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ULTRASOUND-ASSISTED EXTRACTION OF NATURAL ANTIOXIDANTS FROM THE HAZELNUT SKIN: OPTIMIZATION AND COMPARISION WITH CONVENTIONAL METHOD

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ABSTRACT

This study focused on extracting antioxidants from hazelnut skin, an industrial food waste, using two different methods: conventional extraction (CE) and ultrasound-assisted extraction (UAE). The Response Surface Methodology (RSM) has been utilized using the total phenolic content (TPC) and antioxidant capacity (AC) results as responses in optimizing both method conditions. The independent variables and their levels for the optimal experimental design were adjusted as follows: temperature (50-90°C), time (2-62 min), and loading capacity (5-15%) for CE; and temperature (25-50°C), time (1-30 min), loading capacity (5-15%), and ultrasonic amplitude (20-50%) for UAE. The optimum conditions were determined to be 90°C for 35 min with a 5% loading capacity for CE, and 50°C for 27 min with a 5% loading capacity and 50% amplitude for UAE. The TPC of the extracts were found to be 142.62 mg GAE/g and 129.69 mg GAE/g, while the AC values were 127.02 µmol TE/g and 116.00 µmol TE/g for CE and UAE methods, respectively. In conclusion, it has been demonstrated that hazelnut skin extracts obtained by optimizing CE and UAE methods can serve as natural antioxidant alternatives in food products and may hold significant potential for further applications.

Keywords: Hazelnut skin, conventional extraction, ultrasound-assisted extraction, phenolic, antioxidant capacity

ULTRASON DESTEKLİ EKSTRAKSİYON YÖNTEMİYLE FINDIK ZARINDAN DOĞAL ANTİOKSİDANLARIN EKSTRAKSİYONU: OPTİMİZASYON VE GELENEKSEL YÖNTEMLE KARŞILAŞTIRMA

ÖZ

Bu çalışmada, endüstriyel bir gıda atığı olan fındık zarının ekstraksiyonu geleneksel ekstraksiyon (GE) ve ultrases destekli ekstraksiyon (UDE) olmak üzere iki farklı yöntemle gerçekleştirilmiştir. Her iki yöntem koşullarının optimize edilmesinde cevap olarak toplam fenolik madde miktarı (TFM) ve

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antioksidan kapasite (AK) sonuçları kullanılarak Yanıt Yüzey Metodu (YYM)'ndan yararlanılmıştır. Optimal deneysel tasarım için bağımsız değişkenler ve seviyeleri: GE için sıcaklık (50-90°C), süre (2-62 dakika) ve besleme oranı (%5-15); UDE için ise sıcaklık (25°C-50°C), süre (1-30 dakika), besleme oranı (%5-15) ve ultrasonik genlik (20-50%) seçilmiştir. Optimal koşullar GE için %5 besleme oranı ile 35 dakika boyunca 90°C sıcaklık ve UDE için ise %5 besleme oranı, %50 genlik ile 27 dakika boyunca 50°C sıcaklık olarak belirlenmiştir. Ekstraktların toplam fenolik madde miktarı değerleri GE ve UDE yöntemleri için sırasıyla 142.62 mg GAE/g ve 129.69 mg GAE/g olarak; antioksidan kapasiteleri ise GE ve UDE yöntemleri için sırasıyla 127.02 µmol TE/g ve 116.00 µmol TE/g olarak belirlenmiştir. Sonuç olarak, GE ve UDE yöntemlerinin optimize edilmesiyle elde edilen fındık zarı ekstraktlarının gıdalarda alternatif doğal antioksidan olarak kullanılabileceği ve ileri uygulamalar için önemli bir kaynak olabileceği görülmüştür.
Anahtar kelimeler: Fındık zarı, geleneksel ekstraksiyon, ultrason destekli ekstraksiyon, fenolik, antioksidan kapasite

INTRODUCTION

Food processing wastes or by-products are generated on a large scale in the food industries worldwide annually. This poses one of the biggest challenges for the food industry, potentially leading to negative ecological effects. Recycling of by-products is a critical measure for the sustainability of food production, playing a significant role in society, the environment, and the economy. Recently, there has been increased attention to the composition of by-products in studies, with researchers suggesting that many of these can be recycled as valuable bioactive components (Yılmaz et al., 2019; Tezel and Yıldız, 2020; Kandemir et al., 2022).

