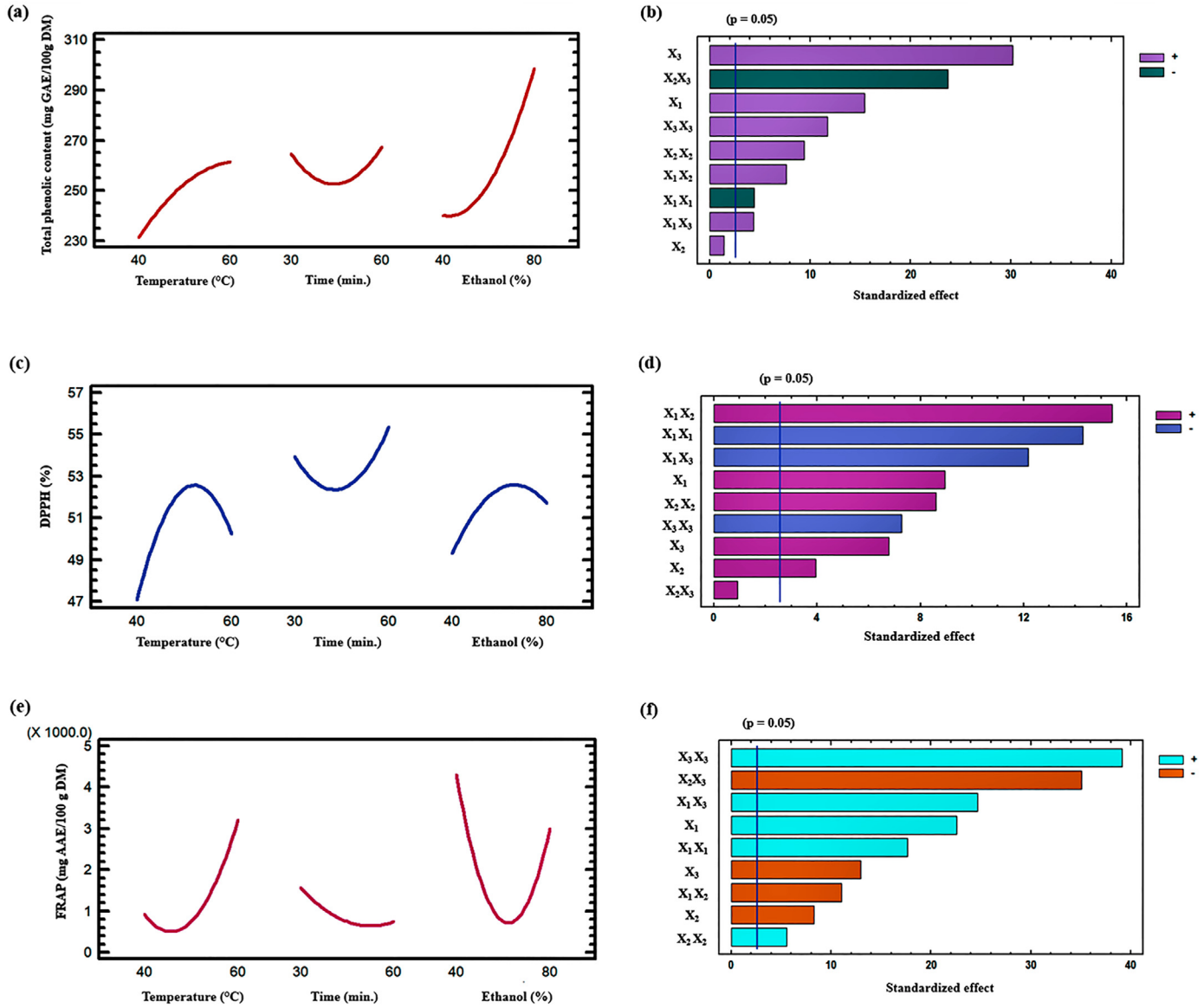

Figure 1. Main effects plot and Pareto chart of temperature, time, and ethanol concentration on (a, b) total phenolic content; (c, d) DPPH: 2,2-diphenyl1-picrylhydrazyl radical scavenging activity; (e, f) FRAP: Ferric reducing antioxidant power.

elevated temperatures. According to Santos et al. [66], increasing the temperature during UAE extraction enhances the vapor pressure of the solvents, resulting in decreased cavitation force and a descended yield of phenolic contents. Taking prior findings into account, the current study considered that higher temperatures may be detrimental to extracting the TPC. Thus, the extraction temperature range was set between 40 and 60 °C for subsequent extraction optimization.

Extraction yields for biomolecules such as polyphenols are very time-dependent [67, 68]. A precise determination of the extraction time will save time and save energy. The time required for extraction is typically determined by the kind of material and the extraction procedure. The main effects plot of TPC (Figure 1(a)) illustrates the steady increase in TPC with the extension of the extraction period from 45 to 60 min, at higher extraction temperature, most likely due to the prolonged extraction time, which allowed polyphenols to migrate from the hog plum pulp into the extraction solvent. Several researchers have noticed a proportionate rise in the extraction yield with increasing extraction time [69, 70, 71, 72]. Nevertheless, the lengthy extraction presents a drawback. Since more polyphenols are extracted over a longer period, they are exposed to other variables such as temperature, light, and oxygen for a longer time or other components they can react with [73, 74, 75]. Then, a decrease in the yield of extraction might be detected. The decline in extraction yield can also be attributed to some minor degradation of unstable polyphenols at high temperatures under a long extraction time. In a study on peaches fruit pulp, the optimal time for the UAE extraction of total phenolics was approximately 30 min [23]. In another study on Genipap berry fruit pulp, the optimal UAE extraction time was 49 min for the TPC [21]. On the contrary, Rocha et al. [76] optimized the process variables for extracting phenolic compounds from blueberry fruit in the UAE, achieving an extraction time of more than 50 min, for TPC. Similarly, Saci et al. [77] recorded approximately 57 min, UAE extraction time for TPC extraction from the carob fruit pulp. Therefore, the present study considered the UAE extraction time between 30 to 60 min, for optimization study.

