



Optimization and kinetics modeling of phenolics extraction from coffee silverskin in deep eutectic solvent using ultrasound-assisted extraction

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ABSTRACT

This research investigates the effect of extraction parameters on total phenolic content (TPC) and the antioxidant capacity of coffee silverskin (CS) extract using ultrasound-assisted extraction (UAE) in deep eutectic solvent (DES). The optimization was carried out in two stages: (i) the optimization of the UAE condition with the highest TPC; and (ii) a four-factor Box-Behnken design (BBD) to optimize the UAE condition with the optimal TPC; 2,2 diphenyl-1-picrylhydrazyl (DPPH) radical scavenging capacity; and ferric reducing antioxidant power (FRAP). The results showed that the optimal UAE condition with the highest TPC was 150–250 μm CS particle size; 1,6-hexanediol as hydrogen bond donor (HBD); 1:7 HBA:HBD molar ratio; and 30% (w/w) water content, given choline chloride (ChCl) as hydrogen bond acceptor (HBA), 30 min extraction time and 30 ° C extraction temperature. The BBD-based optimal UAE condition was 30% w/w water content, 45 mL/g liquid/solid ratio, 90 min extraction time and 85 ° C extraction temperature, given the CS particle size of 150–250 μm and the HBA:HBD molar ratio of 1 (ChCl): 7 (1,6 hexanediol), achieving 19.19 ± 0.20 mg GAE/g CS for TPC, 24.06 ± 1.77 mg TE/g CS for DPPH radical scavenging capacity, and 59.13 ± 4.55 mg Fe (II)/g CS for FRAP. The experimental results were in good agreement with the BBD-based predicted results (22.40 mg GAE/g CS for TPC, 24.09 mg TE/g CS for DPPH, and 59.43 mg Fe(II)/g CS for FRAP). The two-site kinetics model best fitted the experimental data, with R^2 of 0.991–0.999.

1. Introduction

Coffee silverskin (CS) is a thin tegument that covers the coffee seed. During the roasting process, CS is the main by-product that detaches from coffee beans and is normally disposed of as waste [1]. The conversion of CS into value-added products is thus an eco-friendly and sustainable waste management solution. Existing research revealed the high potential of CS as a source of phenolic compounds and other beneficial chemicals [2–5] and [6]. The phenolic compounds in CS extract exhibit a wide range of biological activities, including hypoglycemic, hepatoprotective, antiviral, antibacterial, anticarcinogenic, and anti-inflammatory properties [7, 8].

Ultrasound-assisted extraction (UAE) has been increasingly adopted as an alternative extraction method to the solvent extraction. Ultrasonication increases the extraction efficiency through cavitation effect, resulting in an increase in the mass transfer between the

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target compound and solvent [9,10]. Since phenolic compounds consist of polar constituents, the ideal solvents are polar protic solvents. Conventionally, water and ethanol are used to extract phenolic compounds because of the extraction efficiency and low toxicity. Alternatively, mixtures of different polarity solvents were experimentally used to enhance the extraction efficiency [11–13] and [14]. More recently, deep eutectic solvents have been adopted as an eco-friendly alternative for phenolics extraction [15–19], and [20].

Table 1 summarizes the existing research works on phenolics extraction from different raw materials using different solvent type, extraction time, extraction temperature and extraction methods. The extraction efficiency depends on the solvent type, solvent concentration, extraction time, extraction temperature and source of raw materials.

As shown in Table 1, deep eutectic solvents (DES) are more efficient in extracting phenolic compounds than conventional solvents. DES are prepared by mixing two or more parent components, consisting of hydrogen bond acceptor (HBA) and hydrogen bond donor (HBD). The advantages of DES include lower melting points, low toxicity, nonflammability, biocompatibility, and chemical tunability by varying the molar ratio of the parent components [18]. DES has been used to extract phenolic compounds from various plants, such as oranges peel [16], *Moringa oleifera* [17], *Chlorella vulgaris* [19], *Rosmarinus officinalis* [20], and ripe mango (*Mangifera indica* L.) peel [23].

Choline chloride-based deep eutectic solvents (ChCl-DES) are efficient in extracting phenolic compounds, compared to the conventional solvents, e.g., water, ethanol, methanol, and acetone [24]. ChCl-DES form strong hydrogen bonding with phenolic compounds, resulting in enhanced extraction efficiency [25]. The physicochemical properties of ChCl-DES, including the polarity, solubility, viscosity, density, and conductivity, promote the phenolics extraction. These physicochemical properties could be manipulated by varying the HBD type and/or the molar ratio [25]. However, ChCl-DES are highly viscous due to the complex hydrogen bonding [26], which limits the mass transfer between the target compound and the solution.

As a result, water is added into ChCl-DES to reduce the viscosity of DES and improve the mass transfer [27]. Higher water content also increases the polarity of DES, which enhances the extraction efficiency. However, excessive water content could reduce the extraction yield due to disruption of hydrogen bonds between the DES parent components or between DES and the target compound. The water content in DES in excess of 30% (w/w) resulted in lower TPC as excessive water limits the formation of hydrogen bonding between the polyphenolic compounds and DES [16].

The extraction temperature, particle size of extracted material, and extraction time also play a crucial role in the extraction efficiency. The extraction temperature is positively correlated to the extraction efficiency as higher temperatures reduce the density, viscosity, and surface tension of DES, resulting in increased diffusivity and higher extraction yield. The optimal extraction temperatures are between 40 and 80 °C [14–17], and [21], while the extraction temperature above 80 °C resulted in the disintegration of phenolic compounds [24]. Excessively high extraction temperatures cause DES to evaporate. However, the phenolic compounds from spent coffee ground (SCG) were extracted using autohydrolysis at very high temperature (200 °C), achieving 40.36 mg GAE/g SCG of total phenolic content [28].

Small particle size also plays a role in the extraction yield due to increased contact area between the solvent and the solid matrix. Higher phenolic compounds were achieved using the smaller CS particle size (80 µm), compared with the larger CS particle size (250 µm) [21]. Meanwhile, the extraction time is positively correlated with TPC. However, upon reaching the equilibrium, longer extraction time has no effect on TPC. Higher liquid/solid ratios increase the concentration gradient and the mass transfer, resulting in improved phenolics yield.

There are numerous studies on the optimization of phenolics extraction. However, research on the effects of water content in DES on the extraction efficiency is limited. In this research, the water content in DES was examined as one of the extraction parameters. Furthermore, the kinetics of the phenolics extraction from CS in DES using UAE are little researched. As a result, this research performed a kinetics study to investigate the complex diffusion and mass transfer of phenolic compounds.

Table 1

Existing research on phenolics extraction from different raw materials using different solvent type, extraction time, extraction temperature and extraction methods.

Raw material	Method	Solvent	Liquid/solid ratio	Temperature	Time	TPC (mg GAE/g dry material)	Ref.
CS	CSE	Ethanol 60% (v/v)	35 ml/g CSS	60 °C	30 min	13.00	[14]
CS	UAE	Ethanol 60% (v/v)	35 ml/g CSS	80 °C	30 min	9.91	[21]
	MAE			80 °C	30 min	5.23	
	CSE			80 °C	45 min	10.01	
Spent coffee ground (SCG)	UAE	DES (ChCl:1,6 Hexanediol) (1:7)	2.6 ml/100 mg SCG	60 °C	10 min	17.20	[15]
Orange peel	CSE	DES (ChCl: Glycerol) (1:4)	5 ml/0.5 g orange peel	60 °C	100 min	5.84	[16]
Olive	UAE	DES (Betaine: Glycerol) (1:2)	0.5 ml/0.5 g olive	Room temperature	20 min	0.77	[22]
Moringa oleifera	UAE	Methanol/water 3:2% (v/v)	80 ml/g material	40 °C	15 min	0.59	[17]
		DES (L-Proline: Glycerol) (2:5)				23.60	

Note: CSE denotes the conventional solvent extraction, UAE denotes the ultrasound-assisted extraction, and MAE denotes the microwave assisted extraction.

Specifically, this research investigates the effect of extraction parameters on TPC and the antioxidant capacity of CS extract. The extraction was conducted using UAE in DES. The extraction parameters included the CS particle size, type of HBD, HBA:HBD molar ratio, water content in DES, liquid/solid ratio, extraction time, and extraction temperature. The optimization was undertaken in two stages: (i) the optimization of the UAE condition with the highest TPC; and (ii) a four-factor Box-Behnken design (BBD) to optimize the UAE condition with the optimal TPC; 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging capacity; and ferric reducing antioxidant power (FRAP). The kinetics modeling was carried out to investigate the complex diffusion, and mass transfer parameters that affect the UAE of CS; and to determine the kinetics model that best fitted the experimental data.

2. Materials and methods

The experimental CS was acquired from *Khao Chong Industry 1979 Co., Ltd.* The CS was ground to increase the surface area and sieved by particle sizes (100–850 μm) before retaining in the dark at 4 °C. The DES were prepared by mixing HBA with HBD at 80 °C for 1 h. In this research, CHCl_3 was used as HBA, while HBD was either 1,6-hexanediol, lactic acid, or glycerol. The molar ratio of HBA:HBD was varied between 1:1–1:9. All the chemicals were used as received.

2.1. Experimental setup

The CS of various particle sizes were weighed and mixed with DES. Water was added to vary the viscosity of DES. The mixture (CS, DES and water) was then immersed in a 40 kHz ultrasonic bath under prespecified extraction times and temperatures. Afterward, the CS extract was centrifuged at 8,000 rpm for 10 min and filtered by vacuum filtration and retained at -4 °C. All experiments were carried out in triplicate.

The optimization was undertaken in two stages: (i) the optimization of the UAE condition that yielded the highest TPC; and (ii) a four-factor BBD to optimize the UAE condition with the optimal TPC, DPPH radical scavenging capacity, and FRAP antioxidant capacity. In the first stage of optimization, the CS particle size was varied between 100 and 850 μm ; the type of HBD between 1,6-hexanediol, lactic acid, and glycerol; the HBA:HBD molar ratio between 1:1–1:9; and the water content in DES between 10 and 80% (w/w), given 30 min extraction time, 30 °C extraction temperature [22], and 15 mL/g liquid/solid ratio. In the second stage, the BBD experimental design was carried out by optimizing four factors: water content in DES (X_1), liquid/solid ratio (X_2), extraction time (X_3), and extraction temperature (X_4), given the CS particle size, HBD type, and HBA:HBD molar ratio. The water content in DES (X_1) was included in the BBD experimental design because the water content plays a significant role in the TPC extraction due to lower DES viscosity as the water content increased.