The nut industry has the potential to generate a significant amount of by-products due to the interesting layered structure of nuts. These by-products (such as shells, green leafy covers, leaves, and skins) are rich in phenolic compounds and antioxidants, which are naturally present in plant-based foods (Wijeratne et al., 2006; Göncüoğlu-Taş and Gökmen, 2017). Like other nuts, hazelnuts (*Corylus avellana* L.), of which Türkiye is the largest producer, also have by-products containing phenolic compounds (Shahidi et al., 2007; Contini et al., 2008; FAO, 2021). Some researchers have shown that hazelnut skins have a higher TPC than other hazelnut by-products (Shahidi et al., 2007). Additionally, researchers have reported that most of the phenolic compounds in hazelnuts are located in the skin, and the AC of unroasted hazelnut skin could be approximately 100 times higher than that of unroasted hazelnut kernels without the skins, proportionally (Shahidi et al., 2007; Göncüoğlu-Taş and Gökmen, 2015). Compared to foods rich in antioxidants, hazelnut skin has shown a higher AC according to various antioxidant assays. It has been reported that 1 g of unroasted hazelnut skin could be equivalent to 1.4 g of cinnamon, 10 g of dark chocolate, and 16.7 g of blueberries (Blomhoff et al., 2006; Göncüoğlu-Taş and Gökmen, 2015). In addition to this comparison, it has been reported that unroasted hazelnut skin (309-1375.00 µmol Trolox equivalent (TE)/g) has a greater AC than other foods such as walnuts (224 µmol TE/g), buckwheat (118 µmol TE/g), coffee silverskin (82.24 µmol TE/g), almonds (27.8 µmol TE/g), and peanuts (14.3 µmol TE/g) according to the QUENCHER (QUick, Easy, New, CHEap, and Reproducible) method, which allows for comparison of AC without any extraction procedure (Serpen et al., 2007; Serpen et al., 2008; Gökmen et al., 2009; Açar et al., 2009; Göncüoğlu-Taş and Gökmen, 2015; Doğan-Cömert and Gökmen, 2017). These previous studies have shown that hazelnut skin is an excellent source of natural antioxidants. The skin of hazelnuts is generally removed during the roasting process because the pectic polysaccharides within the layered structure of the skin are partially denatured by the heat (Saklar et al., 2003). Roasting can also affect antioxidant activity, and the overall impact of roasting depends on the balance between the thermal degradation of natural antioxidant compounds such as polyphenols and the formation of antioxidative Maillard reaction products like melanoidins (Açar et al., 2009). For this reason,

the recycling of hazelnut skin is gaining increasing interest, similar to other food wastes (Bertolino et al., 2015; Longato et al., 2019; Dinkçi et al., 2021).

Synthetic antioxidants such as tert-butylhydroquinone (TBHQ), butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), and ethylenediamine tetraacetic acid (EDTA) have been extensively used in the food industry to delay or prevent lipid oxidation, which leads to the formation of potentially harmful reaction products, off-flavors, and an decrease in shelf life. However, due to consumer concerns regarding the potential health risks associated with synthetic antioxidants in food products, there is a growing demand for natural alternatives (Frankel, 1984; Xu et al., 2021). For this purpose, hazelnut skin, with its high AC, can be used as a natural alternative to synthetic antioxidants in food products.

Extraction is the initial and crucial step in recovering phenolic compounds from plant-based food wastes. Various extraction techniques can be employed for extracting plant materials. Alongside conventional solid-liquid extraction methods, ultrasonic-assisted extraction (UAE), one of the "green extraction methods," has gained significant attention recently due to its advantages of short extraction time and lower energy consumption. The primary mechanism of ultrasonic-assisted extraction is based on a phenomenon called cavitation, which involves the formation and collapse of bubbles generated by the compression and expansion of ultrasonic waves. This cavitation facilitates the release of target compounds by disrupting cell walls and enhancing the penetration of the solvent into the sample matrix (Knorr et al., 2004; Chemat et al., 2017).

Extraction process parameters such as temperature, time, and loading capacity are crucial in the recovery of phenolic compounds from materials in both conventional solid-liquid extraction and ultrasonic-assisted extraction. Additionally, amplitude, which refers to the characteristics of the ultrasonic wave that can affect cavitation, is also an important parameter for ultrasonic-assisted extraction. Optimizing extraction parameters is essential to obtain extracts rich in antioxidants and phenolic compounds (Chemat et al., 2017). Response Surface Methodology (RSM) is a statistical and mathematical methodology that enables the evaluation of the effects of process parameters and their interactions. It can also determine the optimum process conditions through the design of experimental runs (Myers et al., 2002).

Numerous conventional extraction studies have been conducted to recover antioxidant phenolic compounds from hazelnut skin using various solvents (Shahidi et al., 2007; Contini et al., 2008; Alasalvar et al., 2009; Monagas et al., 2009; Locatelli et al., 2010; Del Rio et al., 2011; Göncüoğlu-Taş and Gökmen, 2015; Pelvan et al., 2018). Furthermore, the maceration method, one of the traditional extraction methods, has been compared with novel extraction methods and optimized, including ultrasonic-assisted extraction. In this study, ethyl alcohol is used in different concentrations as a solvent in both maceration and ultrasonic-assisted extraction methods (Odabaş and Koca, 2016). Additionally, there is an optimization study for the recovery of phenolic compounds from hazelnut skin using deep eutectic solvents (Fanali et al., 2021).

In future studies, there is a consideration to transform the extracts obtained with high AC into different forms that can be used as antioxidants in food products through further processing. It has been noted that the use of water as a solvent might be more suitable for the "clean label" trend, which has been a consumer expectation in recent years. For this reason, in this study, water was preferred instead of ethanol or deep eutectic solvents as a solvent for both extraction processes (Chemat et al., 2012; Asioli et al., 2017). In the literature, phenolic compounds from hazelnut skin has been extracted in a closed loop using a continuous set-up using water as solvent (Bertino et al., 2023). However, a study comparing and optimizing ultrasonic-assisted extraction and conventional solid-liquid extraction processes for the recovery of phenolic compounds from hazelnut skin using water as a solvent has not been encountered.