The solvent's nature is critical for the extraction process; it should have a high affinity and an excellent dissolving capacity. The current study examined the effect of ethanol concentration on the UAE extraction efficiency of TPC using three different concentrations (40%, 60%, and 80%, respectively). Since the concentration of ethanol directly affects the solvent's polarity, but ultrasonic absorption depends on the solvent's

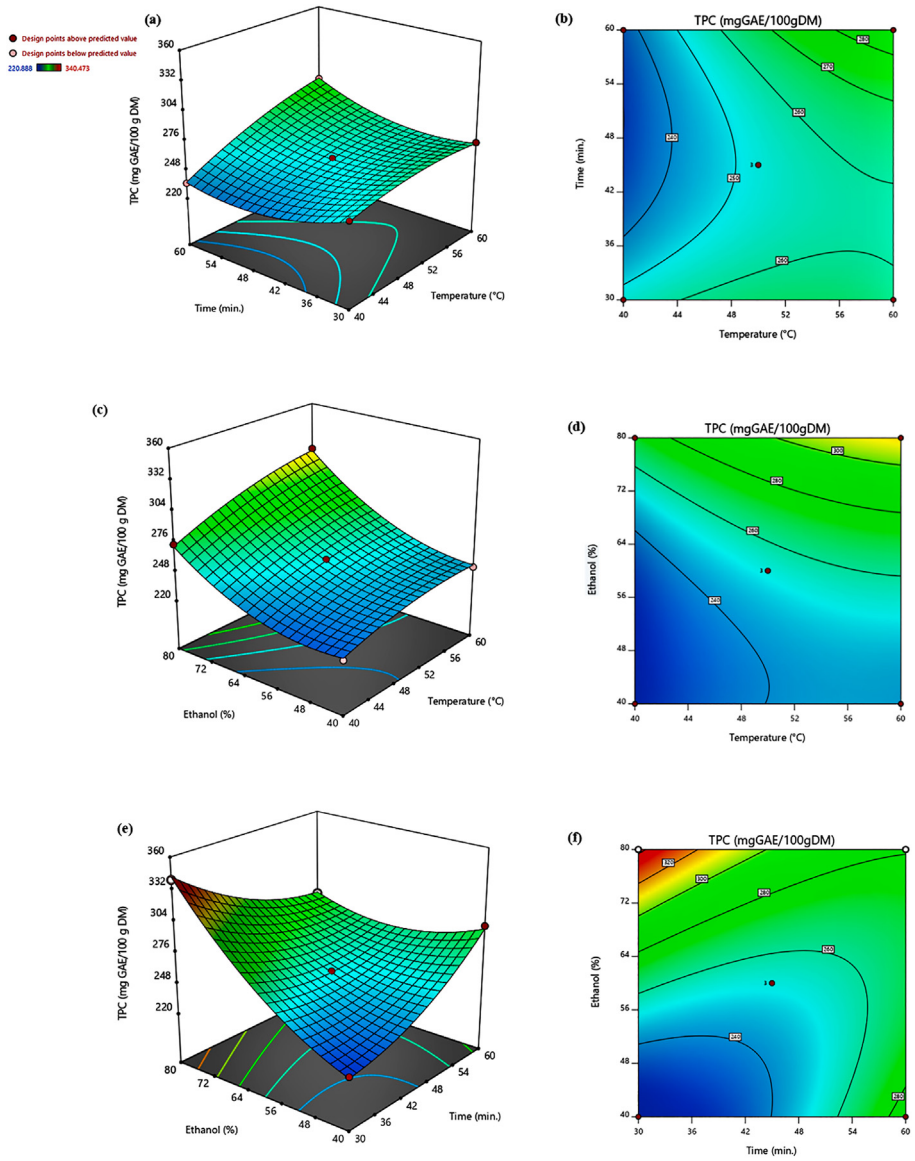

Figure 2. Response surface and contour plots showing the interaction effects of (a, b) time and temperature; (c, d) temperature and ethanol; (e, f) time and ethanol on the total phenolic content of hog plum pulp.

dielectric constant and increases with the amount of water in aqueous ethanol [78]. Galvan et al. [79] reported that high ethanol concentrations could result in protein denaturation, impeding polyphenol solubility and thereby affecting extraction. Therefore, finding an optimal ethanol concentration for the UAE extraction of hog plum pulp is crucial. Figure 1(a) depicts the effect of ethanol concentration on the TPC, and it can be observed that the increase of the ethanol concentration from 40% to 80% determined an increase of TPC. Numerous studies have demonstrated an effect of the ethanol concentration in the extraction medium on phenolic compound production. For instance, in the work of Hammi et al. [80], the optimum ethanol concentration in the UAE extraction was 50% for TPC from the *Zizyphus lotus* (L.) fruit. Similarly, regarding the optimal conditions of UAE extraction for TPC, d'Alessandro et al. [79], Rodrigues et al. [81], Rocha et al. [76], Dumitraşcu et al. [82], Zvicevičius et al. [24], and Aquino et al. [83] reported the ethanol concentration was 50%, 50%, 40–80%, 60%, 70%, 80% for black chokeberry fruit, jaboticaba fruit peel, blueberry fruit, Cornelian cherry fruits, apple pulp, and Sapodilla fruit seed, respectively. The effect of ethanol concentration is owing to its effect on the polarity of the extraction solvent and the phenolic compounds' resultant solubility. The general principle is "like dissolve like'', which means that solvents only extract those compounds, which have a similar polarity to that of the solvent [84].

3.4. Response surface analysis of antioxidant activities

3.4.1. DPPH radical scavenging activity

In general, phenolic compounds with greater polarity can be extracted easily with water. However, phenolic compounds with a high degree of hydroxylation are more soluble in alcohol, such as ethanol [85]. Antioxidant activity is attributed mainly to phenolic components such as phenolic acids and phenolic diterpenes. The antioxidant activity of phenolic compounds is primarily owing to their redox characteristics, which can aid in the absorption and neutralization of free radicals, the quenching of singlet and triplet oxygen, and the degradation of peroxides [86]. The DPPH assay is used to determine a compound's ability to act as a free radical scavenger and is widely used to evaluate the antioxidant capacity of foods.

The average results for the DPPH scavenging activity of the hog plum pulp for each experimental run are shown in Table 3. The highest DPPH scavenging activity (57 ± 7%) was obtained in run 15, which used an

