



## Investigation of Operating Parameters on Ultrasound-Assisted Extraction of Anethole in Fennel Essential Oil

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ARTICLE INFO	ABSTRACT
<p><b>Article History:</b> Received: 05 June 2021 Revised: 13 August 2021 Accepted: 14 August 2021</p> <p><b>Article type:</b> Research</p> <p><b>Keywords:</b> Anethole, Extraction, Fennel, Soxhlet, Ultrasound-Assisted</p>	<p>In this paper, the operational impact of three parameters, including the power of ultrasonic apparatus, size of fennel seeds, and experiment time on the extraction yield of anethole, the major component in fennel essential oil and its concentration, have been studied through ultrasound-assisted extraction (UAE). The ultrasonic extraction from fennel seeds using a solution of 70% water-ethanol was studied at different particle sizes, different ultrasonic powers and three different levels of time. The most effective parameter was particle size, while the experiment time had the least impact on both the efficiency and anethole concentration as well. As a result, compared to the Soxhlet method, the ultrasonic-assisted extraction was more efficient. In this experiment, eighteen constituents were identified for fennel seeds using GC-MS. The major components were anethole (78.12%), fenchone (8.81%), limonene (4.39%), and estragole (4.52%). Furthermore, the analysis of two quadratic models using the box-Behnken design (BBD) indicated that the quadratic polynomial model could be applied for estimating the anethole extraction yield as well as anethole concentration.</p>

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## Introduction

In the past decades, significant attention was dedicated to the production of valuable foods and medical materials. Natural compounds derived from herbal plants have been widely used in the food, pharmaceutical, and perfume industries [1, 2]. Fennel (*Foeniculum Vulgare*) is a type of plant in the umbelliferae family, which normally grows in Asia and the Mediterranean region [3, 4]. The fennel extracts consist of monoterpenes, terpenes that could be utilized in pharmaceutical, health, and food industries [4]. The fennel extract's medicinal purposes include blood pressure reduction.

Furthermore, it has been used as an anti-spasmodic, anti-hypertensive, and anti-inflammatory. Fennel could be applied to cure different diseases and performs as an agent for being carminative and diuretic. Furthermore, it could be utilized as an antioxidant and antimicrobial agent [5-9]. Among the major constituents in fennel seeds' essential oil are anethole, fenchone, and estragole [10, 11]. Anethole (the major component of fennel seeds extract) is an estrogenic agent and, due to its vaso-relaxant and clot destabilizing effect, could be utilized as an antithrombotic agent [9]. Anethole and estragole consist of methoxy and propenyl functional groups. To extract compounds with methoxy, propenyl, and phenolic functional groups, some specific solvents are commonly used, including water, acetonitrile, ethanol, methanol, and ethyl acetate [12]. The combination of organic solvents and water demonstrated higher extraction efficiency compared with the pure solvents [13]. For the extraction of phenolic compounds, the mixture of 80:20% v/v ethanol-water resulted in the highest extraction yield [14].

There are several ways of the extraction of essential oil from herbal plants. These techniques include pressing, crushing, solvent extraction (SE), microwave-assisted extraction (MAE), supercritical fluid extraction (SFE), and ultrasound-assisted extraction (UAE) [15-19]. To choose a suitable extraction method, some factors should be considered, including types of the plant, solvent, sensitivity of the essential oil, and the obtained concentration of the desired component [20, 21]. Traditional solvent extraction techniques require many organic solvents, energy and are time-consuming [14, 22]. The common and conventional method for extraction is distillation. However, this method might cause degradation of sensitive compounds as a result of temperature [17]. There are volatile substances in essential oils that can be easily affected by high temperatures [23]. Thermal effects can degrade the essential oil compounds, and therefore, byproducts might be produced utilizing high intensity of heat [4, 24]. In order to avoid the production of undesired materials, an effective extraction process should be utilized. Steam distillation, solvent extraction, percolation, and centrifugation methods have been applied to extract fennel seed essential oils.

Furthermore, supercritical fluid extraction was used for the extraction of fennel seed essential oils. Although the obtained extraction yield was 22.25 mg/g, however, the operating conditions for achieving this yield were not efficient (temperature 70 °C, pressure 25 MPa, and time 100 min). Moreover, the recovery of anethole extraction was obtained to be 54.08% [9].