2.2. Characterization of CS extracts

2.2.1. Determination of TPC

The TPC of CS extracts was determined by the Folin-Ciocalteu method, following [11] with minor modifications. Specifically, 60 μL of CS extract was mixed with 2.5 mL of 2 N Folin-Ciocalteu reagent 10% (v/v) and incubated in the dark for 2 min. Then, 2 mL of sodium carbonate solution at 7.5% (w/v) was added and shaken well before incubation in the dark at 50 °C for 15 min and left to cool down. The absorbance was measured by a spectrophotometer at 765 nm. A calibration curve was created using gallic acid standard solution (50, 100, 200, 300, 400, 500, 700, 1,000 $\mu\text{g}/\text{mL}$), and the blank was ethanol. The TPC was expressed as milligram gallic acid equivalent per dry weight material (mg GAE/g CS).

2.2.2. Determination of antioxidant capacity

The DPPH radical scavenging capacity of CS extracts was determined according to the procedure in Ref. [29] with minor modifications. In the DPPH analysis, 1 mL of CS extract with 40-fold dilution was mixed with 2 mL of 0.2 mM DPPH solution and incubated in the dark at room temperature for 30 min. The absorbance was measured using the spectrophotometer at 517 nm, with ethanol as blank. The DPPH radical scavenging capacity was calculated by equation (1) and expressed as milligram of Trolox equivalent per dry weight material (mg TE/g CS).

$$\% \text{ radical scavenging capacity} = (A_C - A_S)/A_C \times 100 \quad (1)$$

where A_C is the absorbance of reference standard and A_S is the absorbance of diluted CS extract.

The FRAP antioxidant capacity of CS extracts was determined according to the procedure in Ref. [30] with minor modifications. The FRAP reagent was prepared by mixing 10 mM of TPTZ (2,4,6-tripyridyl-s-triazine) solution in 40 mM HCl with 300 mM sodium acetate buffer (pH 3.6) and 20 mM of ferric chloride (1:10:1 (v/v/v)). Then, 10 μL of CS extract with 10-fold dilution was mixed with 290 μL of FRAP reagent and incubated at 37 °C for 15 min. The absorbance was determined at 595 nm, with ethanol as blank. A calibration curve was constructed using an aqueous solution of ferrous sulfate at 10–250 $\mu\text{g}/\text{mL}$. The FRAP antioxidant capacity were expressed as milligram of ferrous equivalent per dry weight material (mg Fe(II)/g CS).

2.3. Kinetics models for extraction

This research also examined three kinetics models to determine the model that best fitted the experimental data. The kinetics

models under study included the power law model, Elovich kinetics model, and two-site kinetics model. In the kinetics modeling, the extraction temperature was varied between 35, 60 and 85 °C; and the extraction time between 2, 4, 8, 10, 30, 60 and 90 min.

2.3.1. The power law model

The power law model is a straightforward mathematical model for modeling solid-liquid extraction from plant. The power law kinetics model was used to describe the kinetics of UAE of phenolic compounds from grape marc [31]. The power law kinetics model can be mathematically expressed as equation (2)

$$C_t = Bt^n \quad (2)$$

where C_t is the extractable substance content at time t (mg GAE/g CS), n is the power law exponent (<1), and B is a constant related to the extraction rate (g CS/mg GAE. min^{-1}).

2.3.2. Elovich kinetics model

The Elovich kinetics model assumes that the rate of adsorption of solute decreases exponentially as the amount of adsorbed solute increase. The Elovich model was used to describe the kinetics of vanillic acid extraction from pumpkin seeds [32] and can be mathematically expressed as

$$C_t = E_0 + E_1 \ln t \quad (3)$$

where C_t is the extractable substance content at time t (mg GAE/g CS), E_0 is the initial yield, and E_1 is the initial extraction rate.

2.3.3. Two-site kinetics model

The two-site kinetics model was used to model the kinetics of UAE of phenolic compounds from grape marc [33]. The two-site kinetics model was modified from Fick's second law, and it consists of two steps: washing and diffusion. The two-site kinetics model is mathematically expressed in equation (4).

$$\frac{C_t}{C_\infty} = 1 - Fe^{-k_1t} - (1 - F)e^{-k_2t} \quad (4)$$

where C_t is the extractable substance content at time t (mg GAE/g CS), C_∞ is the extractable substance content at time t approaching infinity (mg GAE/g CS), F is the portion of rapidly released solute, $(1 - F)$ is the portion of slowly released solute, k_1 is the first-order rate constant of the rapidly released portion (min^{-1}), and k_2 is the first-order rate constant of the slowly released portion (min^{-1}).

To determine the effective diffusion coefficient of TPC from CS, this research used the unsteady-state diffusion model based on Fick's second law, given the following assumptions:

- The CS particles was of spherical shape of 150–250 μm in diameter, with the mean diameter of 200 μm .
- UAE induced cavitation and subsequent convection in the bulk liquid medium (*i.e.*, DES). In addition, the DES and CS were assumed to be well mixed, given the DES volume of 3–4 mL, resulting in negligible external resistance to mass transfer.
- The effective diffusion coefficient of the extracted solute (*i.e.*, phenolic compounds) remained constant.
- No chemical reaction or ultrasonic degradation of phenolics occurred throughout the extraction.

Given the assumptions, a one-dimensional unsteady-state diffusion model derived from Fick's second law was used to describe the mass transfer of a solute (*i.e.*, TPC) from spherical particles (*i.e.*, CS) [33]. The initial condition for solving the diffusion equation is that C_i is the initial solute concentration at the beginning of extraction (kg/m^3) at any radius of particle (m), and the boundary conditions are no concentration change at the center of particles and no solubility limit. Given the initial and boundary conditions, the analytical solution of one-dimensional unsteady-state diffusion model is obtained and the linear relationship is expressed in equation (5).

$$\ln\left(\frac{C_\infty}{C_\infty - C_t}\right) = \ln\frac{6}{\pi^2} + \frac{D_e\pi^2t}{R^2} \quad (5)$$

The effective diffusion coefficient can be determined from the slope ($\frac{D_e\pi^2}{R^2}$) of the straight line when plotting the logarithm of $\left(\frac{C_\infty}{C_\infty - C_t}\right)$ against time. Although the intercept of the straight line given by equation (5) is $\ln\frac{6}{\pi^2}$, the value depends on the distribution of the solute (*i.e.*, TPC) and the size and shape of particle (*i.e.*, CS).

2.4. Data and statistical analysis

The effects of different extraction factors on TPC were investigated by Duncan's multiple range test using Mstat software (Mstat for Windows, Michigan State University, USA), given the 95% confidence level ($p < 0.05$). MINITAB software was used to optimize the UAE conditions from CS for TPC, DPPH, and FRAP. A t -test statistical analysis was used to compare the averages of the BBD-based predicted TPC, DPPH and FRAP values with the experimental results, given that $p < 0.05$. All experiments were carried out in triplicate and results were expressed as mean \pm standard deviation.

3. Results and discussion

3.1. Factors affecting TPC of CS extracts

3.1.1. Effect of CS particle size

To determine the optimal CS particle size, this research extracted CS of different particle sizes (100–850 μm) using 50% (v/v) ethanol/water, given 40 kHz ultrasonic power, 30 mL/g liquid/solid ratio, 30 ° C extraction temperature, and 30 min extraction time. The rationale behind using ethanol/water in place of DES was that ethanol/water is commonly used for extraction of phenolics [14]. Specifically, the experiments were performed to determine the particle size of CS for subsequent analysis. Fig. 1 shows that TPC increased significantly ($p < 0.05$) as the particle size of CS decreased from 425–850 μm to 106–425 μm . The finding is consistent with [21] who experimentally extracted CS using two particle sizes: 80 μm and 250 μm ; and reported higher phenolic compounds with the smaller CS particle size.

The highest TPC was achieved with the CS particle size of 106–425 μm . The finding could be attributed to increased contact surface area of smaller CS particle size, resulting in higher mass transfer between the solid and liquid. As a result, the CS particle size of 150–250 μm was used in subsequent experiments.

3.1.2. Type of DES

To determine the optimal HBD, this research experimented with three types of HBD: 1,6 hexanediol, lactic acid, and glycerol, given 40 kHz ultrasonic power, 15 mL/g liquid/solid ratio (with DES as liquid), 30 ° C extraction temperature, 30 min extraction time, and ChCl as HBA [24,26]. The HBA:HBD molar ratio was varied between 1:2, 1:4 and 1:6; and the water content in DES between 10 and 30% (w/w).

In Fig. 2, the analysis showed that the HBD type significantly affected TPC from CS. In Fig. 2(a), given 10% (w/w) water content, ChCl-Lactic acid achieved higher TPC than ChCl-1,6 hexanediol and ChCl-Glycerol at all molar ratios ($p < 0.05$). The high viscosity of DES due to low water content (10% (w/w)) limited the mass transfer between the solid and liquid. However, the higher TPC for the DES with lactic acid as HBD could be attributed to free H^+ ions in lactic acid, which promotes the hydrolysis of cellulose and hemicellulose inside the cell wall, resulting in higher TPC [26].

In Fig. 2(b), given 30% (w/w) water content, ChCl-1,6 hexanediol and ChCl-Lactic acid achieved higher TPC than ChCl-Glycerol at all molar ratios ($p < 0.05$). The findings are consistent with [26] who experimentally extracted citrus peel waste and reported higher TPC with 1,2-propanediol as HBD, compared to lactic acid or glycerol as HBD, given 25% (v/v) water content and ChCl as HBA. The TPC yields are correlated to the polarities of alcohol and carboxylic acid-based DES. ChCl-Glycerol has higher polarity than ChCl-1,6 hexanediol and than ChCl-Lactic acid. The phenolic compounds are typically of less-polar substances. Therefore, the TPC yield is strongly dependent on HBD polarity. In addition, the results showed that the molar ratio was positively correlated with TPC. Higher water content in DES (from 10% to 30% (w/w)) significantly increased TPC due to lower viscosity of DES. In this study, 1,6 hexanediol was used as HBD in subsequent experiments.