In this study, temperature, time, and loading capacity were determined as process parameters for the aqueous extraction of antioxidants and phenolic compounds from hazelnut skin, both for CE and UAE. Additionally, amplitude was added as a process factor for UAE. The TPC and AC of the extracts were examined as responses for both extraction methods. Optimization was performed to maximize the TPC and AC of hazelnut skin extract using RSM.

MATERIALS AND METHODS

Materials

Hazelnut (*Corylus avellana* L.) skins, obtained as by-products from different hazelnut varieties (Palaz, Tombul, Kara, and Çakıldak) under different roasting conditions (115°C for 30 min and 140°C for 15 min), were collected from a hazelnut processing plant located in Ordu, Türkiye. The hazelnut skins were ground using a laboratory-type grinding device and sieved through the range of 500 μm and 1 mm sieves. Distilled water (Millipore, USA) was used as the solvent in the extraction processes, and in preparation of the necessary solutions for TPC analysis. All chemicals used in the analyses, including 2,2-diphenyl-1-picrylhydrazyl (DPPH), 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox), Folin-Ciocalteu reagent, gallic acid, and methanol, were of analytical grade and purchased from Sigma-Aldrich (Steinheim, Germany) and Merck (Darmstadt, Germany).

Methods

Conventional extraction

The RSM approach was employed to optimize the process factors (independent variables) to obtain the desired extract. For conventional extraction, the independent variables were determined as temperature (ranging from 50°C to 90°C), time (ranging from 2 to 62 min), and loading capacity (ranging from 5% to 15%). These ranges were based on preliminary extraction studies and literature to maximize the TPC and AC values. An Optimal (custom) Design consisting of 20 trials was performed and the amount of hazelnut skin was determined by using a constant volume of solvent (50 mL) according to the experimental design. After mixing hazelnut skin and distilled water in a 100 mL jar, the mixture was placed into a water bath and shaken using a constant speed (150 rpm) according to the extraction conditions specified in the experimental design. At the end of the process, the extract was filtered through a filter paper followed by subsequent filtration through a Whatman filter paper (110 mm diameter). The filtered extract was then cooled to room temperature and stored at -18°C until analysis.

Ultrasonic-assisted extraction

The independent variables for the extraction process were determined as temperature (ranging from 25°C to 50°C), time (ranging from 1 to 30 min), loading capacity (ranging from 5% to 15%), and ultrasonic amplitude (ranging from 20% to 50%). These ranges were based on preliminary extraction studies and literature to maximize the TPC and AC values. An Optimal (custom) Design consisting of 25 trials was performed according to the RSM approach and the amount of hazelnut skin was determined by using a constant volume of solvent (50 mL) according to the experimental design. After mixing hazelnut skin and distilled water in a jacketed beaker (250 mL volume) coupled to a thermostatic water bath (RW-3025 Lab Companion, Korea), the probe depth was set up as 1 cm. Extraction was carried out using an ultrasonicator (VC750, Sonics and Materials, Inc., Newtown, CT, USA; 20 kHz, 750 W) equipped with a probe (13 mm diameter) according to the determined extraction conditions specified in the experimental design. The temperature of the mixture in the jacketed beaker was monitored using a digital thermometer throughout the process. At the end of the extraction process, the extract was filtered through a filter paper followed by subsequent filtration through a Whatman filter paper (110 mm diameter). The filtered extract was then cooled to room temperature and stored at -18°C until analysis.

Analysis

Total Phenolic Content (TPC)

To determine the TPC, 0.5 mL of the sample (diluted), 2.5 mL of Folin–Ciocalteu reagent (diluted 10 times with water), and 2 mL of sodium carbonate solution (7.5%, w/v) were added into a

test tube. The mixture was then vortexed (DragonLab, MX-S) to ensure thorough mixing. Water was used as a control sample, and all mixtures were incubated at 50°C for 5 min and then cooled to room temperature in a dark place for 10 min. After incubation, the absorbance of the mixtures was measured against the control sample at a wavelength of 760 nm using a spectrophotometer (Shimadzu UV-vis 160A, Japan). The total phenolic components were calculated based on the calibration curve of gallic acid and expressed as milligrams of gallic acid equivalent (GAE) per gram of material (Škerget et al., 2005).

Antioxidant capacity (AC)

The AC of the extracts was analyzed using a free radical scavenging capacity assay with 2,2-diphenyl-1-picrylhydrazyl (DPPH). Initially, 50 µL of the sample (diluted) was transferred into a test tube (Eppendorf, 1.25 mL), followed by the addition of 950 µL of a $6x10^{-5}$ M DPPH radical solution. The mixture was then vortexed (DragonLab, MX-S) to ensure thorough mixing. Water was used as a control sample, and all mixtures were kept in the dark for 30 min at room temperature. After incubation, the absorbance of the mixtures was measured at a wavelength of 516 nm using a spectrophotometer (Shimadzu UV-vis 160A, Japan). The results of the samples were calculated as ($Abs_{control}$ - Abs_{sample}). The AC was determined based on the calibration curve of Trolox, and the results were expressed as µmol Trolox equivalent per gram of material (Fernández-León et al., 2013).