Ultrasound-assisted extraction (UAE) has been utilized to extract a variety of bioactive compounds from the herbal plant [22]. The ultrasonic method can prevent causing damage to vital components. Also, it reduces the extraction time and increases the extraction efficiency [14, 25, 26]. This method improves mass transfer and capillary effects [22]. Furthermore, this technique enables an increased contact surface between the solvent and solid, allowing solvent penetration [27]. The mass transfer operation in the UAE occurs in two stages. The first step involves the explosion of the layer containing the herbal tissue, and the second step involves the mass transfer from the herbal plants into the solution due to the presence of a driving force [8]. The extraction yield of the UAE method can be affected by some parameters, including

sonication time, temperature, solvent composition, size of the chopped plant, and the sonication power [28].

The response surface methodology (RSM), which is a statistical and mathematical method, was used for the optimization of the parameters [29, 30]. In this paper, the UAE technique was applied for the extraction of essential constituents from fennel seeds, and the three-level box-Behnken design (BBD) method was used to optimize the number of tests, and a quadratic mathematical model was proposed to evaluate the parameters. Also, a solution of 70% v/v ethanol-water was used as the solvent because of its low toxicity and acceptability in food applications [31, 32]. This study intends to determine the impact of the three-mentioned operation parameters on the extraction yield and concentration of anethole as the major component in the essential oil of fennel seeds.

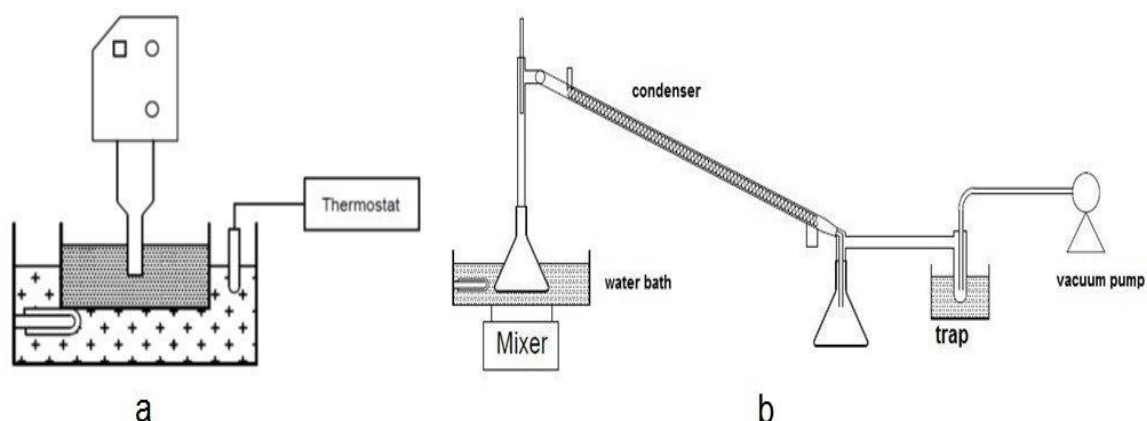
## Materials and Methods

### Soxhlet Method

Fennel seeds were purchased from Hamadan suburban region. The dried seeds were milled and were passed through the vibrating sieve shaker (Novin Tajhiz Azma, Iran) with different mesh sizes of 12, 18, and 50 (ASTM classifications). The optimum solvent to solid ratio was obtained between 10-17 g solvent/ 1 g dried plant [33]. For this purpose, an amount of 15 g of fine milled powders of fennel seeds with the mesh size number of 18 (ASTM classifications) was soaked in the 200 g of ethanol (13.3 g solvent/ g dried plant) Merck, Germany. The runtime of the extraction of essential oil from the fennel seeds in the Soxhlet system was 2 hr. This experiment was carried out as a criterion for analyzing the essential constituents with the gas chromatography-mass spectrometry method.