3.1.3. Molar ratio of DES

To determine the optimal HBA (ChCl):HBD (1,6 hexanediol) molar ratio, this research varied the ratio of ChCl to 1,6 hexanediol between 1:1–1:9; and the water content in DES between 10, 20, and 30% (w/w), given 40 kHz ultrasonic power, 15 mL/g liquid/solid ratio (with DES as liquid), 30 ° C extraction temperature, and 30 min extraction time.

Fig. 3 shows the effect of variable HBA:HBD molar ratios and water content on TPC. TPC increase with increase in the molar ratio and at the same molar ratio, low TPC was observed at low water content of 10% (w/w) (Fig. 3 (a)) and the yield of TPC was improved when 20% (w/w) water (Fig. 3 (b)) and 30% (w/w) water (Fig. 3 (c)) was added. The results indicated that TPC increased with increase

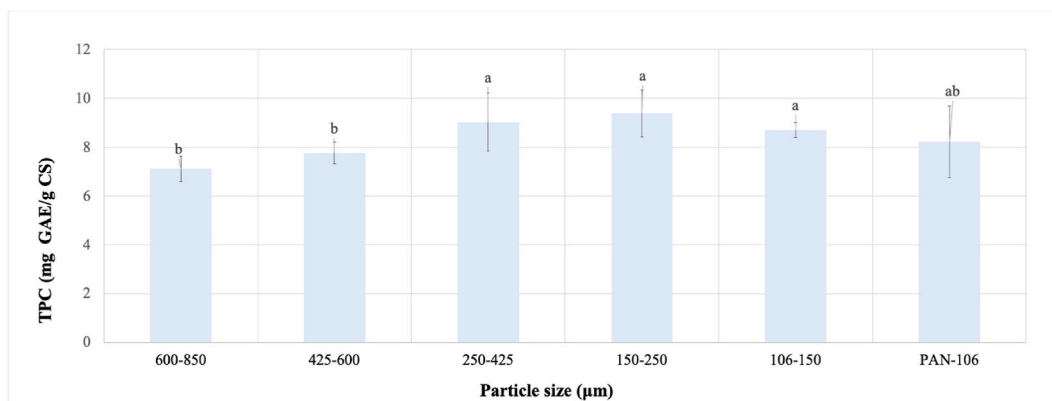


Fig. 1. Effect of CS particle size on TPC, given 40 kHz ultrasonic power, 30 mL/g liquid/solid ratio (with 50% (v/v) ethanol/water as liquid), 30 ° C extraction temperature and 30 min extraction time.

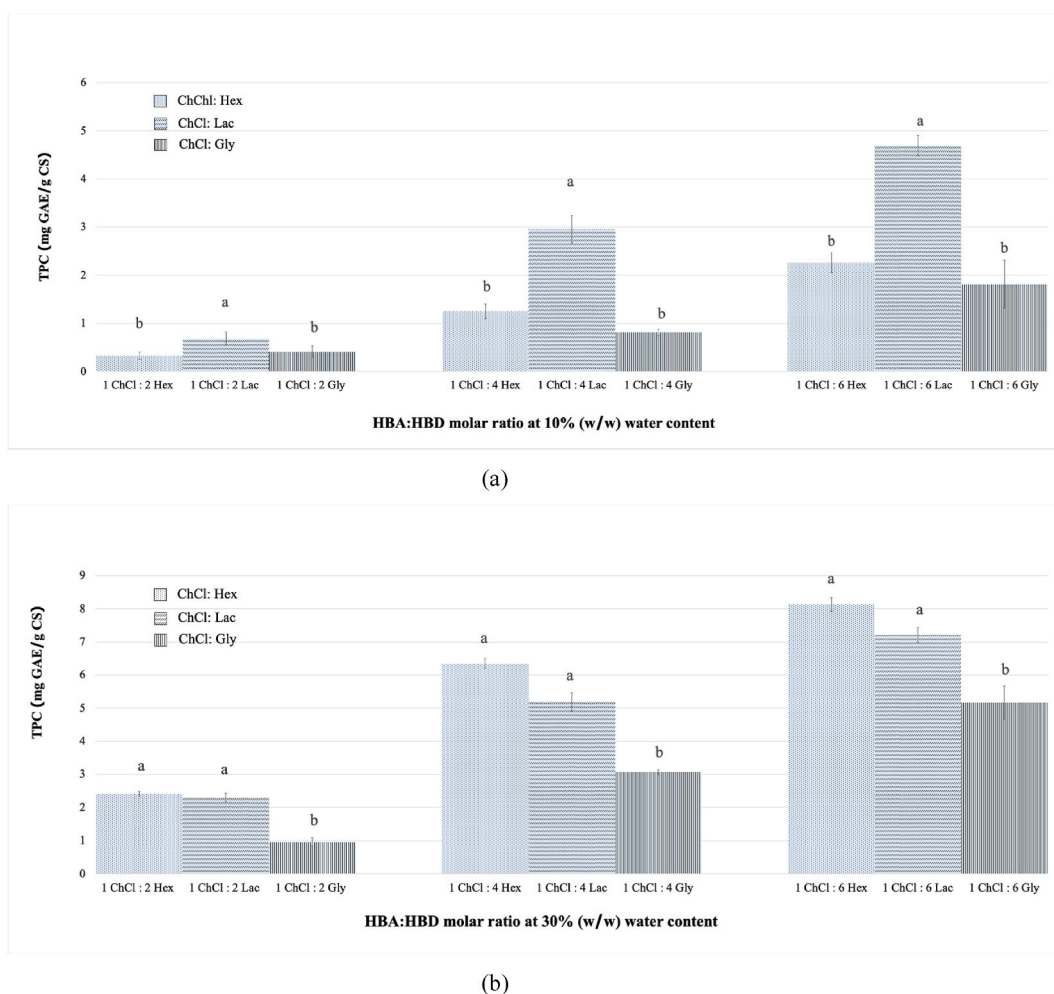


Fig. 2. Effect of HBD type on TPC under variable molar ratios, given 40 kHz ultrasonic power, 15 mL/g liquid/solid ratio (with DES as liquid), 30 °C extraction temperature and 30 min extraction time: (a) 10% (w/w) water content, (b) 30% (w/w) water content.

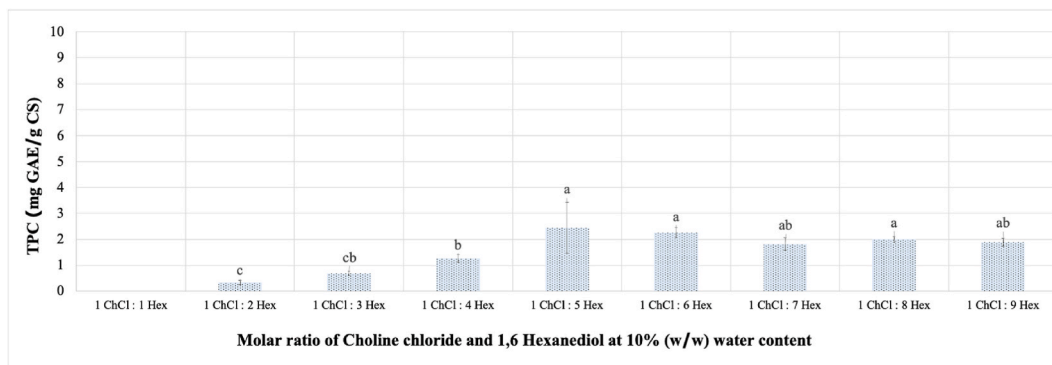
in the molar ratio and the water content ($p < 0.05$). The findings are in line with [26] who reported that the increasing number of hydroxyl groups of HBD molecules surrounding the negatively-charged chloride anion of ChCl strengthened the hydrogen bonds with phenolics. The higher mole of HBD also altered the polarity of DES, leading to higher TPC.

However, excessively high molar ratio of HBA:HBD (*i.e.*, above 1 ChCl:7 Hex) with 20% (w/w) water content resulted in lower TPC (Fig. 3 (b)). The finding could be attributed to higher viscosity and higher surface tension of DES due to excessive 1,6 hexanediol in DES. Excessive 1,6 hexanediol also reduced the interaction between TPC and DES [5]. As a result, the HBA:HBD molar ratio (ChCl: 1,6 hexanediol) of 1:7 was chosen for subsequent analysis.

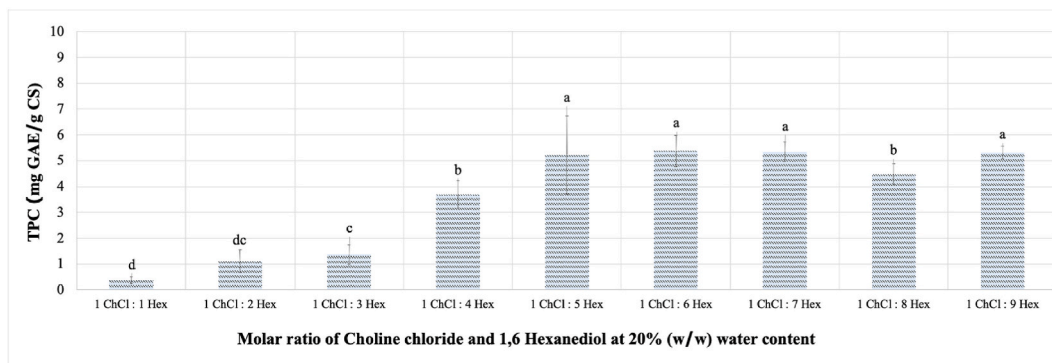
3.1.4. Effect of water content in DES and viscosity

Fig. 4 shows the effect of water content in DES (10–80% w/w) and water (without DES) on TPC, given 40 kHz ultrasonic power, 15 mL/g liquid/solid ratio (with DES as liquid), the molar ratio of 1 ChCl: 7 Hex, 30 °C extraction temperature, and 30 min extraction time.