extraction temperature of 60 °C, an extraction time of 60 min, and an ethanol concentration of 60%. However, the lowest DPPH scavenging activity (41 ± 6%) was reported in experimental run 4, which was performed with 40 °C extraction temperature, 45 min extraction time, and 40% ethanol concentration. Multiple regression analysis of the data (Table 4) revealed that the DPPH scavenging activity of the hog plum pulp was significantly ($p < 0.01$ or $p < 0.05$) affected by the linear term (X_1: ultrasonic temperature, X_2: ultrasonic time, and X_3: ethanol concentration), and the interaction term between extraction temperature and extraction time (X_1X_2) as well as extraction temperature and ethanol concentration (X_1X_3). Also, the quadratic term for extraction temperature (X_1^2), extraction time (X_2^2), and ethanol concentration (X_3^2) showed a significant effect on antioxidant activity. Similar observations were also noted in the Pareto chart (Figure 1(d)), where extraction temperature (X_1), time (X_2), and ethanol concentration (X_3) had a positive effect on the DPPH radical scavenging activity, followed by the interaction between extraction temperature and extraction time (X_1X_2), and the quadratic term for time (X_2^2). To explore the effects of extraction temperature, extraction time, and their interaction on the antioxidant activity of hog plum pulp extracts as assessed by DPPH assay, the main effects plot and the three-dimensional plots are depicted in Figures 1(c) and Figure 3(a)–(f). As the extraction temperature and ethanol concentration increased, the DPPH radical scavenging activities increased. Still, after reaching a maximum value, DPPH radical scavenging activity dropped when the extraction temperature and ethanol concentration increased. Temperature causes the viscosity of substances to decrease and their solubility in the solvent to increase. Additionally, increasing the temperature improves the diffusion coefficient of the extracted solvent by increasing dispersion and diffusion, hence speeding up the extraction process. In the current study, increasing the extraction temperature from 50 to 60 °C results in an increase in the DPPH radical scavenging activity of hog plum pulp. Our results are in line with the report of several studies. For instance, Morelli and Prado [87] found that the optimal UAE extraction temperature for the red grape jam was 50 °C. Similarly, Fadimu et al. [88], Ismail et al. [89], and Hammi et al. [80] reported that the optimal extraction temperature in the UAE for watermelon seeds, baobab seeds, and Tunisian *Zizyphus lotus* fruits were 50.32 °C, 60 °C, and 63 °C, respectively. However, a higher temperature may result in a decrease in antioxidant activity. The reduction activity of phenolic acids and their esters is proportional to the number of free hydroxyl groups present in the molecule, as evidenced by their high capacity to donate protons and stabilize the DPPH radical [90]. Higher exposure to

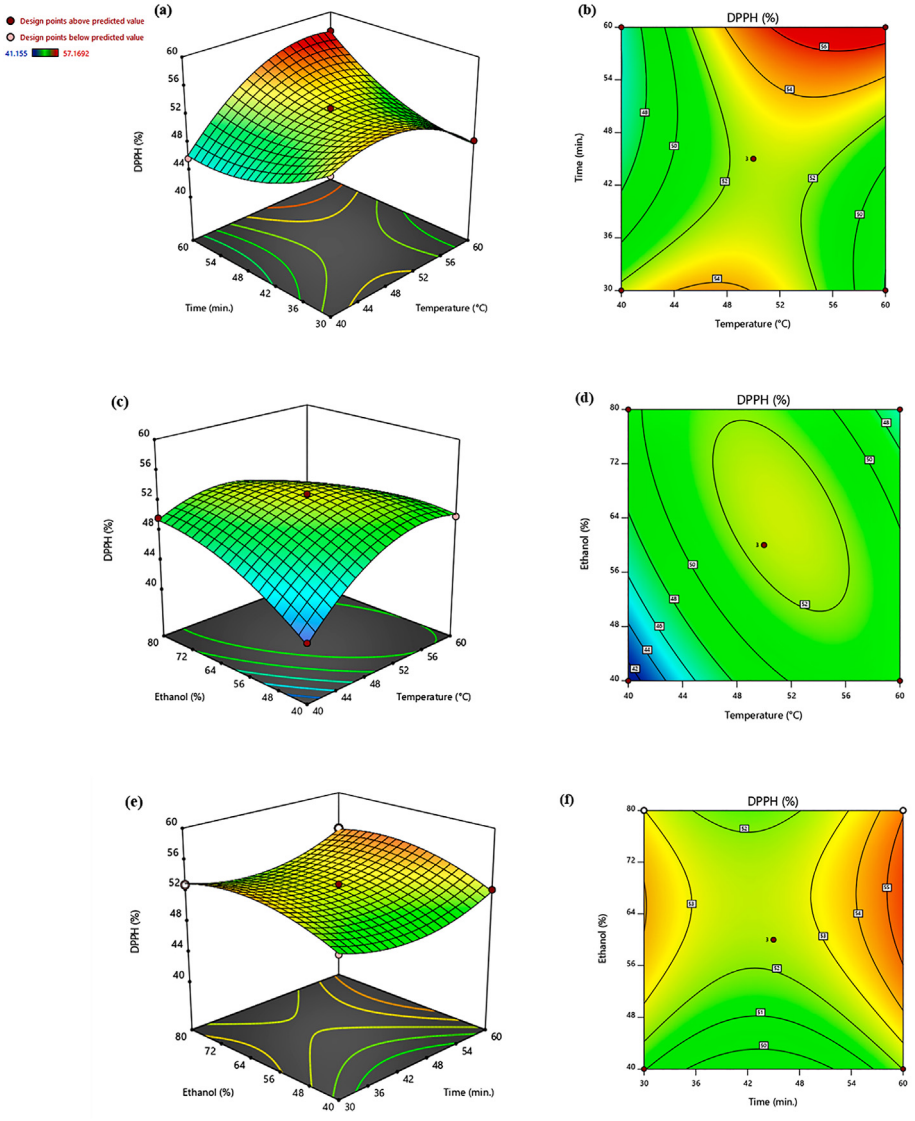

Figure 3. Response surface and contour plots showing the interaction effects of (a, b) time and temperature; (c, d) temperature and ethanol; (e, f) time and ethanol on the DPPH (2,2-diphenyl1-picrylhydrazyl radical scavenging activity) of hog plum pulp.

ultrasound may result in the formation of free radicals or the destruction of the conjugated double bond, hence decreasing the free radical scavenging activity [91]. On the other hand, the maximum DPPH value was obtained when the range of the ethanol concentration was from 40 – 60%; beyond that value, the DPPH value started to decrease. One probable explanation is that raising the ethanol level alters the solvent's polarity, diminishing the solvent's ability to efficiently extract molecules that react with DPPH [92]. Sady et al. [93] recorded the highest DPPH activity in the UAE extraction with 60% ethanol concentration as an optimal value from chokeberry pomace. Similar results have been reported by Morelli and Prado [87], where the UAE extraction of antioxidant phenolic compounds from red grape jam was excellent at 60% ethanol. In another study, Rodsamran and Sothornvit [94] found that UAE was more effective in extracting total phenolics from lime peel waste with high antioxidant activity at a concentration of 55% ethanol. An increase in extraction time positively impacted the DPPH radical scavenging activity of hog plum pulp. Both DPPH and TPC displayed a similar pattern. Increasing the extraction time from 30 to 40 min caused a decrease in the DPPH activity. The reason is most likely the result of insufficient contact time between the solid particle and the solvent. Surprisingly, an abrupt increase in DPPH activity was observed approximately after 40 min, followed by a further increase in extraction time (Figure 1c). Increased antioxidant activity can be attributed to the high TPC content in hog plum pulp as a result of bound phenolics released. Additionally, it has been claimed that hydroxyl radicals' formation increases the hydroxylation of dietary components, hence increasing their antioxidant activity [95]. Our findings agree with the previous investigation by Chen et al. [96], who reported the DPPH radical scavenging activity of litchi seed under the optimal UAE extraction time of 45 min. In another investigation, Sengkhamparn and Phonkerd [97] reported that the UAE extraction time for 50 min showed the highest antioxidant activity (DPPH radical scavenging activity) from industrial tomato waste. Similarly, Nag and Shit [98] found that the UAE extraction time of 41.45 min was optimal for the DPPH radical scavenging activity from pomegranate peels.