### Ultrasound-Assisted Extraction

An amount of 5 g of fennel seeds fine powder (mesh sizes of 12, 18, and 50 ASTM classifications) were added to 80 ml of 70% v/v ethanol-water solution. Subsequently, the mixture was sonicated at different times, using UP4000S Hielscher at 400W and 24 kHz and the constant temperature of 40 °C. Afterward, the mixture was transferred to the centrifuge (Iran, KTS) and was centrifuged at 4000 rpm for 20 min. Fig. 1a demonstrates the schematic of the ultrasound-assisted extraction. The supernatant was transferred to the rotary evaporator, as shown in Fig. 1b. The rotary evaporator decreased the pressure and boiling point and was utilized for the separation of solvents with low boiling points. The rotary evaporator device consisted of a mixer (ALFA, D500) used for feed agitation. The water bath maintained the temperature at 50 °C. The condenser and pressure controller was utilized for vapor condensation and for maintaining constant pressure, respectively. Afterward, the samples were dried in the oven for 24 hours at a temperature of 60 °C. Subsequently, the dried samples were weighted and made up to 1 ml by dissolving in the n-hexane through the utilization of Thermo-mixer (LongGene, China) at 300 rpm for 20 min. Subsequently, the samples were centrifuged at 4000 rpm for 10 min before the GC analysis. The composition of the constituents of the samples was measured by GC analysis.



**Fig. 1.** (a) The schematic diagram of the ultrasound-assisted extraction, (b) The rotary evaporator for the separation of the ultra-sonicated components

## Identification Procedure

The extracts and essential constituents were analyzed through gas chromatography using the Agilent Technologies 7890A Gas chromatograph and the 5975C VL MSD with triple-Axis detector as a mass selective detector. The GC was equipped with the 30 m×0.25 mm silica capillary Rtx 5 MS column with the 25  $\mu$ m film. The device operating temperature had the range of 40-250 °C at 3°C/min, the injector temperature of 250 °C, the detector temperature of 230 °C, and carrier gas was 99.99%. The liquid extract (volume of 0.2  $\mu$ L) was injected to be tested. The percentage of the constituents was calculated by Agilent MSD Chemstation (Rev E.02.02. 1413).

## Design of Experiments

In this study, the design-expert software was utilized for the design of experiments (DOE). The DOE proposes the best experiments according to the parameter levels. For the box-Behnken design, 3 parameters, including time (A), power (B), particle size (A) in 3 levels were selected: -1, 0, and +1, representing low, middle, and high levels, respectively. [Table 1](#) shows the parameters and levels. Totally, a list of 17 runs with 5 central points was selected to be conducted in the laboratory, which can be seen in [Table 2](#). These experiments were carried on to evaluate the extraction yield and concentration of the anethole by the three selected parameters.

**Table 1.** Factors and levels for the Box-Behnken design

Factor	Notation	Level		
		-1	0	1
Time (min)	A	20	40	60
Power (W)	B	80	240	400
Particle Size (mm)	C	0.3	1	1.7

## Results and Discussion

### Characterization of the Volatile Components in Fennel Essential Oil

The constituents of the essential oil extracted from the Iranian fennel seeds through the Soxhlet system were determined from the GC. Overall, 18 compounds were identified, and the most constituents in the essential oil were anethole, fenchone, estragole, and limonene.

Besides, the constituents of the essential oils obtained through the UAE method were determined through the GC analysis, tabulated in Table 2, which there are higher figures in percentages of four major components each through the ultrasonic-assisted extraction in comparison with Soxhlet method.

**Table 2.** The percentage of major components in the ultrasonic experiments

No.	Time (min)	Power (w)	particle size (mm)	anethole	fenchone	estragole	limonene
1	40	240	1	80.06	9.14	5.54	5.24
2	40	240	1	81.26	9.78	4.78	4.16
3	20	80	1	80.71	9.72	4.88	4.67
4	60	240	0.3	82.00	9.31	4.58	4.09
5	40	400	0.3	81.02	9.57	4.87	4.52
6	40	240	1	81.14	9.59	4.7	4.56
7	20	240	0.3	80.94	9.77	4.71	4.56
8	40	240	1	83.62	8.48	4.12	3.76
9	20	240	1.7	80.78	9.79	4.88	4.53
10	20	400	1	81.53	9.7	4.63	4.13
11	60	400	1	80.58	9.76	4.84	4.8
12	60	80	1	80.48	9.93	4.88	4.69
13	40	80	1.7	81.86	9.24	4.62	4.26
14	40	80	0.3	80.70	9.76	4.88	4.65
15	60	240	1.7	80.89	9.74	4.82	4.53
16	40	400	1.7	80.86	9.65	4.75	4.72
17	40	240	1	81.07	9.55	4.83	4.53