Statistical Analysis

The statistical analysis was conducted using Design-Expert software (Stat-Ease Inc., Version 10, Minneapolis, USA) based on Response Surface Methodology (RSM). This software includes functions such as experimental design, modeling, and optimization studies. Model adequacies were evaluated using various metrics including the regression coefficient (R^2), adjusted regression coefficient (adj-R^2), predicted regression coefficient (pre-R^2), lack of fit value, coefficient of variance (C.V.), and adequate precision (Adeq.Precision). Additionally, insignificant terms (P >0.1) were removed to improve the model without compromising its hierarchy, and the statistical analysis was repeated. Furthermore, SPSS version 22.0 (IBM, USA) was utilized to verify the optimization by comparing the predicted and experimental responses. A one-sample t-test was conducted for this purpose. This statistical approach helps to assess the accuracy of the predicted values obtained from the optimization process.

RESULTS AND DISCUSSION

Effects of conventional extraction factors, model analysis, and optimization

The results of all trials for conventional extraction are presented in Table 1. The TPC varied from 75.27 to 155.06 mg GAE/g, while the AC, measured by DPPH free radical scavenging activity, ranged from 72.44 to 127.21 µmol TE/g. The optimal extraction condition, yielding the highest AC, involved extraction at 90°C for 24 min with a loading capacity of 15%. Conversely, the least favorable condition, resulting in the lowest AC, was extraction at 50°C for 6 min with a loading capacity of 15%.

The highest TPC and AC values were observed under the same condition (Run 19). Overall, there was a positive correlation between the TPC and AC values of the samples, as expected. However, some results suggested that the TPC and AC results could not be directly correlated with each other. This discrepancy may be due to the presence of other antioxidant components in hazelnut skin, such as tocopherols, carotenoids, and melanoidins, in addition to phenolic compounds (Shahidi et al., 2007; Açar et al., 2009; Göncüoğlu-Taş and Gökmen, 2015).

The regression coefficients of the proposed and reduced models, along with the effects of independent variables statistically on both responses (TPC and AC), are presented in Table 2. The lack of fit values of the models was found to be insignificant (P >0.05) for both TPC and AC values. For the TPC response, the R^2, adj-R^2, and pre-R^2 were determined as 0.8554, 0.8283, and 0.7733, respectively. Similarly, for the AC response, these coefficients were determined as

0.9174, 0.8879, and 0.7566, respectively. The difference between the pre-R^2 and the adj-R^2 was less than 0.2 for both TPC and AC, indicating that there are statistically insignificant terms in the model. Additionally, the low difference suggests that the model is effective. Moreover, the Adeq.Precision, which is desired to be greater than 4 for the model to be considered reasonable and to have adequate signals, was calculated as 14.579 and 17.066 for TPC and AC, respectively.

Table 1. Optimal (custom) design and responses for conventional extraction of hazelnut skin

Run	A: Temperature (°C)	B: Time (min)	C: Loading capacity(%)	Antioxidant capacity (μmol TE/g)	Total phenolic content (mg GAE/g)
1	90	48	5	118.07±3.29	126.72±1.36
2	70	48	10	106.09±0.38	124.18±0.14
3	70	48	10	107.31±0.45	123.75±0.57
4	50	48	15	81.94±1.38	91.19±1.28
5	70	48	10	104.58±1.06	130.01±0.00
6	50	12	10	80.28±2.12	75.27±1.07
7	50	48	10	85.41±0.46	103.95±0.59
8	50	6	15	72.44±0.65	91.80±1.00
9	50	62	5	83.90±0,00	93.69±0.54
10	90	2	10	106.25±0.61	130.58±2.84
11	90	48	5	117.82±4.05	150.48±0.23
12	70	12	5	106.43±1.27	124.69±0.68
13	70	48	10	97.81±2.12	111.94±1.00
14	90	24	15	122.75±5.41	136.87±0.93
15	90	6	5	123.13±4.81	138.27±1.13
16	50	24	5	89.72±0.76	99.39±0.54
17	70	48	15	95.79±0.93	118.02±1.73
18	90	62	15	120.84±2.55	152.81±2.52
19	90	24	15	127.21±0.95	155.06±2.66
20	70	2	15	72.50±1.27	108.15±0.12

The temperature of the extraction (ranging from 50 to 90°C) played a significant role ($P < 0.01$) in both the TPC and AC for CE, with the results showing an increasing trend as the temperature increased. This can be attributed to the temperature's effect, which triggers a higher diffusion rate and solubility of the extracted compounds. Additionally, it is considered that phenolic compounds are more easily recovered due to the softening or disruption of the cell wall and the decrease in the viscosity and surface tension of water used as the solvent (Hemwimol et al., 2006; Torun et al., 2015). Similarly, Amirabbasi et al. (2021) and Jesus et al. (2019) reported that temperature had a significant ($P < 0.01$) and positive effect on both the TPC and AC in CE. On the other hand, the extraction time (ranging from 2 to 62 min) and the loading capacity (ranging from 5% to 15%) demonstrated an insignificant effect on both responses ($P > 0.05$). However, the independent parameters and their interactions were found to significantly affect the AC ($P < 0.05$). The response surface graph illustrating this interaction effect is presented in Figure 1, and according to the graph, it was observed that the process conditions can be maximized if a longer extraction time (up to 35 min) and a lower loading capacity are applied.