3.4.2. Ferric reducing antioxidant power (FRAP)

In most cases, more than one approach uses to determine the antioxidant activity of natural complexes of plant materials. Therefore, the ferric reducing antioxidant power (FRAP) assay was employed in the present study to determine the antioxidant activity of the hog plum pulp extracts in addition to the DPPH radical scavenging assay. FRAP demonstrates a sample's ability binding metal ions to reduce metals, inhibiting the metal ion-catalyzed formation of reactive species [99].

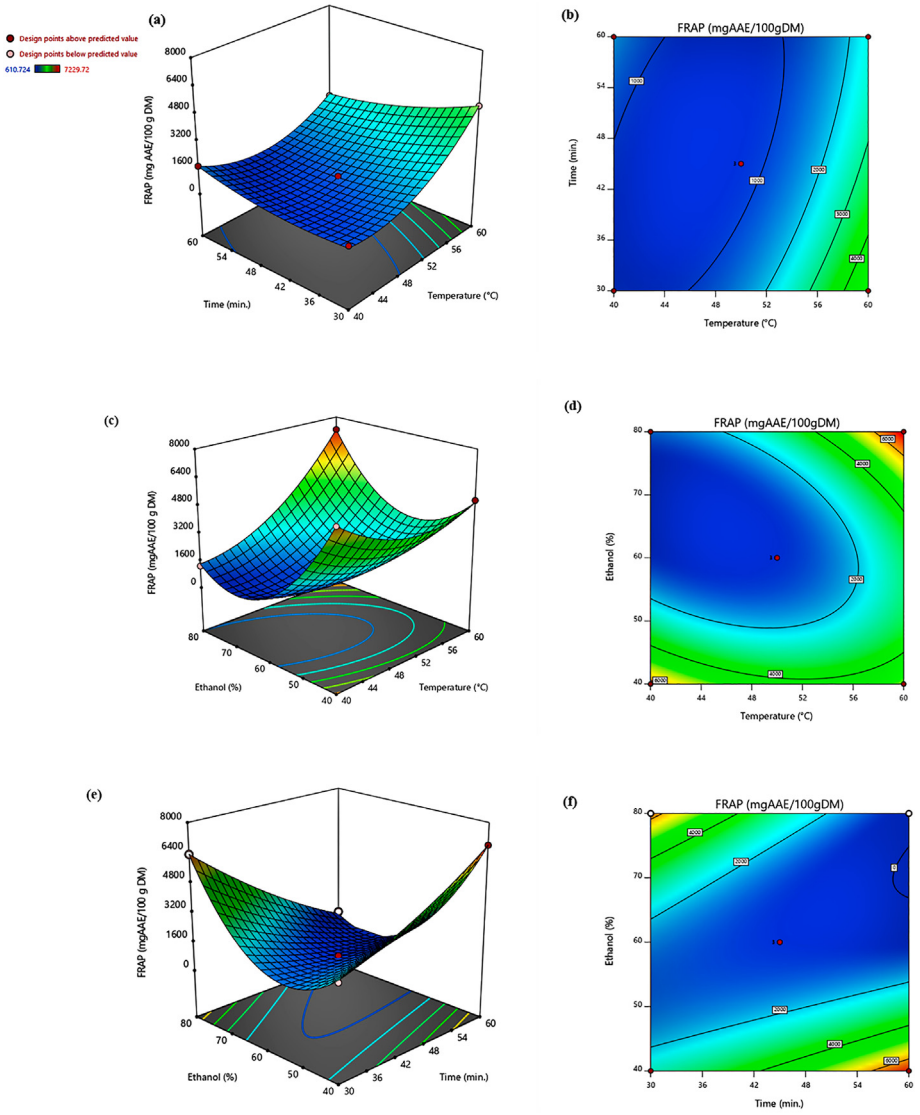

Figure 4. Response surface and contour plots showing the interaction effects of (a, b) time and temperature; (c, d) temperature and ethanol; (e, f) time and ethanol on the FRAP (Ferric reducing antioxidant power) of hog plum pulp.

The main effects plot, Pareto chart, three-dimensional response surfaces and contour plots for FRAP assay are shown in Figures 2(e), (f), and 4(a)–(f), respectively. Figure 2(e) represents the main effects plot of UAE extraction temperature, time, and ethanol concentration on the FRAP activity of hog plum pulp. It is clear from Figure 2(e) and the ANOVA test for FRAP (Table 4) that extraction temperature (X_1), extraction time (X_2), and ethanol concentration (X_3) significantly ($p < 0.01$) affect the FRAP assay of hog plum pulp. It was observed that the hog plum pulp extracts with higher temperature ranges from 60 to 80 °C showed increased FRAP value. The temperature-dependent trend in FRAP activity observed experimentally could be explained by changes in solvent characteristics with temperature and decomposition or alteration of the extract. As the temperature rises, more compounds may be extracted due to increased diffusivity within the extraction media and relaxation of the food matrix, which may account for the increase in FRAP activity from 60 to 80 °C. Hossain and Hossain [100] reported the maximum FRAP activity in Burmese grape pulp at 80 °C. In previous investigations, Hani et al. [101] and Deng et al. [92] recorded 60 °C and 68 °C as the optimal temperature in the UAE for bitter gourd and sugar apple, respectively. Similarly, the results showed a significant ($p < 0.01$) effect of extraction time on FRAP activity of hog plum pulp extract. Precisely, the values were decreased when the extraction time was increased from 30 to 60 min. The decline of FRAP activity may be related to the oxidation of phenolic compounds caused by prolonged exposure to environmental variables such as light and oxygen [102]. The results were also explained by Fick's second rule of diffusion, which states that after a specific time, there will be a final equilibrium between the solute concentration in the solid matrix (plant sample) and the bulk solution (extraction solvent) [103]. Hence, an optimal time is required to extract more phenolic compounds from hog plum pulp. The present study recorded the highest FRAP activity between 30 to 45 min. Chen et al. [104], Kashyap et al. [105], and Deng et al. [92], all demonstrated the maximum FRAP activity for *Lycium ruthenicum* Murr. Sequentially, fruit, Meghalayan cherry fruit, and sugar apple under an optimum extraction time of 30 min, 31 min, and 42.54 min.