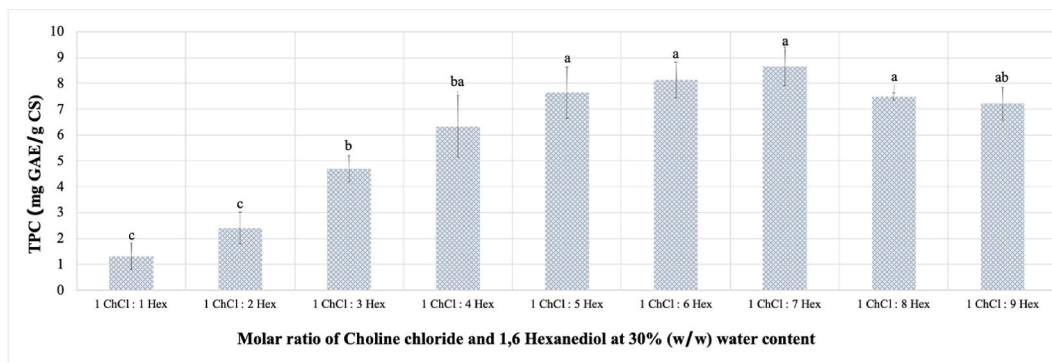
The TPC yield significantly increased ($p < 0.05$) as the water content increased from 10% to 30% (w/w), as shown in Fig. 4. The water molecules were embedded in the DES structure, resulting in lower DES viscosity (Fig. 5) and higher TPC. However, the TPC yields were insignificantly different when the water content in DES increased from 30% (w/w) to 70% (w/w); and the TPC yield decreased for the water content beyond 70% (w/w) (Fig. 4). The reduction in TPC was attributable to excessive water molecules surrounding the DES, thereby hindering the interaction between DES and phenolic compounds [34]. Excessive water content also increased the polarity of DES and reduced the TPC yield [27]. The experimental results were consistent with [26], who extracted flavonoids from citrus peel waste using DES and reported that the optimal water content was 20–25% (v/v) and excessively high water content in DES (*i.e.*, more than 30% (v/v)) lowered the flavonoid yields.



(a)



(b)



(c)

Fig. 3. Effect of the molar ratio of ChCl (HBA) to 1,6 hexanediol (HBD) on TPC under variable molar ratios (1:1–1:9) and water content, given 40 kHz ultrasonic power, 15 mL/g liquid/solid ratio (with DES as liquid), 30 ° C extraction temperature and 30 min extraction time: (a) 10% (w/w) water content, b) 20% (w/w) water content, (c) 30% (w/w) water content.

3.2. Optimization of the extraction condition by experimental design

3.2.1. Influential variables for CS extraction

Table 2 presents the four significant UAE variables that affect the TPC, DPPH and FRAP antioxidant capacity of CS extract: the water content in DES (X_1), liquid/solid ratio (X_2), extraction time (X_3), and extraction temperature (X_4). The design of experiments is based on BBD with the objective to select the optimal UAE condition.

The liquid/solid ratio is positively correlated with the extraction efficiency, and the optimal liquid/solid ratio is between 15 and 45 mL/g, depending on the extracted material [14,15], and [25]. The extraction time is inversely related to the extraction temperature and is subject to the limit of equilibrium. In this research, the extraction time for the BBD experimental design was 10–90 min in order to account for the limit of equilibrium. Meanwhile, higher extraction temperatures enhanced the extraction efficiency due to improved diffusivity and increased mass transfer. Existing research documented that the optimal extraction temperatures for phenolics

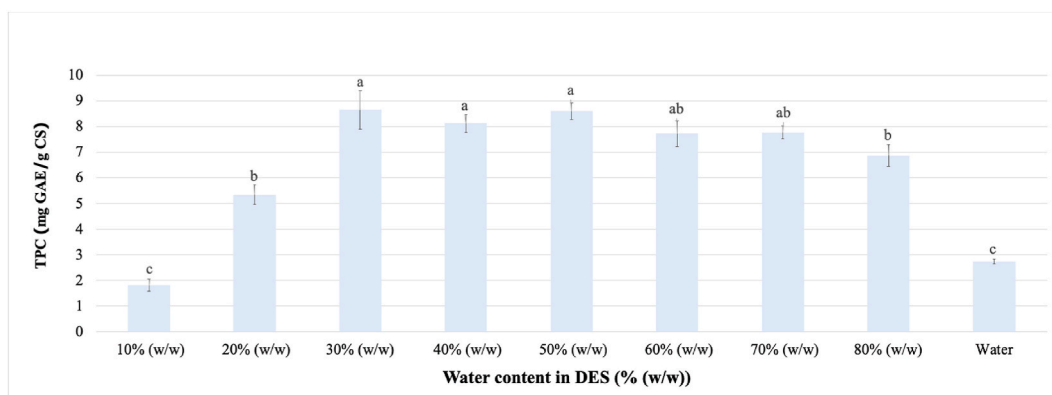


Fig. 4. Effect of water content in DES on TPC, given 40 kHz ultrasonic power, 15 mL/g liquid/solid ratio (with DES as liquid), 1 ChCl: 7 Hex molar ratio, 30 ° C extraction temperature and 30 min extraction time.

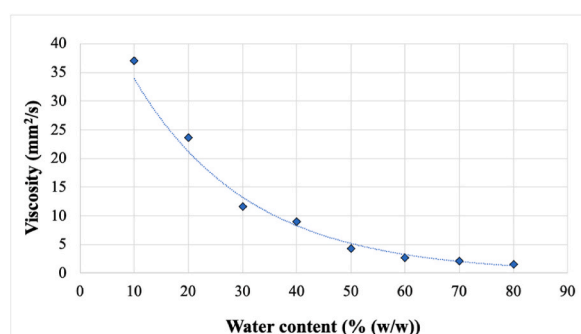


Fig. 5. Viscosity of DES under variable water content.

Table 2

The experimental design factor and levels of design of experiments.

Independent variable/UAE parameters	Symbol	Experiment value		
		Low (-1)	Center (0)	High (+1)
Water content in DES (% (w/w))	X_1	10	30	50
Liquid to solid ratio (mL/g)	X_2	15	30	45
Extraction time (min)	X_3	10	50	90
Extraction temperature (°C)	X_4	35	60	85

extraction were between 40 and 80 °C [14–17], and [21]. The BBD experimental design consisted of three levels of temperature (low, moderate and high) to investigate the effect of varying temperatures on the TPC yield.

3.2.2. Effect of UAE parameters on TPC

Table 3 shows the TPC results of the design of experiments. The highest TPC of 21.14 ± 1.90 mg GAE/g CS was achieved under the UAE condition of 30% (w/w) water content in DES (X_1), 45 mL/g liquid/solid ratio (X_2), 50 min extraction time (X_3) and 85 °C extraction temperature (X_4), given 40 kHz ultrasonic power, 150–250 μ m CS particle size and the HBA:HBD molar ratio of 1 ClCh:7 Hex.

In Fig. 6 (a) and Table 6, the water content in DES (X_1) had a significant positive linear effect on TPC ($p < 0.05$) but a significant negative quadratic effect (X_1X_1) on TPC ($p < 0.05$), suggesting that TPC initially increased with increase in the water content and decreased after a certain threshold. The finding is consistent with [26] who extracted flavonoids from citrus peel waste. The extraction temperature had a significant positive quadratic effect (X_4X_4 ; $p < 0.05$) on TPC. The interaction between water content in DES and temperature (X_1X_4) had a significant negative effect ($p < 0.05$) on TPC, indicating that increased water content and extraction temperature lowered TPC, as shown in Fig. 7.

In [35], the TPC yield was positively correlated with the ultrasonic power and extraction time (linear effect), while the extraction temperature had a negative quadratic effect on the TPC yield.

In Fig. 6 (b), the high coefficient of determination (R^2) of the quadratic model (equation (6)) of 0.9702 and low root mean squared

Table 3

The TPC results of the BBD experimental design.

Exp.	Independent variables/UAE parameters				TPC (mg GAE/g CS)	
	Water content (X_1 ; % (w/w))	Liquid to solid ratio (X_2 ; mL/g)	Extraction Time (X_3 ; min)	Temperature (X_4 ; °C)	Experimental result	Predicted result (Equation (6))
1	10	15	50	60	7.03 ± 0.81	7.48
2	50	15	50	60	11.75 ± 0.17	11.30
3	10	45	50	60	11.32 ± 1.15	11.39
4	50	45	50	60	19.59 ± 1.15	18.76
5	30	30	10	35	10.52 ± 0.21	9.93
6	30	30	90	35	14.43 ± 0.78	13.61
7	30	30	10	85	16.67 ± 0.74	17.14
8	30	30	90	85	17.88 ± 0.03	18.09
9	10	30	50	35	5.64 ± 0.99	5.02
10	50	30	50	35	14.03 ± 0.79	14.51
11	10	30	50	85	16.20 ± 0.42	14.77
12	50	30	50	85	16.79 ± 1.65	16.46
13	30	15	10	60	11.33 ± 0.32	10.41
14	30	45	10	60	15.74 ± 0.86	15.74
15	30	15	90	60	13.33 ± 0.87	12.37
16	30	45	90	60	18.43 ± 0.48	18.40
17	10	30	10	60	7.15 ± 0.44	7.77
18	50	30	10	60	13.67 ± 0.51	14.13
19	10	30	90	60	9.96 ± 0.711	10.85
20	50	30	90	60	14.98 ± 0.77	15.68
21	30	15	50	35	8.83 ± 0.26	9.88
22	30	45	50	35	13.40 ± 0.67	13.90
23	30	15	50	85	13.25 ± 0.78	14.07
24	30	45	50	85	21.14 ± 1.90	21.41
25	30	30	50	60	13.00 ± 1.46	13.47
26	30	30	50	60	13.74 ± 1.34	13.47
27	30	30	50	60	13.66 ± 0.64	13.47

Note: The experimental results were expressed as mean ± standard deviation (n = 3).