The extraction yield was measured by Eq. 1, where  $W_C$  represents the weight of the dried sample, and  $W_s$  represents the initial weight of the powdered fennel seeds.

$$\text{Extraction Yield (g/g)} = \frac{W_C(g)}{W_s(g)} \times 100 \quad (1)$$

The designed matrix of variables and the responses obtained from the experiments are presented in Table 3. Table 4 indicates the sum of squares, F value, and P-value (Probability). A value of 109.95 for the F-value reveals that the model is significant. The quadratic model proposed by the Design-Expert was the most suitable method for the prediction of the extraction yield. This model is established based on the F-value and lower lack of fit (LOF), and the prediction error sum of squares (PRESS), in order to fit the experimental data. The  $R^2$  is the percentage of variation of the dependent variable from the independent variables in the model. It is used to measure the fitting degree. The  $R^2$ ,  $R^2_{\text{adjusted}}$ , and  $R^2_{\text{predicted}}$  values were 0.985, 0.976, and 0.945, respectively, as stated in Table 5.

Additionally, the F-value (109.95) and the value of probability (<0.0001), confirmed the significance of the predicted model. The predicted data versus the actual values of the extraction yield are shown in Fig. 2. The mathematical model measuring the extraction yield is expressed in Eq. 2:

$$\text{yield} = 1.55746 + 0.01475A - 0.000492188B - 1.40689C - 0.00014375A^2 - 0.000003B^2 + 0.37755C^2 \quad (2)$$

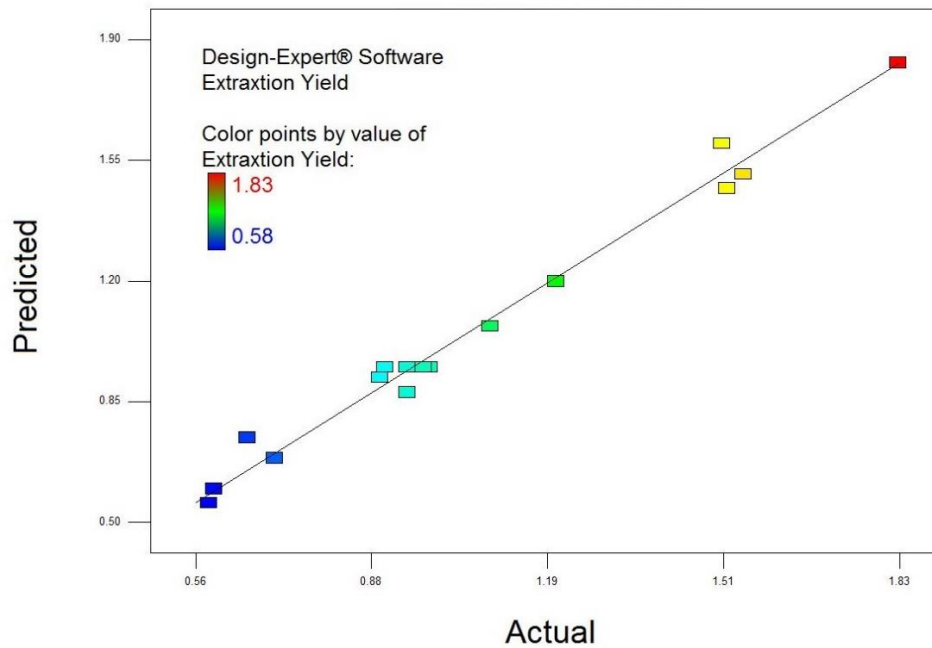


Fig. 2. The predicted values versus actual values of the extraction yield

Table 3. Design matrix and the responses for the BBD of the extraction yield

No.	A: Time (min)	B: Power (w)	C: particle size ( mm)	Response%
1	20	240	1.70	0.58
2	40	400	1.70	0.89
3	60	240	1.70	0.7
4	40	80	1.70	0.59
5	40	400	0.30	1.83
6	40	240	1.00	0.9
7	20	80	1.00	0.65
8	40	240	1.00	0.96
9	20	400	1.00	1.09
10	40	240	1.00	0.94
11	60	80	1.00	0.94
12	40	80	0.30	1.55
13	60	400	1.00	1.21
14	20	240	0.30	1.52
15	60	240	0.30	1.51
16	40	240	1.00	0.98
17	40	240	1.00	0.97