On the other hand, the ethanol concentration had a weak positive linear effect on the FRAP value. According to Figure 2(e), the optimal ethanol concentration was either at the lowest or the highest of the investigated range. The difference in FRAP activity of the hog plum pulp extracts at various ethanol concentrations indicated that the ethanol concentration affected the type of compounds extracted from the hog plum pulp. Furthermore, with the polarity of the solvent varying from very polar (lower concentration of ethanol) to less polar (higher concentration of ethanol), the solvent's capacity to dissolve selected groups of antioxidants would also fluctuate, which would affect the antioxidant activity [106]. Moreover, extraction temperature affects the polarity of the solvent by changing the dielectric constant; this might have significantly influenced the extraction of phenolic compounds by interacting with ethanol concentration [107]. Three-dimensional response surfaces and contour plots are shown in Figure 4(a)–(f) to illustrate the interaction impact on the FRAP activity of hog plum pulp. The interaction effects of temperature and time with a fixed ethanol concentration (60%) are depicted in Figure 4(a) and (b). When the temperature increased from 40 to 60 °C, FRAP activity increased, but an increased time from 30 to 60 min, causing a decrease in the FRAP activity. However, it is also clear from Figure 2(f) and the ANOVA test (Table 4) that the interaction effect of temperature and time (X_1X_2) had a significant negative impact on the FRAP activity. The interaction effects of time and ethanol concentration (X_2X_3) also had a similar trending effect on FRAP activity (Figure 4(e) and (f)). In contrast, the interaction of temperature and ethanol concentration (X_1X_3) showed a substantial positive impact (Figure 4(c) and (d)).

3.5. Optimization of extraction parameters and models validation

One of the primary objectives of the present study was to determine the optimal process parameters of the UAE for hog plum pulp, precisely the temperature, time, and ethanol concentration, that result in maximizing TPC and antioxidant activities (DPPH and FRAP assays).

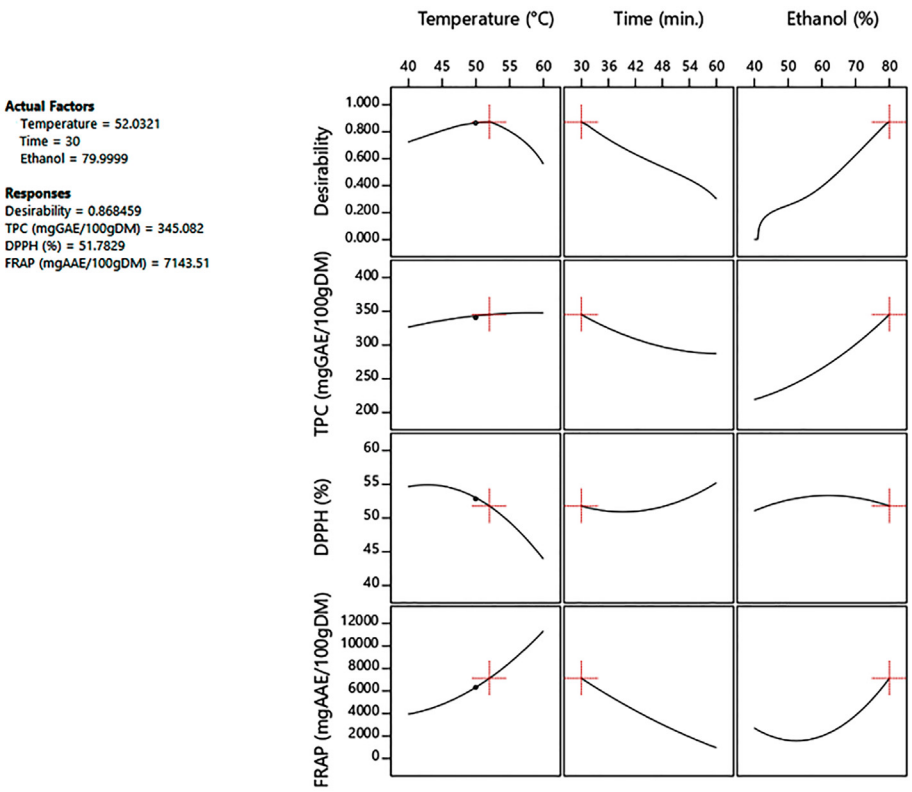

Figure 5. Graphical presentation of response optimization for hog plum pulp.