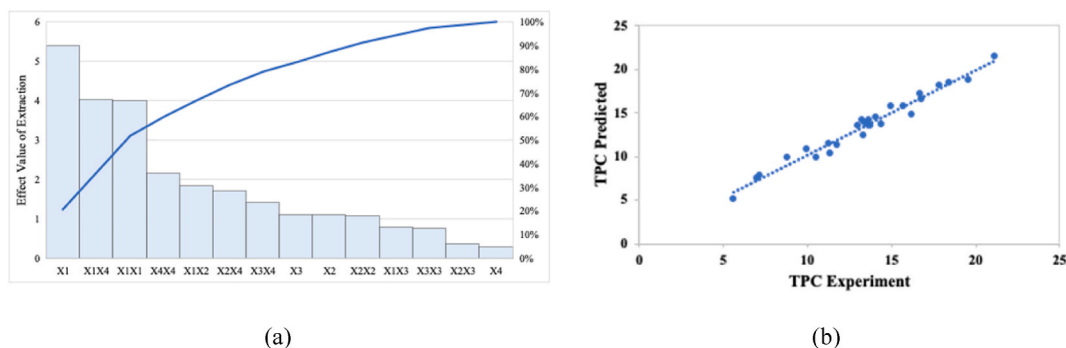


Fig. 6. (a) Pareto chart for the factors X_1 (water content in DES), X_2 (liquid/solid ratio), X_3 (extraction time), X_4 (extraction temperature) and their interaction with respect to TPC given the 95% confidence level ($p < 0.05$), (b) Correlation between the experimental and predicted TPC with $R^2 = 0.9702$, R^2 adjusted = 0.9690, p -value = 1, RMSE = 0.64.

error (RMSE) of 0.64 indicate the high predictive ability of the quadratic model, as evidenced by a close resemblance between the experimental results and the BBD-based predicted results (Table 3 and Fig. 6 (b)).

$$\begin{aligned} \text{TPC} = & -3.87 + 0.561 X_1 - 0.165 X_2 + 0.0554 X_3 + 0.0281 X_4 - 0.00420 X_1^2 + 0.00198 X_2^2 + 0.000201 X_3^2 + 0.001447 X_4^2 \\ & + 0.00295 X_1 X_2 - 0.000479 X_1 X_3 - 0.003899 X_1 X_4 + 0.000291 X_2 X_3 + 0.00221 X_2 X_4 - 0.000682 X_3 X_4 \end{aligned} \quad (6)$$

Fig. 7 shows the significant influence of the interaction term $X_1 X_4$ (the water content in DES and extraction temperature) on the TPC yield, indicating the combined effect of water content and temperature on the lower TPC yield. Fig. 7 depicts only the interaction effect between water content in DES and extraction temperature ($p < 0.05$) because no statistical significance was observed in the other interaction terms ($p > 0.05$).

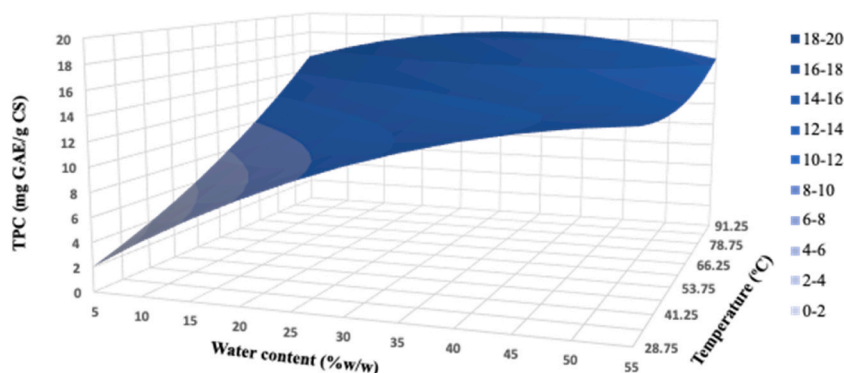


Fig. 7. The 3D response surface area plot and contour plot showing the mutual effect of the water content in DES (X_1) and extraction temperature (X_4) on TPC, given the liquid/solid ratio (X_2) = 30 mL/g and the extraction time (X_3) = 50 min.

3.2.3. Effect of UAE parameters on DPPH radical scavenging capacity

Table 4 tabulates the DPPH results of the design of experiments. The highest DPPH radical scavenging capacity of 24.05 ± 0.67 mg TE/g CS was achieved under the UAE condition of 10% (w/w) water content in DES (X_1), 45 mL/g liquid/solid ratio (X_2), 50 min extraction time (X_3) and 60 °C extraction temperature (X_4), given 40 kHz ultrasonic power, 150–250 μ m CS particle size, and the HBA: HBD molar ratio of 1 ClCh:7 Hex.

In Fig. 8 (a) and Table 6, the water content in DES (X_1) had a significant positive linear effect on DPPH antioxidant capacity while the interaction term X_1X_4 had a significant negative effect ($p < 0.05$), indicating that increased water content contributed to higher DPPH antioxidant capacity; but the DPPH antioxidant capacity decreased with increased in both water content and extraction temperature, as shown in Fig. 9. The finding could be attributed to the thermal oxidation, resulting in the degradation of phenolic compounds. Since no statistical significance was observed in the other interaction terms ($p > 0.05$), only the interaction effect between water content in DES and extraction temperature ($p < 0.05$) was shown in Fig. 9.

In Fig. 8 (b), R^2 of the quadratic model is 0.7432 and RMSE is 2.08, indicating that the BBD-based predicted results reasonably

Table 4

The DPPH results of the BBD experimental design.

Exp.	Independent variables				DPPH radical scavenging capacity (mg TE/g CS)	
	Water content (X_1 ; % (w/w))	Liquid to solid ratio (X_2 ; mL/g)	Extraction Time (X_3 ; min)	Temperature (X_4 ; °C)	Experimental result	Predicted result (Equation (7))
1	10	15	50	60	10.72 ± 1.28	9.04
2	50	15	50	60	13.61 ± 0.74	12.18
3	10	45	50	60	24.05 ± 0.67	20.39
4	50	45	50	60	19.37 ± 0.53	15.96
5	30	30	10	35	18.01 ± 0.12	14.36
6	30	30	90	35	19.86 ± 1.21	16.36
7	30	30	10	85	19.21 ± 1.01	17.63
8	30	30	90	85	21.01 ± 0.73	19.57
9	10	30	50	35	8.77 ± 1.08	8.56
10	50	30	50	35	14.92 ± 0.52	15.87
11	10	30	50	85	19.70 ± 1.39	19.75
12	50	30	50	85	9.95 ± 1.01	11.16
13	30	15	10	60	12.79 ± 0.47	12.95
14	30	45	10	60	20.63 ± 1.45	20.15
15	30	15	90	60	13.07 ± 0.55	14.55
16	30	45	90	60	21.65 ± 0.72	22.49
17	10	30	10	60	11.50 ± 0.93	14.97
18	50	30	10	60	12.38 ± 1.25	14.46
19	10	30	90	60	15.05 ± 2.96	17.07
20	50	30	90	60	15.68 ± 1.07	16.29
21	30	15	50	35	8.20 ± 0.60	10.11
22	30	45	50	35	13.48 ± 2.22	18.00
23	30	15	50	85	14.09 ± 1.99	13.67
24	30	45	50	85	18.74 ± 1.14	20.92
25	30	30	50	60	15.33 ± 0.49	14.68
26	30	30	50	60	13.85 ± 1.23	14.68
27	30	30	50	60	14.85 ± 0.98	14.68

Note: The experimental results were expressed as mean \pm standard deviation ($n = 3$).

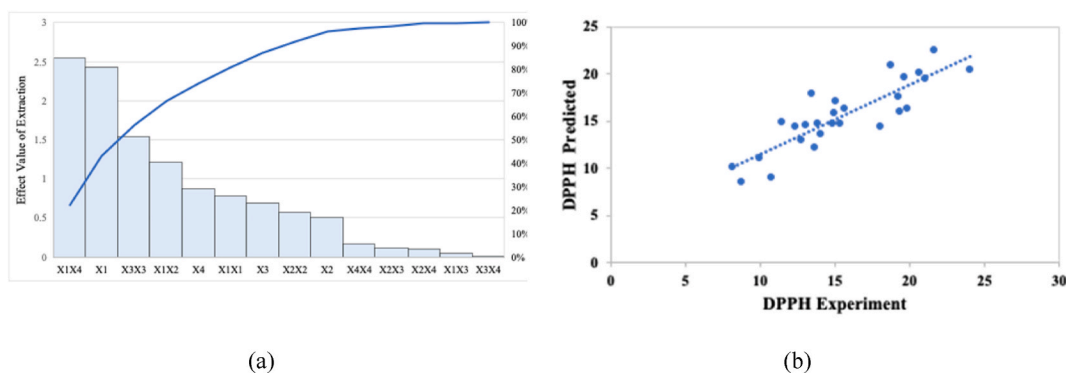


Fig. 8. (a) Pareto chart for the factors X_1 (water content in DES), X_2 (liquid/solid ratio), X_3 (extraction time), X_4 (extraction temperature) and their interaction with respect to DPPH antioxidant capacity given the 95% confidence level ($p < 0.05$), (b) Correlation between the experimental and predicted DPPH antioxidant capacity with $R^2 = 0.7432$, R^2 adjusted = 0.7330, p -value = 1, RMSE = 2.08.