Table 2. ANOVA results for antioxidant capacity and total phenolic content of extracts from conventional extraction (after removing the insignificant factors (P >0.1) from the models)

Source	Sum of Squares	df	Mean Square	F-value	Coefficient Estimate	p value
Antioxidant capacity						
Model	5388.79	5	1077.76	31.09		< 0.0001**
A-Temperature	4246.07	1	4246.07	122.48	18.38	< 0.0001**
B-Time	87.30	1	87.30	2.52	3.20	0.1349
C- Loading capacity	131.81	1	131.81	3.80	-3.20	0.0715
BC	171.09	1	171.09	4.94	5.34	0.0433*
B^2	280.28	1	280.28	8.08	-12.05	0.0130*
Residual	485.36	14	34.67			
Lack of Fit	421.43	9	46.83	3.66		0.0833
Pure Error	63.92	5	12.78			
Cor Total	5874.14	19				
C.V.: 5.83						
Adeq.Precision: 17.066						
R^2=0.9174						
Adj-R^2 =0.8879						
Pre-R^2=0.7566						
Final Equation in Terms of Coded Factors:						
R1=+105.79+18.38*A+3.20*B-3.20*C+5.34*BC-12.05*B^2						
Final Equation in Terms of Actual Factors:						
R1=+42.109+0.919*Temperature+0.608*Time-1.778*Loading capacity+0.036*Time*Loading capacity-0.013*$Time^2$						
Total phenolic content						
Model	8010.89	3	2670.30	31.54		<0.0001**
A-Temperature	7871.85	1	7871.85	92.99	24.70	<0.0001**
B-Time	291.52	1	291.52	3.44	5.67	0.0820
C- Loading capacity	2.99	1	2.99	0.035	0.48	0.8533
Residual	1354.44	16	84.65			
Lack of Fit	734.57	11	66.78	0.54		0.8177
Pure Error	619.87	5	123.97			
Cor Total	9365.33	19				
C.V.: 7.71						
Adeq.Precision: 14.579						
R^2=0.8554						
Adj-R^2 =0.8283						
Pre-R^2=0.7733						
Final Equation in Terms of Coded Factors:						
R2=+117.82+24.70*A+5.67*B+0.4812*C						
Final Equation in Terms of Actual Factors:						
R2=+24.355+1.235*Temperature+0.189*Time+0.096*Loading capacity						

*Statistically significant at a significance level of 0.05 **Statistically significant at a significance level of 0.01.

The temperature of the extraction (ranging from 50 to 90°C) played a significant role (*P <0.01*) in both the TPC and AC for CE, with the results showing an increasing trend as the temperature increased. This can be attributed to the temperature's effect, which triggers a higher diffusion rate and solubility of the extracted compounds. Additionally, it is considered that phenolic compounds are more easily recovered due to the softening or disruption of the cell wall and the decrease in the viscosity and surface tension of water used as the solvent (Hemwimol et al., 2006; Torun et al., 2015). Similarly, Amirabbasi et al. (2021) and Jesus et al. (2019) reported that temperature had a significant (*P <0.01*) and positive effect on both the TPC and AC in CE. On the other hand, the extraction time (ranging from 2 to 62 min) and the loading capacity (ranging from 5% to 15%) demonstrated an insignificant effect on both responses (*P >0.05*). However, the independent parameters and their interactions were found to significantly affect the AC (*P <0.05*). The response surface graph illustrating this interaction effect is presented in Figure 1, and according to the graph, it was observed that the process conditions can be maximized if a longer extraction time (up to 35 min) and a lower loading capacity are applied.