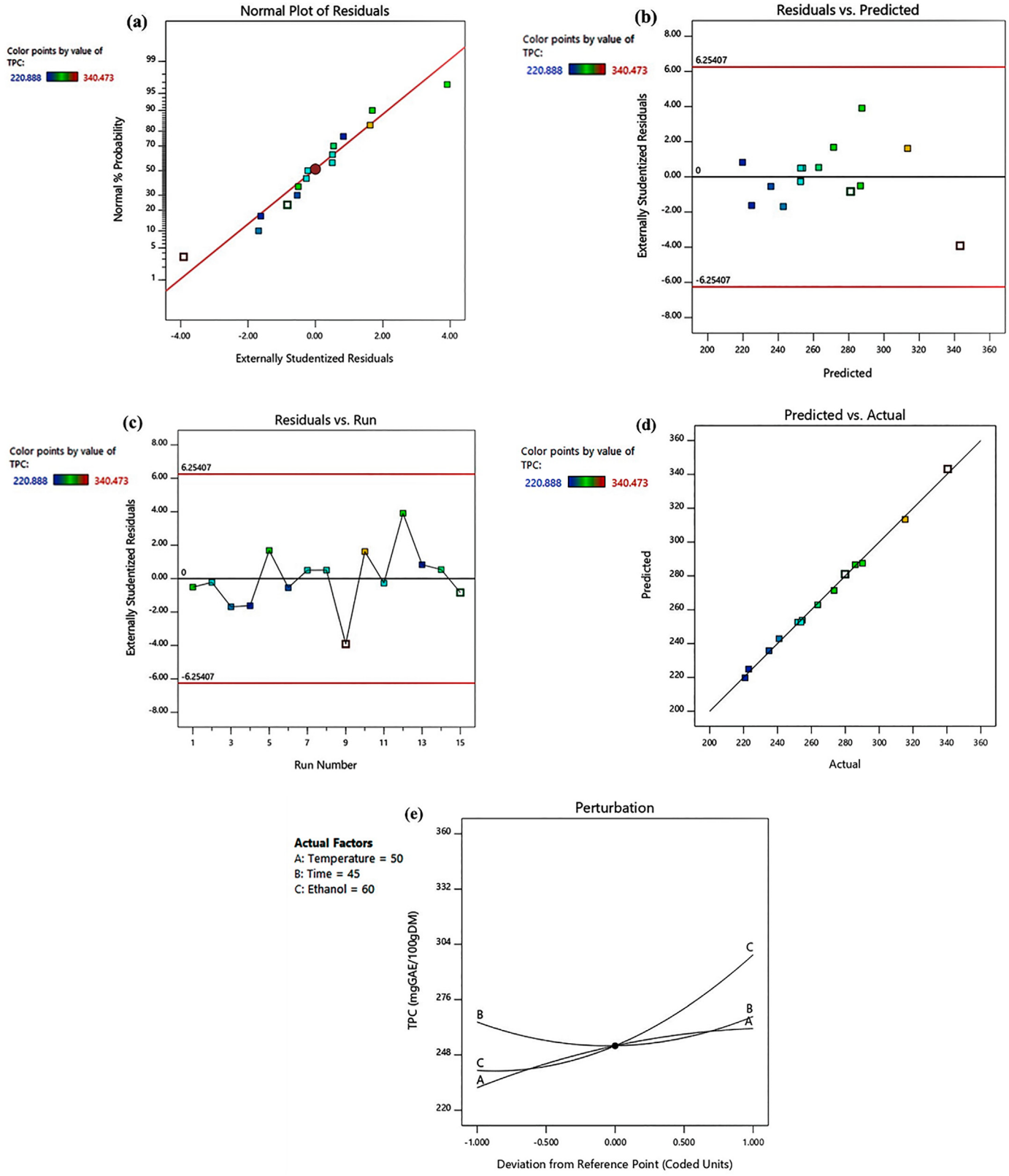

Figure 6. Diagnostic plots of TPC (total phenolic content) for validation of RSM model. (a) Normal Plot of Residuals; (b) Residuals vs. Predicted; (c) Residuals vs. Run; (d) Predicted vs. Actual; (e) Perturbation plot showing the effect of all factors on the TPC.

However, obtaining these responses under the same condition is difficult since factors have distinct interest regions. In RSM optimization, two methodologies are most typically employed. The first approach is the superimposition of response contour plots and manual derivation of the desired value. Notwithstanding, Granato et al. [108] assert that this graphical approach is inefficient and incapable of being automated. Therefore, the second strategy, desirability function, was applied using Design Expert Software version 12.0.3 to compromise between these

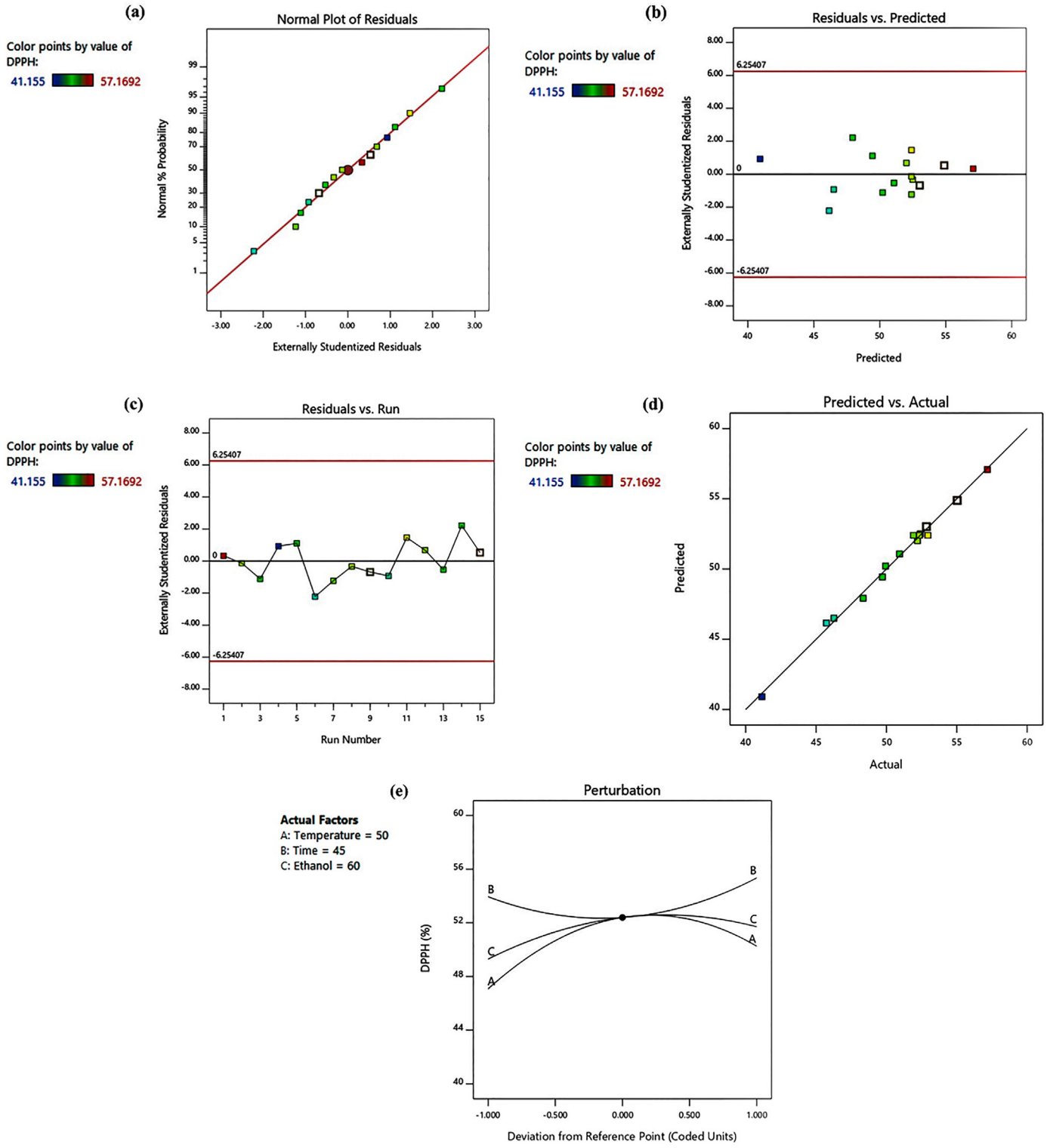

Figure 7. Diagnostic plots of DPPH for validation of RSM model. (a) Normal Plot of Residuals; (b) Residuals vs. Predicted; (c) Residuals vs. Run; (d) Predicted vs. Actual; (e) Perturbation plot showing the effect of all factors on the DPPH.