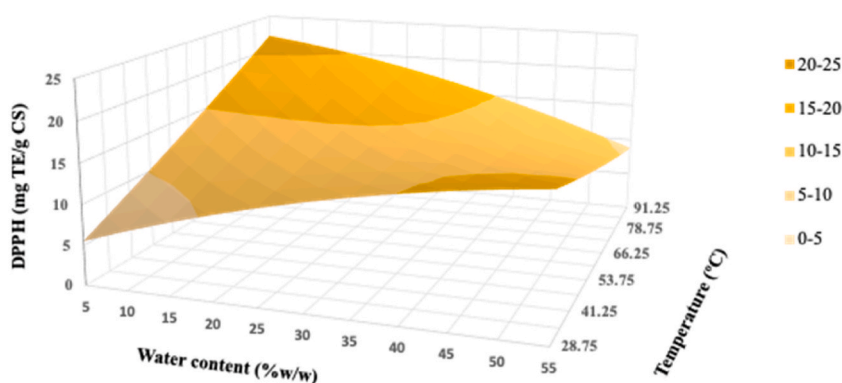


Fig. 9. The 3D response surface area plot and contour plot showing the interaction effect of the water content in DES (X_1) and extraction temperature (X_4) on DPPH antioxidant activity, given $X_2 = 30$ mL/g and $X_3 = 50$ min.

resemble the experimental results, as shown in Table 4 and Fig. 8 (b). Similarly, a low R^2 of 0.78 was reported in Ref. [17] who experimentally extracted phenolic compounds from *Moringa oleifera* with DES using UAE method. The BBD-based quadratic model that describes the relationship between independent variables and the interaction terms and the response (i.e., DPPH antioxidant capacity) is mathematically expressed in equation (7).

$$\text{DPPH} = -12.7 + 0.813 X_1 + 0.245 X_2 - 0.111 X_3 + 0.274 X_4 - 0.00266 X_1^2 + 0.00345 X_2^2 + 0.001300 X_3^2 + 0.00035 X_4^2 - 0.00631 X_1 X_2 - 0.00008 X_1 X_3 - 0.00795 X_1 X_4 + 0.00031 X_2 X_3 - 0.00042 X_2 X_4 - 0.00001 X_3 X_4 \quad (7)$$

3.2.4. Effect of UAE parameters on FRAP antioxidant capacity

Table 5 tabulates the FRAP results of the design of experiments. The highest FRAP antioxidant capacity of 61.82 ± 4.53 mg Fe (II)/g CS was achieved under the UAE condition of 30% (w/w) water content in DES (X_1), 45 mL/g liquid/solid ratio (X_2), 50 min extraction time (X_3) and 85 °C extraction temperature (X_4), given 40 kHz ultrasonic power, 150–250 μ m CS particle size, and the HBA:HBD molar ratio of 1 ClCh:7 Hex.

In Fig. 10 (a) and Table 6, the water content in DES (X_1) had a significant positive linear effect on FRAP antioxidant capacity but a significant quadratic negative effect on FRAP ($p < 0.05$), suggesting that the FRAP antioxidant capacity initially increased with increase in the water content and decreased after a certain threshold. The interaction effect of water content and liquid to solid ratio (X_1X_2) contributed positively to the FRAP antioxidant capacity, indicating that increased water content in DES and liquid to solid ratio improved the FRAP recovery, as shown in Fig. 11 (a). The interaction between the liquid to solid ratio and extraction temperature (X_2X_4) has a positive effect on the FRAP antioxidant capacity, as shown in Fig. 11 (b). However, the interaction between water content in DES and extraction temperature (X_1X_4) had a negative effect on the FRAP antioxidant capacity (Fig. 11(c)), similar to that of TPC and DPPH.

In Fig. 10 (b), high R^2 of 0.9749, despite RMSE of 1.83, indicates the high predictive ability of the quadratic model, as evidenced by a close resemblance between the experimental results and the BBD-based predicted results (Table 5 and Fig. 10 (b)). The BBD-based

Table 5

The FRAP results of the BBD experimental design.

Exp.	Independent variables				FRAP antioxidant capacity (mg Fe (II)/g CS)	
	Water content (X ₁ ; % (w/w))	Liquid to solid ratio (X ₂ ; mL/g)	Extraction Time (X ₃ ; min)	Temperature (X ₄ ; °C)	Experimental results	Predicted result (Equation (8))
1	10	15	50	60	19.89 ± 1.87	19.85
2	50	15	50	60	34.01 ± 2.10	35.13
3	10	45	50	60	24.39 ± 2.03	25.15
4	50	45	50	60	52.45 ± 1.72	54.48
5	30	30	10	35	30.39 ± 4.88	29.09
6	30	30	90	35	36.08 ± 4.46	34.03
7	30	30	10	85	42.50 ± 1.22	46.53
8	30	30	90	85	46.92 ± 3.79	50.21
9	10	30	50	35	9.16 ± 0.99	8.35
10	50	30	50	35	43.32 ± 0.93	42.45
11	10	30	50	85	38.86 ± 3.35	36.95
12	50	30	50	85	49.44 ± 0.74	47.47
13	30	15	10	60	33.32 ± 1.65	30.99
14	30	45	10	60	47.12 ± 2.29	44.32
15	30	15	90	60	36.28 ± 1.43	36.30
16	30	45	90	60	48.07 ± 8.5	47.63
17	10	30	10	60	16.03 ± 4.89	17.77
18	50	30	10	60	43.17 ± 4.66	43.81
19	10	30	90	60	25.68 ± 6.57	25.81
20	50	30	90	60	45.36 ± 0.39	44.39
21	30	15	50	35	27.99 ± 0.22	30.73
22	30	45	50	35	31.52 ± 1.38	33.80
23	30	15	50	85	39.79 ± 1.20	38.29
24	30	45	50	85	61.82 ± 4.53	59.87
25	30	30	50	60	40.94 ± 6.35	42.78
26	30	30	50	60	43.20 ± 3.80	42.78
27	30	30	50	60	44.21 ± 3.27	42.78

Note: The experimental results were expressed as mean ± standard deviation (n = 3).

quadratic model that describes the relationship between the independent variables and the interaction terms and the FRAP antioxidant capacity is mathematically expressed in equation (8).

$$\text{FRAP} = -34.4 + 2.230 X_1 - 0.336 X_2 + 0.283 X_3 + 0.523 X_4 - 0.01999 X_1^2 - 0.00504 X_2^2 - 0.001149 X_3^2 - 0.00156 X_4^2 + 0.01172 X_1 X_2 - 0.00233 X_1 X_3 - 0.01179 X_1 X_4 - 0.00084 X_2 X_3 + 0.01234 X_2 X_4 - 0.00032 X_3 X_4 \quad (8)$$

In Fig. 11 (a), the water content in DES (X₁) and liquid/solid ratio (X₂) were positively correlated to the FRAP antioxidant activity. The findings could be attributed to the lower DES viscosity and improved mass transfer as the water content increased. Higher liquid/solid ratio provided an ample amount of solvent to react and create strong hydrogen bonding with phenolic compounds. In Fig. 11 (b), high FRAP antioxidant capacity was achieved with high liquid to solid ratio (X₂) and high temperature (X₄). In Fig. 11 (c), higher FRAP antioxidant activity was achieved under 30–40% w/w water content and 80 °C. Higher water content in DES and higher extraction temperature lowered the FRAP antioxidant capacity.

3.2.5. The correlation between three responses (TPC, DPPH and FRAP)

Fig. 12 shows the correlation between the three responses (TPC, DPPH radical scavenging capacity and FRAP antioxidant capacity). The results indicated that TPC and FRAP antioxidant capacity were strongly correlated (r = 0.938), while TPC and the DPPH antioxidant capacity were moderately correlated (r = 0.608). The correlation between DHHP and FRAP antioxidant capacity was low (r = 0.434) due to different assay methods for DPPH and FRAP. Certain phenolic compounds exhibit no antioxidant capacity, partly contributing to the low correlation between DPPH and FRAP [34]. The findings are consistent with [17], who reported a strong correlation between TPC and FRAP antioxidant activity (R² = 0.9385) but a low correlation between TPC and DPPH antioxidant capacity; and between FRAP and DPPH antioxidant activity. A weak correlation exists between TPC and the DPPH antioxidant capacity of the extracts from brewer's spent grain (R² = 0.2) [36].

3.2.6. Optimized UAE conditions and model prediction

Fig. 13 shows the optimization of the UAE conditions from CS that achieve the optimal TPC, DPPH radical scavenging capacity, and FRAP antioxidant capacity. The optimal extraction conditions were obtained by optimizing the four influential variables: water content in DES, liquid/solid ratio, extraction time, and extraction temperature.

In Fig. 13, higher water content contributed positively to TPC and the FRAP antioxidant capacity but negatively to the DPPH radical scavenging capacity. The optimal water content in DES was 30.2% (w/w). The liquid/solid ratio and the extraction temperature had a strong influence on TPC, DPPH and FRAP antioxidant capacity, as evidenced by the steep positive slope. On the other hand, the

Table 6

Regression coefficients of the fitted polynomial equation (equation (6), equation (7), equation (8)) for TPC, DPPH, and FRAP of CS extracts, respectively.

Regression Coefficient	TPC				DPPH				FRAP			
	Coefficients	Standard Error	t Stat	p-value	Coefficients	Standard Error	t Stat	p-value	Coefficients	Standard Error	t Stat	p-value
Intercept Linear	-3.8724				-12.7448				-34.3513			
X1	0.5609	0.1036	5.4123	0.0002*	0.8135	0.3343	2.4331	0.0315*	2.2298	0.2943	7.5775	6.52E-06*
X2	-0.1650	0.1508	-1.0942	0.2953	0.2447	0.4863	0.5031	0.6240	-0.3364	0.4280	-0.7860	0.4471
X3	0.0554	0.0498	1.1117	0.2881	-0.1114	0.1608	-0.6928	0.5016	0.2827	0.1415	1.9976	0.0689
X4	0.0281	0.0975	0.2884	0.7780	0.2745	0.3144	0.8732	0.3997	0.5234	0.2767	1.8918	0.0829
Quadratic effect												
X1X1	-0.0042	0.0010	-4.0120	0.0017*	-0.0027	0.0034	-0.7869	0.4466	-0.0200	0.0030	-6.7320	2.10E-05*
X2X2	0.0020	0.0019	1.0635	0.3085	0.0034	0.0060	0.5751	0.5759	-0.0050	0.0053	-0.9549	0.3585
X3X3	0.0002	0.0003	0.7677	0.4575	0.0013	0.0008	1.5416	0.1491	-0.0011	0.0007	-1.5472	0.1478
X4X4	0.0014	0.0007	2.1619	0.0515	0.0004	0.0022	0.1627	0.8735	-0.0016	0.0019	-0.8233	0.4264
Interaction effect												
X1X2	0.0030	0.0016	1.8328	0.0917	-0.0063	0.0052	-1.2150	0.2477	0.0117	0.0046	2.5620	0.0249*
X1X3	-0.0005	0.0006	-0.7929	0.4432	-0.0001	0.0019	-0.0413	0.9677	-0.0023	0.0017	-1.3601	0.1988
X1X4	-0.0039	0.0010	-4.0349	0.0016*	-0.0079	0.0031	-2.5497	0.0254*	-0.0118	0.0027	-4.2967	0.0010*
X2X3	0.0003	0.0008	0.3608	0.7245	0.0003	0.0026	0.1184	0.9077	-0.0008	0.0023	-0.3654	0.7211
X2X4	0.0022	0.0013	1.7153	0.1120	-0.0004	0.0042	-0.1015	0.9209	0.0123	0.0037	3.3720	0.0055*
X3X4	-0.0007	0.0005	-1.4117	0.1834	0.0000	0.0016	-0.0096	0.9925	-0.0003	0.0014	-0.2301	0.8219

* Significant at $p < 0.05$.