Table 4. Analysis of variance (ANOVA) of the quadratic response surface model for Eq. 2

Source	Sum of Squares	D F	F - Value	P-value Prob > F	
Model	2.0850	6	109.95	< 0.0001	Significant
A-Time	0.0356	1	10.65	0.0085	
B-Power	0.2088	1	65.57	< 0.0001	
C-Particle Size	1.6603	1	524.92	< 0.0001	
A <sup>2</sup>	0.0119	1	4.39	0.0626	
B <sup>2</sup>	0.0278	1	8.49	0.0154	
C <sup>2</sup>	0.1405	1	45.42	< 0.0001	
Residual	0.032	10			
Lack of Fit	0.0280	6	4.62	0.0801	Not significant

<b>Pure Error</b>	0.004	4
<b>Corrected Total</b>	2.12	16

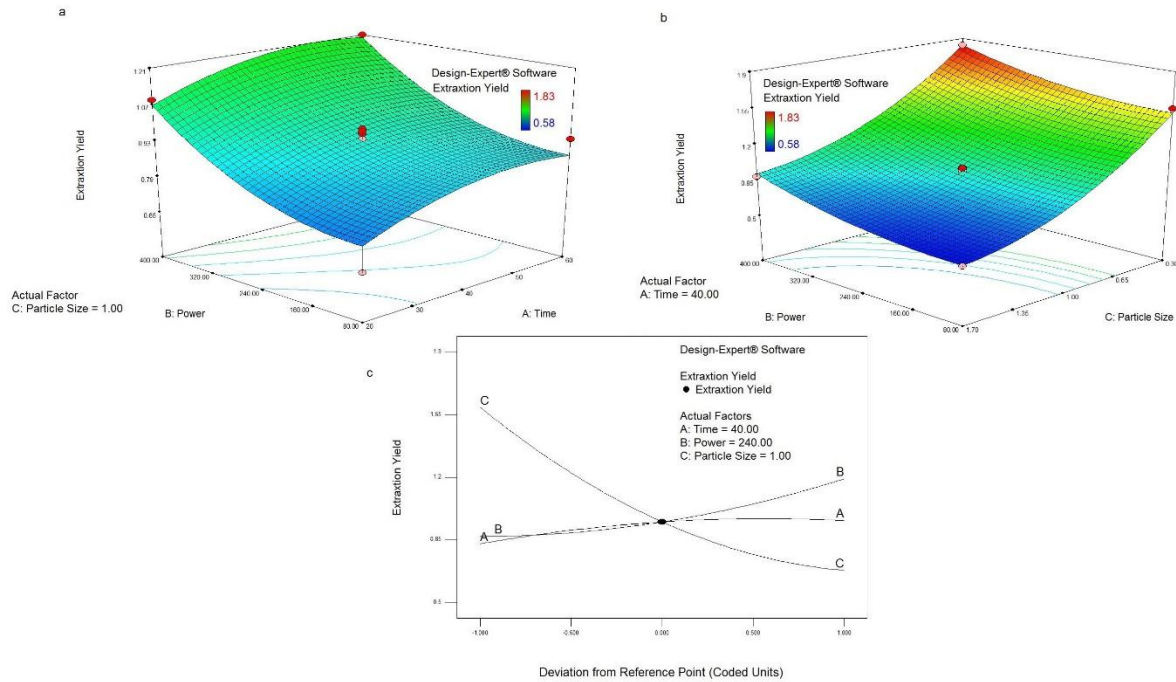
**Table 5.** Statistical parameters for the quadratic model in Eq. 2

<b>Std. Dev.</b>	<b>0.056</b>	<b>R<sup>2</sup></b>	<b>0.9851</b>
<b>Mean</b>	1.05	<b>R<sup>2</sup><sub>Adjusted</sub></b>	0.9761
<b>C.V. %</b>	5.38	<b>R<sup>2</sup><sub>Predicted</sub></b>	0.9449
<b>PRESS</b>	0.12	<b>Adequate Precision</b>	35.311