responses. The optimization process assigned desirability values ranging from 0 to 1 to each model's minimum and maximum responses. Following that, the optimum condition showed an overall desirable property of 0.868459 (Figure 5). The optimal conditions were determined by maximizing the desirability of the responses. These optimal conditions were used for the extraction process, and all the responses were replicated three times at optimized conditions. The results are presented in Table 5. The optimal conditions were temperature of 52.03 °C, time of 30 min, and ethanol concentration of 79.99%. Under the optimal conditions, the experimental values were 370 ± 26 mg GAE/100 g DM for TPC, 57 ± 7% for DPPH, and 7650 ± 460 mg AAE/100 g DM for FRAP. These experimental results were in agreement with the predicted values for TPC (345.09 mg GAE/100 g DM), DPPH (51.78%), and FRAP (7143.51 mg AAE/100 g DM). The residual

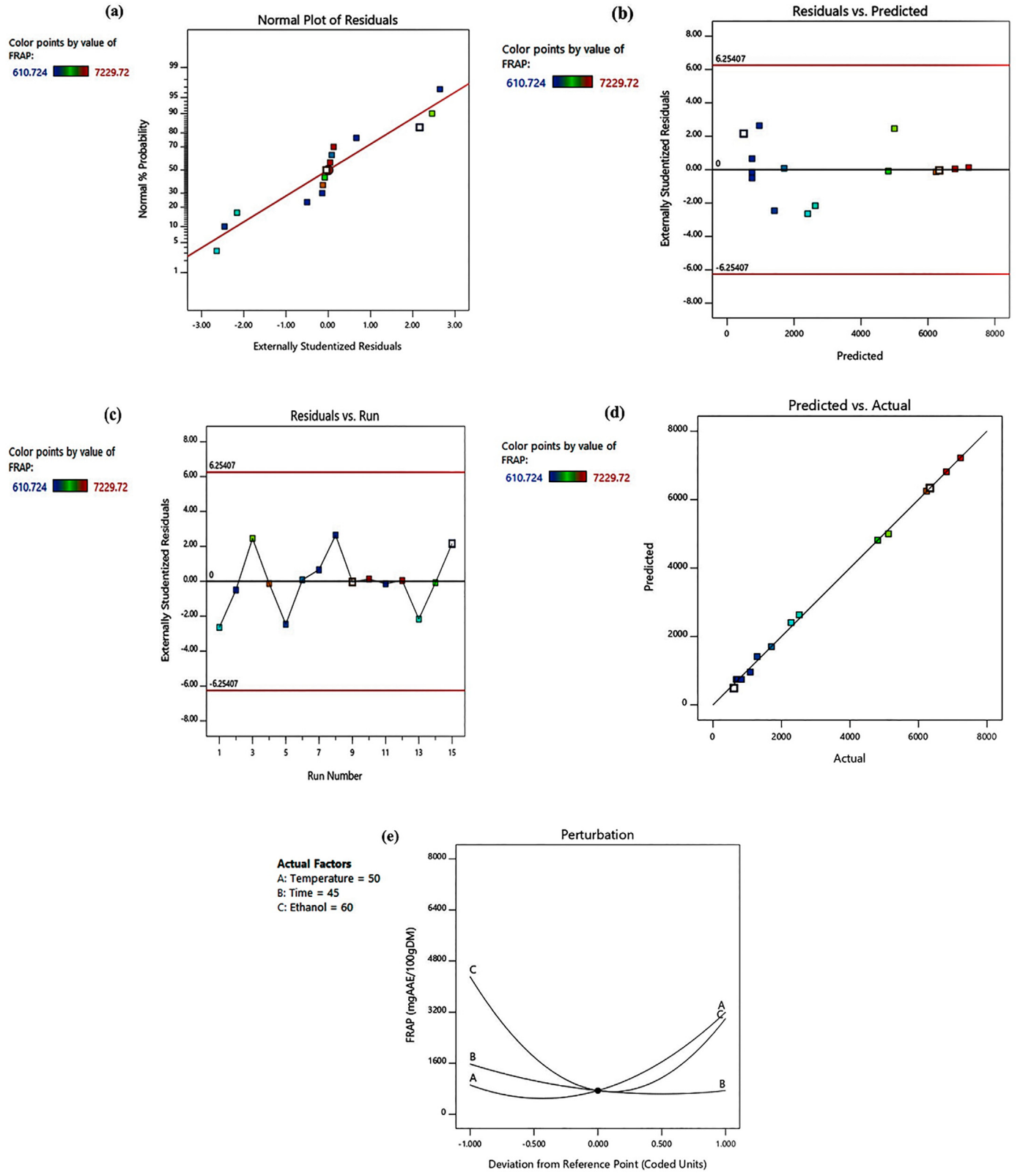

Figure 8. Diagnostic plots of FRAP for validation of RSM model. (a) Normal Plot of Residuals; (b) Residuals vs. Predicted; (c) Residuals vs. Run; (d) Predicted vs. Actual; (e) Perturbation plot showing the effect of all factors on the FRAP.

standard error (RSE) percentages were used to compare the experimental results with the predicted values. In the present study, we considered RSE values lower than ±0.5 to be in agreement with the prediction [109]. The obtained RSE values for the extracts of hog plum pulp demonstrated no significant disparities between the experimental and predicted values. The excellent high fit degree between the experimental and predicted values suggest that the model obtained by BBD can accurately predict the optimal conditions of extraction temperature, time, and ethanol concentration in the UAE for TPC and antioxidant activities from hog plum pulp.

Table 5. Experimental values of TPC, DPPH, and FRAP under the optimized conditions.

Optimized conditions	Temperature (°C)	52.03			
	Time (min.)	30			
	Ethanol (%)	79.99			
		Target	Predicted value	Experimental value	RSE (%)
Response variables	TPC (mg GAE/100 g DM)	Maximum	345.09	370 ± 26	0.07
	DPPH (%)	Maximum	51.78	57 ± 7	0.12
	FRAP (mg AAE/100 g DM)	Maximum	7143.51	7650 ± 460	0.07

RSE: Residual Standard Error; Experimental values expressed as mean ± standard deviation of the mean (n = 3).

Table 6. Pearson's correlations between TPC and antioxidant activities (DPPH, and FRAP assays).