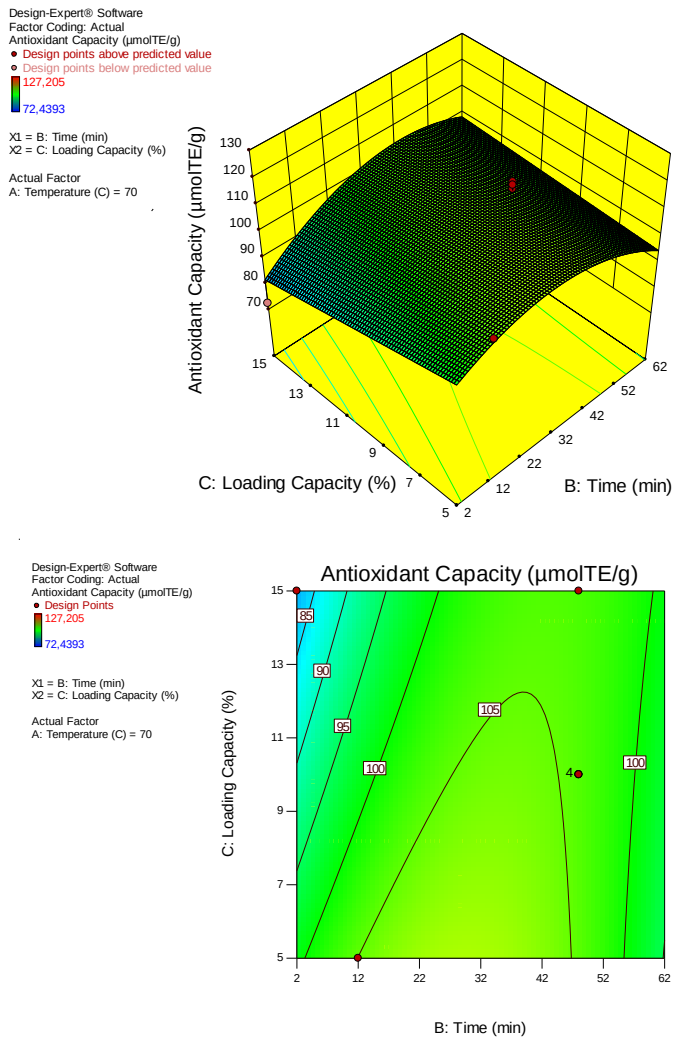

Figure 1. Effects of time (min) and loading capacity (%) on the antioxidant capacity of the hazelnut skin extract in CE

In conclusion, the optimum process conditions for CE of hazelnut skin were determined to be 90°C for 35 min with a loading capacity of 5%, resulting in a desirability function of 0.92. While the predicted TPC and AC were 142.62 mg GAE/g and 127.02 μmol TE/g, respectively, in the optimum conditions, experimental results were 136.52 mg GAE/g and 126.03 μmol TE/g, respectively. Statistical analysis using a t-test revealed no significant difference between the predicted and experimental TPC and AC values. Therefore, it can be concluded that the response surface methodology (RSM) model effectively predicts these responses in the CE of hazelnut skin.

Effects of ultrasonic-assisted extraction factors, model analysis, and optimization

The results of all trials for ultrasonic-assisted extraction were presented in Table 3. The TPC ranged from 54.76 to 134.51 mg GAE/g, while the AC (DPPH free radical scavenging activity) ranged from 47.93 to 117 μmol TE/g. Although the TPC results were consistent with those reported by Odabaş and Koca (2016) (ranging from 40.38 to 127.88 mg GAE/g), variations may occur due to factors such as climatic conditions during hazelnut growth, harvesting methods, storage conditions, and the parameters of hazelnut skin extraction.

Table 3. Optimal (custom) design and responses for ultrasonic-assisted extraction of hazelnut skin

Run	A:Temperature (°C)	B:Time (min)	C:Loading capacity (%)	D:Amplitude (%)	Antioxidant capacity (μmol TE/g)	Total phenolic content (mg GAE/g)
1	25	1	5	20	57.78±0.72	58.20±2.81
2	25	1	5	50	70.51±1.30	70.20±0.95
3	25	10	5	35	78.03±2.17	84.72±3.26
4	50	15	15	35	86.78±1.46	105.88±0.33
5	50	30	10	50	102.94±7.96	112.37±0.47
6	40	30	15	20	77.86±3.21	105.41±2.12
7	40	1	10	35	79.72±1.36	87.12±0.59
8	40	1	10	35	79.84±1.25	81.20±0.12
9	50	1	15	20	77.86±2.27	92.47±0.93
10	25	30	5	35	93.94±0.87	95.86±1.09
11	50	15	15	35	86.25±2.78	116.33±0.50
12	25	15	10	20	58.01±0.06	72.83±0.95
13	25	15	15	35	93.08±0.85	108.26±0.23
14	40	1	10	35	76.77±1.14	82.86±0.12
15	50	1	15	50	69.98±3.94	99.97±0.66
16	40	1	10	35	83.25±1.93	82.26±0.47
17	50	1	5	20	64.71±1.08	92.46±0.75
18	50	1	5	50	111.28±1.45	103.91±1.09
19	25	1	15	20	47.93±1.59	54.76±0.33
20	40	15	15	50	93.97±3.10	107.14±3.32
21	25	15	10	20	73.58±5.23	85.16±0.38
22	40	15	5	50	117.00	134.51±0.18
23	25	30	15	50	89.30±1.86	107.70±1.49
24	40	15	5	20	92.35±4.77	91.92±1.22
25	50	30	5	20	94.69±0.87	112.78±0.18

The highest TPC and AC values were achieved under the same extraction conditions, with a temperature of 40°C, extraction time of 15 min, loading capacity of 5%, and ultrasonic amplitude of 50% (Run 22). Similarly, the lowest values for both responses were obtained at identical extraction conditions, with a temperature of 25°C, extraction time of 1 min, loading capacity of 15%, and ultrasonic amplitude of 20% (Run 19). This high concordance between the AC and TPC values could be attributed to the presence of phenolic compounds in hazelnut skin, known for its high AC. Similar findings have been reported in previous studies on the composition of hazelnut skin in the literature (Shahidi et al., 2007; Contini et al., 2008; Pelvan et al., 2012; Göncüoğlu-Taş and Gökmen, 2015; Pelvan et al., 2018). Furthermore, it can be inferred that there exists a strong correlation between the antioxidant mechanism of phenolic compounds and the AC assay, particularly the DPPH free radical scavenging capacity (Bibi-Saader et al., 2020).