### Effects of the Time, Temperature and Ultrasonic Power on the Extraction Yield

Fig. 3a represents the response surface plot for the extraction yield as the function of time and power at the constant particle size of 1 mm. According to Fig. 3a, increasing the extraction time leads to an increase in the yield of extraction. Due to an optimum value in the extraction time for different power values, the extraction time range of 20-60 min was suitable for the extraction. The effect of time on the extraction yield is negligible in the range of 30-60 min. Fig. 3c is the perturbation plot, representing the extraction yield versus the deviation from the reference point. According to Fig. 3c, the slope of parameter a (time) is low, indicating the negligibility of time impact on the extraction yield. This could be due to the degradation of bioactive compounds, caused as a result of the usage of ultrasonic waves for a long period of time [30]. According to Fig. 3a, Power has a positive impact on the extraction yield. The slope of extraction yield versus power increases with increasing ultrasound power, which indicates that the influence of power is greater than the effect of time and it is shown in Fig. 3c.

The effect of ultrasonic power and particle size on the extraction yield was investigated at different power levels of 80-400 W and different particle sizes of 0.3-1.7 mm. Fig. 3b demonstrates the response surface plot of the extraction yields as the function of power, and particle size at the constant time of 40 min. According to Fig. 3b, particle size has a greater effect on the extraction yield compared to the power, and the extraction yield is not significantly affected by the low ultrasonic powers and high particle sizes. The increase in the extraction yield with power is a result of cell tissue disruption due to the higher energy, which leads to the release of more constituents. Moreover, by milling the fennel seeds, the necessity of increasing the power, and time for the purpose of extraction decreases since essential oil compounds can be released more easily in a short period, due to the increased contact area and higher concentration gradient [28, 34, 35].



**Fig. 3.** (a) the effect of the ultrasonic power and time on the extraction yield at the particle size of 1 mm, (b) the effect of the ultrasonic power and particle size on the extraction yield, (c) the perturbation plot

### Investigation of Anethole Concentration Extracted through the Ultrasound Method

The concentration of anethole present in the extract was investigated through the response surface methodology from the box-Behnken design. The value of Anethole concentration (mole/lit) in the extract is calculated by using Eq. 3, where  $X_j$  is the mass fraction of anethole (gr/gr),  $\rho$  is the solution density (gr/lit), and  $M_w$  is the Molecular mass (gr/mole) of anethole in the sample.

$$C_j^{Anethole} = \rho \frac{x_j^{Anethole}}{M_w^{Anethole}} \quad (3)$$

The design matrix and the responses from the box-Behnken method are reported in Table 6. Statistical criteria for evaluating the anethole concentration model are also mentioned in Table 7 and Table 8. The best-fitted correlation proposed by the DOE is presented in Eq. 4, where  $C_{anethole}$  (mole/lit) is the concentration of anethole. The predicted values versus actual values of  $C_{anethole}$  is shown in Fig. 4.

$$C_{anethole} = 0.165 - 0.00034A - 0.000049B - 0.0982C + 8.4 \times 10^{-6}A^2 + 3.3 \times 10^{-7}B^2 + 0.0276C^2 \quad (4)$$