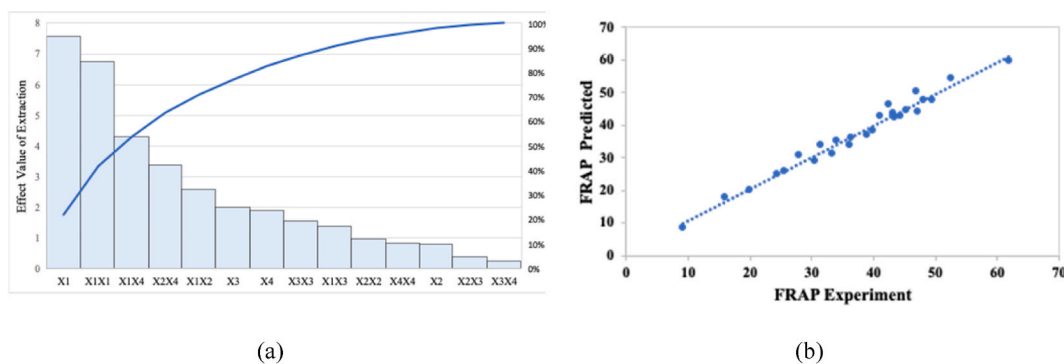


Fig. 10. (a) Pareto chart for the factors X_1 (water content in DES), X_2 (liquid/solid ratio), X_3 (extraction time), X_4 (extraction temperature) and their interaction with respect to FRAP antioxidant capacity given the 95% confidence level ($p < 0.05$), (b) Correlation between the experimental and predicted FRAP antioxidant capacity with $R^2 = 0.9749$, R^2 adjusted = 0.9739, p -value = 1, RMSE = 1.83.

extraction time had a minimal influence on the responses, as indicated by the relatively flat slope.

The optimal UAE condition for CS extraction with DES was 30.2% (w/w) water content in DES, 45 mL/g liquid/solid ratio, 90 min extraction time and 85 °C extraction temperature, achieving 22.39 mg GAE/g CS for TPC, 24.09 mg TE/g CS for DPPH radical scavenging capacity, and 59.43 mg Fe(II)/g CS for FRAP antioxidant capacity, with the composite desirability (D) of 0.9847.

To validate, experiments were carried out in triplicate under the BBD-based optimal UAE condition (Table 7). The experimental results were 19.188 ± 0.20 mg GAE/g CS for TPC, which was significantly different from the predicted value ($p < 0.05$). The discrepancy (*i.e.*, significant difference) could be attributed to failure to account for the degradation of certain phenolic compounds of the BBD-based model. The DPPH antioxidant capacity was 24.058 ± 1.77 mg TE/g CS for DPPH radical scavenging capacity, which was insignificantly different from the predicted value ($p > 0.05$). The FRAP antioxidant capacity was 59.125 ± 4.55 mg Fe (II)/g CS, which was significantly different from the predicted value ($p < 0.05$). The discrepancy could be attributed to a large standard deviation.

3.3. Kinetics models for CS extraction

This research examined three kinetics models to determine the model that best fitted the experimental data. The kinetic models under study included the power law kinetics model, Elovich kinetics model, and two-site kinetics model. In the kinetics modeling, the extraction temperature was varied between 35, 60, and 85 °C; and the extraction time between 2, 4, 8, 10, 30, 60, and 90 min, given 30% (w/w) water content, 45 mL/g liquid/solid ratio, 1 ChCl: 7 hexanediol, 40 kHz ultrasonic power, and 150–250 μ m CS particle size.

3.3.1. The power law kinetics model

In Fig. 14, the TPC yield was positively correlated to the extraction temperature since higher extraction temperature reduced the density, viscosity and surface tension of DES, resulting in increased diffusivity and higher extraction efficiency. The predicted results of the power law kinetics model and the experimental results were agreeable.

In Table 8, R^2 of 0.992–0.999 and the root mean square error (RMSE) of 0.224–0.579 indicated that the predicted and experimental results were in good agreement. The finding also suggested that the power law kinetics model could be used to predict TPC from CS in DES.

3.3.2. Elovich kinetics model

In Fig. 15, the TPC yield was positively correlated to the extraction temperature. The predicted results of the Elovich kinetics model were agreeable with the experimental results. However, the Elovich model failed to predict the TPC extraction at $t = 0$ due to the natural logarithm term (equation (3)).

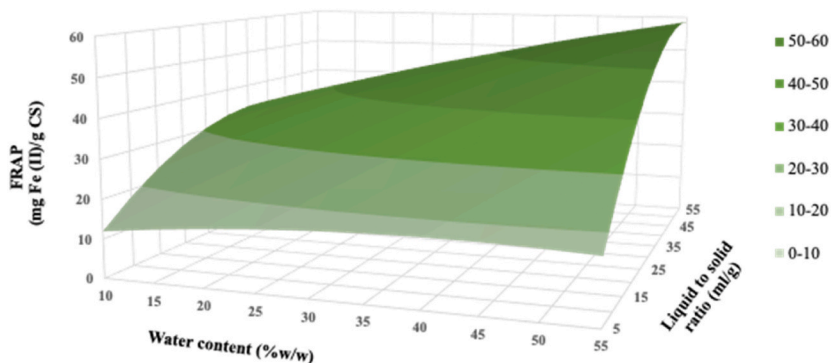
In Table 9, the predicted results and the experimental results were agreeable, as indicated by R^2 of 0.917–0.975 and RMSE of 0.555–0.707. As a result, the Elovich kinetics model could be reasonably used to predict TPC from CS in DES using UAE.

3.3.3. Two-site kinetics model

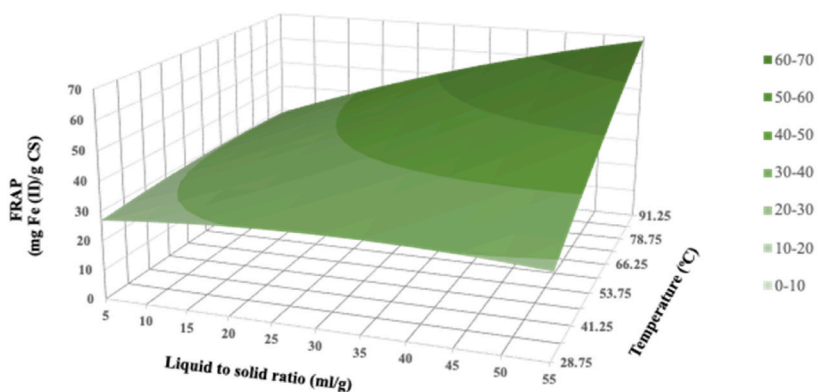
Fig. 16 shows the effect of extraction temperature on TPC under variable extraction time using the two-site kinetics model. Specifically, TPC was positively correlated with the extraction temperature. In Fig. 16, the kinetics modeling consisted of two steps: washing and diffusion. However, the washing step was unobservable due to its brevity and rapidity [33].

In Table 10, the high R^2 of 0.990–0.999 and small RMSE of 0.199–0.501 indicated that the predicted and experimental results were in good agreement. Generally, the extraction curve of UAE is of exponential function [37]. By comparison, the predicted results of the two-site kinetics model best fitted the experimental results, as evident in the highest R^2 and smallest RMSE.

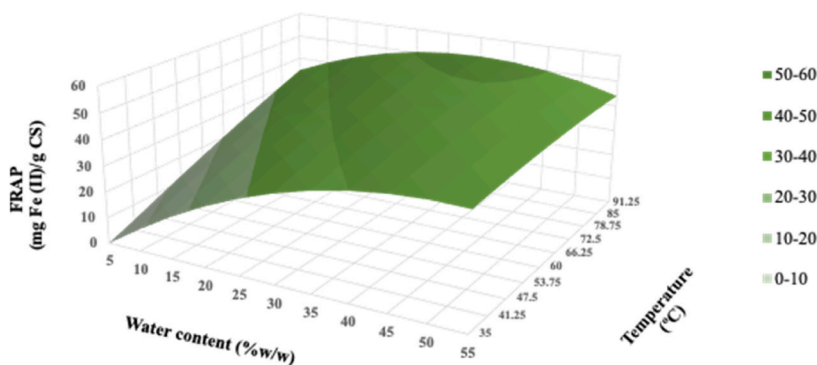
In Table 11, due to the brevity and rapidity of the washing stage, the effective diffusion coefficients of the washing stage (D_{e-fast}) under variable extraction temperatures were approximated by the by two-site kinetics model (equation (5)). Besides, the effective



(a)



(b)



(c)

Fig. 11. 3D response surface area plot and contour plot showing the effect of the water content in DES (X_1), liquid/solid ratio (X_2), extraction time (X_3), and extraction temperature (X_4) on FRAP antioxidant activity: (a) mutual effect of X_1 and X_2 , given $X_3 = 50$ min and $X_4 = 60^\circ\text{C}$, (b) mutual effect of X_2 and X_4 , given $X_1 = 30\%$ (w/w) and $X_3 = 50$ min, (c) mutual effect of X_1 and X_4 , given $X_2 = 30$ mL/g and $X_3 = 50$ min.

diffusion coefficients of the washing stage ($D_{e\text{-fast}}$) were higher than those of the diffusion stage ($D_{e\text{-slow}}$), and the effective diffusion coefficients of both stages increased with increase in the extraction temperature.