The regression coefficients of the proposed and then reduced models, along with the effects of independent variables statistically on both responses (TPC and AC), are presented in Table 4. The lack of fit values of the models was insignificant ($P > 0.05$) for both of them. The R^2, adj-R^2, and pre-R^2 were determined as 0.6719, 0.6063, and 0.4602 for AC, respectively, indicating a lower correlation between experimental and predicted values. However, for TPC, these coefficients were determined as 0.8216, 0.7747, and 0.6706, respectively, suggesting a relatively higher correlation. The difference between the pre-R^2 and the adj-R^2 was less than 0.2 for both TPC and AC, indicating statistically insignificant terms in the model, thus showing the model's effectiveness. Additionally, the Adeq.Precision, which is desired to be greater than 4 for the model to have adequate signals, was 15.410 and13.050 for TPC and AC, respectively, in the present results.

From the process conditions, temperature (25-50 °C), time (1-30 min), and amplitude (20-50%) had a significant effect ($P < 0.01$) individually on the TPC and AC values. An increase in extraction temperature led to an increase in both TPC and AC in both responses. This effect of the temperature parameter in ultrasonic-assisted extraction is similar to the effect of increasing temperature in CE, such as increasing the diffusion rate, mass transfer, and solubility (Hemwimol et al., 2006). Consistent with our findings, Hefied et al. (2023) reported a significant increase in TPC with increasing temperature from 20 °C to 50 °C, with the highest TPC value observed at 50 °C in preliminary experiments of the optimization study. Additionally, it was noted that increasing the extraction temperature from 25 to 50 °C resulted in higher TPC and AC in extracts, while exceeding 50 °C led to a decrease in TPC due to the heat-sensitive compounds (Bouafia et al., 2021). The effect of the temperature factor aligns with many studies reported in the literature (Chakraborty et al., 2020; Dinçel-Kasapoğlu et al., 2021; Sirichan et al., 2022).

According to our findings, extraction time (1-30 min) has shown a significant ($P < 0.01$) and positive effect on the TPC and AC values. Similarly, it has been reported that a higher extraction time leads to an increase in TPC and AC values in the recovery study from hazelnut skin by Odabaş and Koca (2016). Additionally, Wani and Uppaluri (2022) reported that extraction time had a significant and positive effect ($P < 0.01$) on the TPC and AC values. These studies are consistent with our results regarding the effect of extraction time.

Concerning the extraction time, it is stated that ultrasonic-assisted extraction occurs in two main stages: "washing" and "slow extraction," respectively. Initially, soluble components on the surface of the plant matrix are rapidly dissolved by the solvent penetrating the matrix, leading to the release of bioactive compounds at maximum levels. Then, in the second stage of "slow extraction," solute compounds are transferred from the plant matrix into the solvent via a diffusion mechanism. Although this stage has disadvantages such as longer time, higher energy consumption, and potential degradation of polyphenols, increasing the extraction time could

result in higher TPC until a certain value of time (Vinatoru, 2001; Şahin and Şamlı, 2013). Furthermore, the limiting effect of time is related to the cessation of mass transfer when the solute and extraction solution reach equilibrium (Ciğeroğlu et al., 2018). These findings underscore the importance of optimizing the time parameter.

Table 4. ANOVA results for antioxidant capacity and total phenolic content of extracts from ultrasonic-assisted extraction (after removing the insignificant factors (P >0.1) from the models)

Source	Sum of Squares	df	Mean Square	F-value	Coefficient Estimate	p value
Antioxidant capacity						
Model	4265.20	4	1066.30	10.24		0.0001**
A-Temperature	848.63	1	848.63	8.15	7.12	0.0098**
B-Time	1388.47	1	1388.47	13.33	9.89	0.0016**
C- Loading capacity	486.22	1	486.22	4.67	-5.26	0.0430*
D-Amplitude	1595.73	1	1595.73	15.32	10.13	0.0009**
Residual	2082.59	20	104.13			
Lack of Fit	1940.17	15	129.34	4.54		0.0518
Pure Error	142.42	5	28.48			
Cor Total	6347.79	24				
C.V.: 12.40						
Adeq.Precision: 13.050						
R^2=0.6719						
Adj-R^2 =0.6063						
Pre R^2=0.4602						
Final Equation in Terms of Coded Factors:						
R1=+85.57+7.12*A+9.89*B-5.26*C+10.13*D						
Final Equation in Terms of Actual Factors:						
R1=+40.502+0.570*Temperature+0.682*Time-1.0514*Loading capacity+0.676*Amplitude						
Total phenolic content						
Model	6806.32	5	1361.26	17.50		< 0.0001**
A-Temperature	2417.51	1	2417.51	31.08	12.15	< 0.0001**
B-Time	2213.22	1	2213.22	28.46	12.70	< 0.0001**
C- Loading capacity	3.81	1	3.81	0.049	-0.47	0.8271
D-Amplitude	1044.95	1	1044.95	13.44	8.20	0.0016**
B^2	635.33	1	635.33	8.17	-11.07	0.0101*
Residual	1477.73	19	77.78			
Lack of Fit	1326.80	14	94.77	3.14		0.1064
Pure Error	150.93	5	30.19			
Cor Total	8284.05	24				
C.V.:9.40						
Adeq.Precision:15.410						
R^2=0.8216						
Adj-R^2 =0.7747						
Pre-R^2=0.6706						
Final Equation in Terms of Coded Factors:						
R2=+104.75+12.15*A+12.70*B-0.47*C+8.20*D-11.07*B^2						
Final Equation in Terms of Actual Factors:						
R2=+23.863+0.972*Temperature+2.508*Time-0.094*Loading capacity+0.547*Amplitude-0.053*$Time^2$						