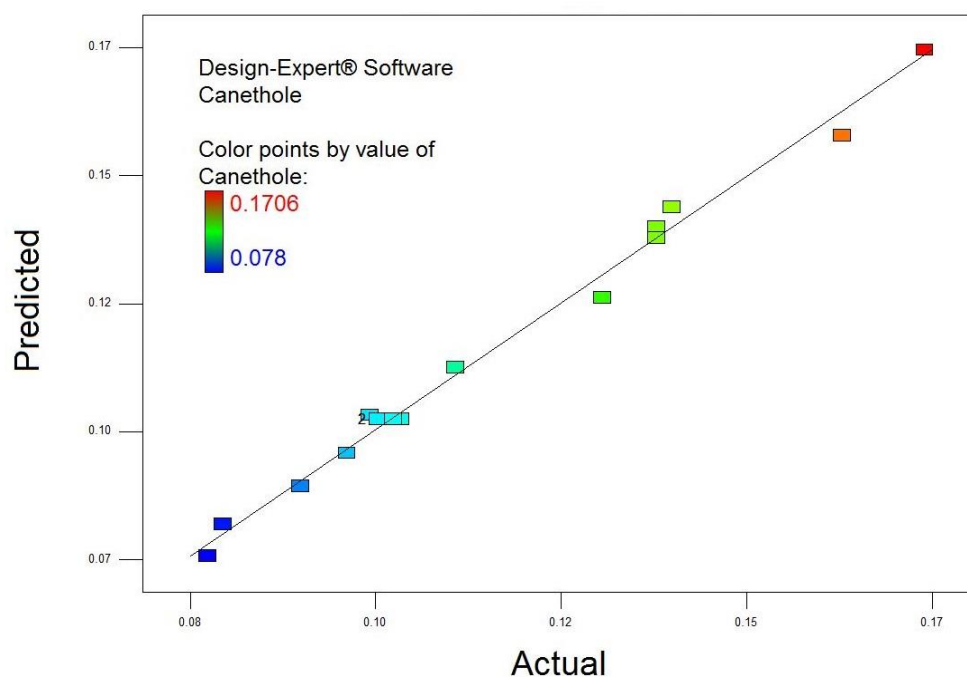


Fig. 4. The predicted data versus the actual values of  $C_{anethole}$

Table 6. Design matrix and the responses from the BBD for anethole Concentration

Number (j)	A: Time (min)	B: Power (watt)	C: particle size ( mm)	$C_{anethole}$ (mole/lit)
1	40	80	1.70	0.078
2	60	240	0.30	0.16
3	40	80	0.30	0.136
4	60	400	1.00	0.136
5	40	400	0.30	0.1706
6	60	240	1.70	0.096
7	20	240	1.70	0.08
8	40	240	1.00	0.103
9	20	80	1.00	0.09
10	40	400	1.70	0.11
11	40	240	1.00	0.102
12	40	240	1.00	0.1
13	20	240	0.30	0.138
14	20	400	1.00	0.129
15	40	240	1.00	0.103
16	40	240	1.00	0.101
17	60	80	1.00	0.099

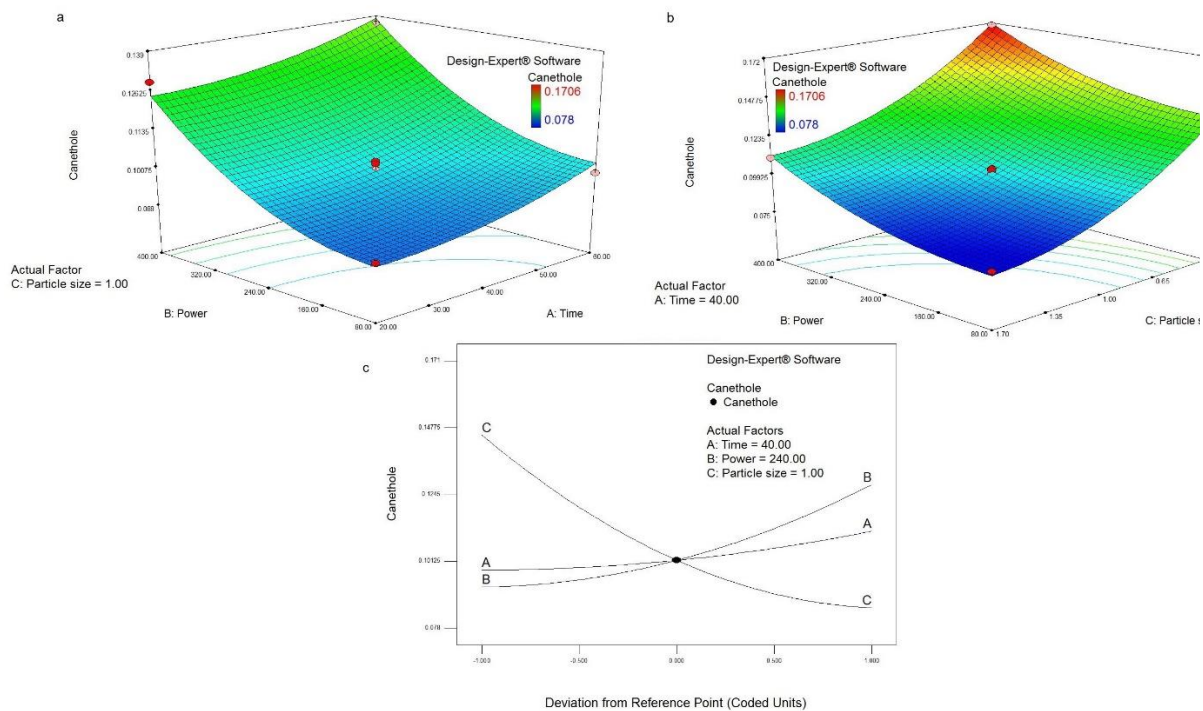
Table 7. Analysis of variance (ANOVA) of the quadratic response surface model for Eq. 4