Assay	DPPH	FRAP
TPC	0.3508	0.3963

3.6. Correlation between total phenolic content and antioxidant activities

In the present study, the contribution of TPC in ethanolic extracts of hog plum pulp to the antioxidant activities was evaluated by Pearson's correlation coefficients (r). At different combinations of extraction parameters (Table 3), TPC values were compared with DPPH and FRAP values using the Pearson correlation coefficient. Several recent studies used the Pearson correlation coefficients to determine the TPC and antioxidant assays correlation. For instance, in a survey conducted by Casagrande et al. [110], a strong and positive correlation between TPC and antioxidant activities assays (DPPH, ABTS, and FRAP) was determined by Pearson correlation coefficients in *Baccharis dracunculifolia*. A similar approach was also observed in the study of Tembo et al. [111], Viapiana and Wesolowski [112]. The Pearson correlation between the TPC of hog plum pulp extracts and antioxidant activity determined by DPPH and FRAP is tabulated in Table 6. The correlations were classified based on the value of strength: ≤ 0.35, representing weak correlation, from 0.36 to 0.67, moderate correlation, and from 0.68 to 1.00, strong correlation as suggested by Taylor [113]. The present study's findings demonstrate that the TPC showed a weak positive correlation with DPPH ($r = 0.3508$) and moderate correlation with FRAP ($r = 0.3963$). These correlations may suggest that the antioxidant activity of hog plum pulp extracts cannot be entirely predicted based on their TPC. Although several studies have shown a strong linear correlation, antioxidant activity may not necessarily correspond with phenolic content, according to Ghasemi et al. [114]. Besides, the non-significant correlation between TPC and antioxidant activity is consistent with the studies of Chang and Azrina [115], Islam et al. [116], Toh et al. [117] and Tsai et al. [118].

Numerous factors may contribute to the following weak correlations. Firstly, the antioxidant activity observed was not contributed solely by phenolic content. However, other compounds such as carotenoids, ascorbic acid, terpenes, tocopherols, reduced carbohydrates, protein, and other phytochemical compounds were not quantified in the present study could also contribute to the total antioxidant activity of hog plum pulp extracts [119]. Additionally, hog plum pulp's crude fibre and dietary fibre content may have antioxidant properties [120]. Second, the synergistic effects of phenolic chemicals may account for the total antioxidant activity [121]. Zaporozhets et al. [122] reported that, in addition to the content of antioxidants, the interaction between antioxidants and other elements might impact antioxidant activity. On the other hand, the antioxidant activity of plant extracts should be assessed using a variety of assays such as DPPH, FRAP, Trolox equivalent antioxidant capacity (TEAC), reducing power assay (RPA), and total antioxidant content (TAC) to cover the range of endogenous compounds. Antioxidants are diverse polyphenols, nucleophiles, and reducing agents with varying degrees of solubility, localization, redox potential, mechanism of action, and specificity [123]. Some methods measure the antioxidant activity based on only hydrophilic (i.e., FRAP) properties, while other methods consider either both hydrophilic and lipophilic (i.e., TEAC) or solubility in organic solvents (i.e., DPPH) [124].

Moreover, according to Jemli et al. [125], the DPPH and FRAP assays do not always show correlation when determining the antioxidant activity, as each approach has different mechanisms and limitations. DPPH radical scavenging activity was weakly correlated to the TPC in the hog plum pulp extract. The reason might be that the polar phenolic compounds in the extracts didn't interact well with the DPPH powder dissolved in ethanol. Lee et al. [126] described that most antioxidants found in plant extracts, such as ascorbic acid and phenolic acids, are poorly soluble in ethanol; hence, the DPPH radical cation's reducing function may be reduced be disrupted. Regarding FRAP, Prior et al. [127] noted that FRAP couldn't be capable of detecting substances that act via radical quenching (H transfer), such as thiols and proteins. Having mentioned that, the authors also suggested that the determination of antioxidant activity using the FRAP method should be followed by another method to determine which mechanism is compatible with the sample. Besides, correlations of the antioxidant activities determined by various assay techniques can also be influenced by the solvent systems. Extraction of unique phenolic substances by the selected solvent systems may have different degrees of contributions to the overall antioxidant activities. Therefore, extraction solvents for antioxidant or physiological study must be carefully chosen.

The current study's findings exposed that the TPC in extracts of hog plum pulp didn't show a strong correlation with antioxidant activity by DPPH and FRAP. Consequently, the identification and quantification of particular phenolic compounds utilizing an accurate analytical platform should be conducted in future studies. Additionally, future research on hog plum pulp extracts should focus on identifying, isolating, and purifying the extracted phenolic components for usage in food supplements and other industrial applications. Perhaps, hog plum pulp may have contained unknown compounds that contributed to its antioxidant properties. Therefore, it is recommended that the extracts be fractionated to determine which compounds are primarily responsible for the antioxidant activity and determine the relationship between these unknown and their antioxidant activities.

Overall, from the ecological perspective, the proposed procedure can be considered acceptable due to the use of non-toxic solvent that are suitable for other industries, such as the food and pharmaceutical industries. Furthermore, the RSM-based approach for quantifying TPC concentration and antioxidant activity can solve the problem of disposing of industrial waste. Due to the current widespread use of ultrasound batch reactors in the industry to extract antioxidants, the developed procedure is suitable for scaling up. It is expected that the optimized conditions of the proposed procedure will have a significant impact on the extraction quality since the thermolabile substances will not be destroyed by the effect of these factors.

4. Conclusion

To the best of our knowledge, this is the first prospective study to optimize the extraction conditions of TPC and antioxidant activities from hog plum pulp. The present work was performed to find an optimal extraction condition of TPC and antioxidant activities (DPPH and FRAP)

from hog plum pulp. RSM was successfully applied to optimize the extraction process and analyze the effects of extraction temperature, time, and ethanol concentration and their interactions. All models generated using the RSM approach demonstrated an adequate level of prediction accuracy. The optimal condition was predicted using the desirability function and subsequently validated. During the optimization process, the primary objective of this study was to maximize TPC and antioxidant activity as determined by DPPH and FRAP. An optimized condition was determined using RSM to be a UAE temperature of 52.03 °C, 30 min, and an ethanol concentration of 79.99%. However, these models can be employed further to obtain desired responses with increasing efficacy from the hog plum pulp, considering economic aspects. Furthermore, it is worth mentioning that it may be possible for the power, frequency, and duty cycle of ultrasound to affect the antioxidant activity and the total phenolic content of hog plum pulp. Therefore, further studies should be conducted to understand the system behavior based on the aforementioned variables to improve and optimize extraction efficiency for industrial applications. Overall, this study should be considered a first step for the extraction, separation, and nutraceuticals analysis of antioxidative compounds, contributing to the further research of hog plum pulp as a health food.

Declarations

Author contribution statement

Tanvir Ahmed: Analyzed and interpreted the data; Wrote the paper.

Md Rahmatuzzaman Rana: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Mahjabin Rahman Maisha: Performed the experiments; Wrote the paper.

ASM Sayem: Conceived and designed the experiments.

Mizanur Rahman: Analyzed and interpreted the data.

Rowshon Ara: Contributed reagents, materials, analysis tools or data.

Funding statement

This work was supported by Shahjalal University of Science and Technology (AS/2021/1/28).

Data availability statement

Data will be made available on request.

Declaration of interest's statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

Acknowledgements

The authors acknowledge with thanks for the technical assistance and other supports received from the Department of Food Engineering and tea Technology of Shahjalal University of Science and Technology, Sylhet, Bangladesh.

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