*Statistically significant at a significance level of 0.05 **Statistically significant at a significance level of 0.01.

The ultrasonic amplitude parameter is crucial for ultrasonic-assisted extraction as it can influence the cavitation phenomenon, which facilitates the release of target compounds by disrupting cell walls and enhancing solvent penetration into the sample matrix (Hemwimol et al., 2006). This factor (20-50%) exhibited a significant effect ($P < 0.01$) on both TPC and AC, showing a positive correlation. Similarly, Rakshit and Srivastav (2020) reported that ultrasonic amplitude (40-60%) had significant effects on TPC and AC ($P < 0.01$), with the optimum amplitude value determined as 50% by RSM. Additionally, Rohilla and Mahanta (2021) indicated that phenolic compounds increased with increasing ultrasonic amplitude from 10 to 50%, but beyond 70%, phenolic compounds started to decrease due to heat sensitivity. Furthermore, it was reported that TPC and AC values increased significantly with increasing amplitude value (30-50%) by Sirichan et al. (2022).

The loading capacity (5-15%) exhibited a significant linear effect ($P < 0.05$) on antioxidant activity, with decreasing loading capacity positively impacting AC. This result could be attributed to the increase in the diffusion rate of bioactive compounds triggered by concentration differences, acting as the driving force (Cacace and Mazza, 2003). Moreover, it can also be explained by the effective production of cavitation bubbles, resulting in a high volume-to-surface area ratio (Pandey et al., 2018). However, this factor did not have a significant effect ($P > 0.05$) on the total phenolic compounds within the range of 5-15% loading capacity in our results. In summary, while loading capacity (5-15%) affected AC, it did not statistically affect TPC. This result could indicate the presence of other antioxidant components such as tocopherols, carotenoids, and melanoidins apart from phenolic compounds.

In conclusion, the optimal process conditions for ultrasonic-assisted extraction of hazelnut skin were determined as 50 °C for temperature, 27 min for time, 5% for loading percentage, and 50% for amplitude, resulting in a desirability function of 0.96. In these conditions, the model predicted a TPC of 129.69 mg GAE/g and an AC of 116.00 μmol TE/g. Upon experimental validation, the actual TPC and AC values were measured as 132.41 mg GAE/g and 125.03 μmol TE/g, respectively. Statistical analysis using the t-test revealed no significant difference between the predicted and experimental values for TPC and AC, indicating that the response surface methodology (RSM) model effectively predicted these responses in the ultrasonic-assisted extraction of hazelnut skin.

CONCLUSION

In this study, aqueous extracts rich in phenolic compounds and antioxidants were obtained from hazelnut skin using both CE and UAE methods. The effects of extraction conditions on TPC and AC were investigated using RSM. Optimal parameters were determined as 90°C temperature, 35 min time, and 5% loading capacity for CE, and 50°C temperature, 27 min time, 5% loading capacity, and 50% amplitude for UAE. The responses of the optimized extracts were similar between the two extraction methods, with TPC values of 136.52 mg GAE/g for CE and 132.41 mg GAE/g for UAE, and AC values of 126.03 μmol TE/g for CE and 125.03 μmol TE/g for UAE. Furthermore, there were no significant differences between the predicted and experimental values of TPC and AC for the optimized extracts. In summary, while both extraction methods yielded similar results, UAE offers the advantage of shorter extraction time. Therefore, UAE may be preferred for its efficiency. The aqueous extracts obtained from hazelnut skin, rich in phenolic compounds, can delay or prevent lipid oxidation and serve as natural antioxidants in the food industry, potentially replacing synthetic antioxidants. From an engineering point of view, understanding of optimum conditions in hazelnut skin extraction is crucial for scaling up to pilot and subsequently developing industrial applications.

CONFLICT OF INTEREST

There are no conflicts of interest or competing with the results of the presented article.

AUTHOR CONTRIBUTION

Merve ÖZDEMİR: Carrying out the experiments, data analysis, writing draft.
Mehmet TORUN: Writing, review, editing, supervision.

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