Source	SS	DF	F Value	Prob > F	
Model	0.011	6	201.72	< 0.0001	Significant
A-Time	3.645E-004	1	38.83	0.0011	
B-Power	2.542E-003	1	270.75	< 0.0001	
C-Particle Size	7.236E-003	1	770.78	< 0.0001	
B <sup>2</sup>	4.796E-005	1	5.11	0.0054	
C <sup>2</sup>	3.060E-004	1	32.60	0.0010	
Residual	7.702E-004	10			
Lack of Fit	8.468E-005	6	6.14	0.0547	Not significant
Pure Error	9.200E-006	4			
Corrected Total	0.011	16			

**Table 8.** Statistical parameters for the quadratic model in Eq. 4

<b>Std. Dev.</b>	<b>0.003</b>	<b>R<sup>2</sup></b>	<b>0.9918</b>
<b>Mean</b>	0.11	<b>R<sub>Adj</sub><sup>2</sup></b>	0.9869
<b>C.V. %</b>	2.70	<b>R<sub>Pred</sub><sup>2</sup></b>	0.9692
<b>PRESS</b>	0.0003	<b>Adequate Precision</b>	48.725

Fig. 5a demonstrates the influence of power and time on the concentration of anethole. Despite the reduction in extraction yield with increasing the time (40-60 min), the rate of anethole concentration increases by time, as shown in Fig. 5a. Furthermore, this has been demonstrated in Fig. 5c. This results from longer sonication, which leads to the release of more anethole from the fennel seeds. Additionally, the impact of ultrasonic power is higher than the impact of time for the extraction of anethole from the fennel seeds. Fig. 5b shows the effect of the ultrasonic power and particle size on the anethole concentration. It can be concluded that the impact of particle size is greater than ultrasonic power, and time has less impact on the extraction of anethole from the fennel seeds.



**Fig.5.** (a) the effect of the ultrasonic power and time on the anethole concentration at the particle size of 1 mm, (b) the effect of the ultrasonic power and particle size on the anethole concentration, (c) the perturbation plot

## Conclusion

This study demonstrates that the ultrasound-assisted extraction method is an effective technique for extracting essential oil from the fennel seeds, and consequently medicinal plants, at a constant temperature of 40 °C. The GC analysis revealed that Iranian fennel seeds' major constituents are anethole, fenchone, estragole, and limonene. Particle size and ultrasonic power greatly influenced the extraction yield, although the experiment time did not significantly contribute to the process results. The maximum extraction yield was obtained to be 18.3 mg/g

with an 80% percent anethole recovery. In addition, a positive impact and statistically significant relationship between the extraction yield and anethole concentration and the operative variables were determined. As a result, the reduction in particle size from 1.7 mm to 0.3 mm enhanced essential oil extraction. The application of box–Behnken experimental design was suitable for estimating the amount of extracted essential oils. Additionally, a comparative analysis between the UAE and the Soxhlet method reveals that the ultrasound-assisted extraction is more economical and environmentally friendly than Soxhlet due to the limited consumption of ethanol instead of water and less heat energy and operational time is needed by this method. Hence, as a result, it prevents some volatile compounds from being degraded because of operating at lower temperatures.

## Nomenclature

$C$	Concentration (mole/Lit)
$x_j$	Mass fraction
$W$	Weight (g)
$M_w$	Molecular weight
$P$	Solution density ( $\text{kg/m}^3$ )

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## Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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