4. Conclusion

This research investigates the effect of UAE parameters on TPC, DPPH radical scavenging capacity, and FRAP antioxidant capacity of CS extract using DES. The UAE parameters included the CS particle size, type of HBD, HBA:HBD molar ratio, water content, liquid/

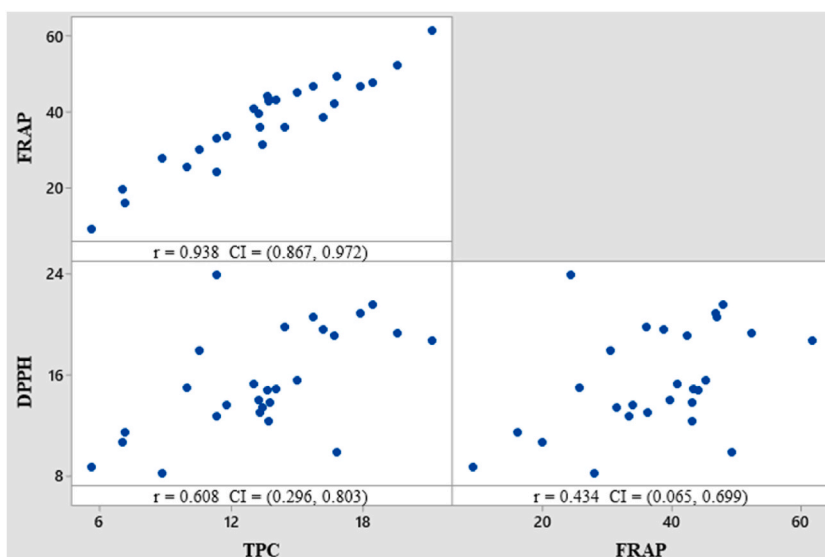


Fig. 12. Correlation analysis chart of the BBD responses (i.e., TPC, DPPH radical scavenging capacity and FRAP antioxidant capacity).

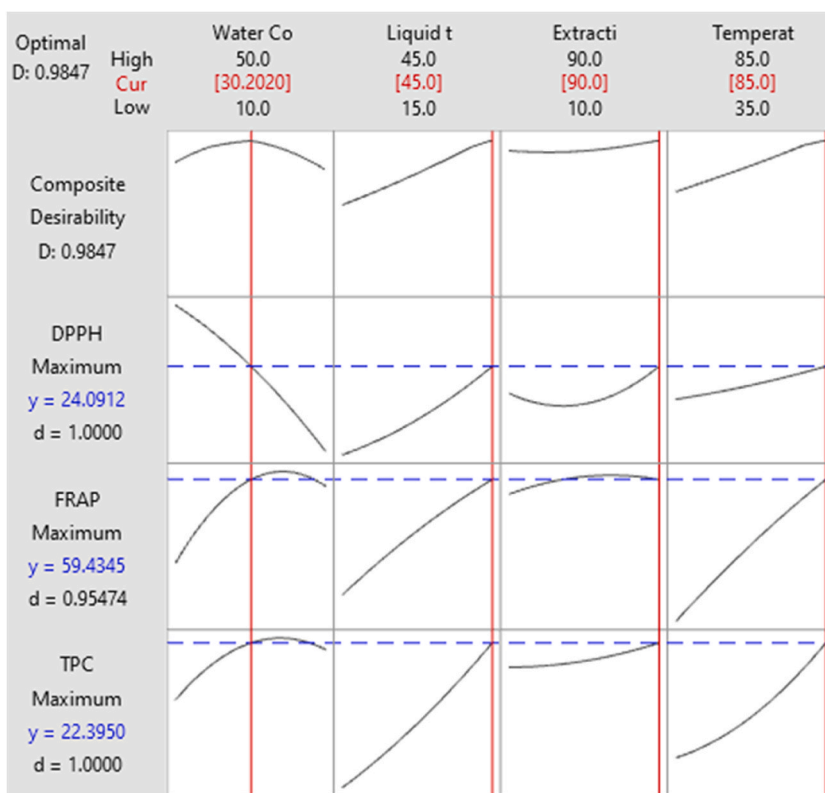


Fig. 13. Optimized UAE condition for CS extraction with DES for maximum TPC, DPPH and FRAP antioxidant capacity.

solid ratio, extraction time, and extraction temperature. The optimization was performed in two stages: The first stage involved optimizing the UAE condition that achieved the highest TPC. In the second stage, a four-factor BBD was used to optimize the UAE conditions that achieved the optimal TPC, DPPH and FRAP antioxidant capacity. The optimal UAE condition with the highest TPC was 150–250 μm CS particle size, 1:7 M ratio (ChCl as HBA and 1,6 hexanediol as HBD), and 30% (w/w) water content, given 30 min extraction time and 30 ° C extraction temperature. Meanwhile, the BBD-based optimal UAE condition was 30% (w/w) water content in DES, 45 mL/g liquid/solid ratio, 90 min extraction time and 85 ° C extraction temperature, given the CS particle size of 150–250 μm

Table 7

Comparison between the experimental and predicted results under the BBD-based optimal UAE conditions.

Exp.	BBD-based optimal UAE conditions				Responses		
	X ₁	X ₂	X ₃	X ₄	TPC (mg GAE/g CS)	DPPH (mg TE/g CS)	FRAP (mg Fe (II)/g CS)
1	30	45	90	85	19.06	22.02	54.58
2	30	45	90	85	19.10	25.29	63.67
3	30	45	90	85	19.42	24.86	59.13
Average experimental results					19.19 ± 0.20 ^a	24.06 ± 1.77 ^a	59.13 ± 4.55 ^a
Predicted results (equations (6)–(8))					22.40 ^b	24.09 ^a	59.43 ^b

Note: The experimental results were expressed as mean ± standard deviation (n = 3). The values with different superscripts in the same column are significantly different (p < 0.05).

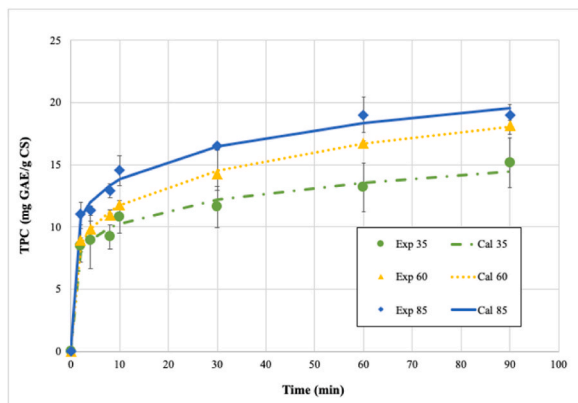


Fig. 14. Effect of extraction temperature on TPC under variable extraction time using the power law kinetics model, given 30% (w/w) water content, 45 mL/g liquid/solid ratio, 1 ChCl: 7 hexanediol, 40 kHz ultrasonic power and 150–250 μ m CS particle size.

Table 8

Coefficients and statistical parameters for the power law kinetics model.

Temperature ($^{\circ}$ C)	B	n	R ²	RMSE
35	7.205	0.155	0.986	0.579
60	7.502	0.195	0.999	0.224
85	9.631	0.158	0.992	0.578

Note: B is a constant related to the extraction rate (g CS/mg GAE.min⁻¹) and n is the power law exponent (<1).

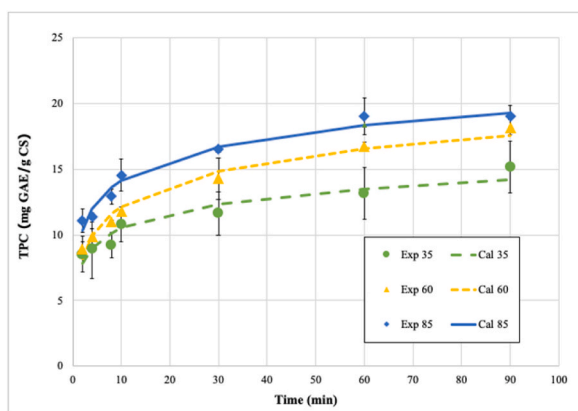


Fig. 15. Effect of extraction temperature on TPC under variable extraction time using the Elovich kinetics model, given 30% (w/w) water content, 45 mL/g liquid/solid ratio, 1 ChCl: 7 hexanediol, 40 kHz ultrasonic power and 150–250 μ m CS particle size.

Table 9
Coefficients and statistical parameters for the Elovich kinetics model.

Temperature (°C)	E_0	E_1	R^2	RMSE
35	6.681	1.663	0.917	0.707
60	6.439	2.474	0.975	0.555
85	8.721	2.346	0.968	0.604

Note: E_0 is the initial yield and E_1 is the initial extraction rate.

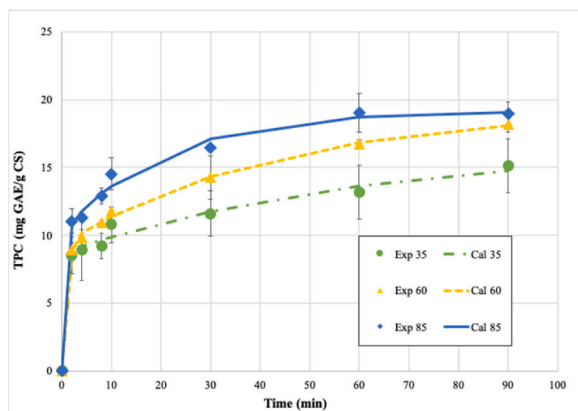


Fig. 16. Effect of extraction temperature on TPC under variable extraction time using the two-site kinetics model, given 30% (w/w) water content, 45 mL/g liquid/solid ratio, 1 ChCl: 7 hexanediol, 40 kHz ultrasonic power and 150–250 μm CS particle size.

Table 10
Coefficients and statistical parameters for the two-site kinetics model.

Temperature (°C)	C_∞	F	k_1 (min^{-1})	k_2 (min^{-1})	R^2	RSME
35	16.552	0.527	1.448	0.016	0.990	0.491
60	19.428	0.481	1.148	0.023	0.999	0.199
85	19.168	0.530	1.944	0.049	0.994	0.501

Note: C_∞ is the extractable substance content at time t approaching infinity (mg GAE/g CS), F is the portion of rapidly released solute, k_1 is the first-order rate constant of the rapidly released portion (min^{-1}), and k_2 is the first-order rate constant of the slowly released portion (min^{-1}).

Table 11
Effective diffusion coefficients (D_e) of phenolic compounds in DES using UAE, where $D_{e\text{-fast}}$ and $D_{e\text{-slow}}$ denote the washing and diffusion stages, respectively.

Temperature (°C)	$D_{e\text{-fast}} \times 10^{11}$ (m^2/s)	$D_{e\text{-slow}} \times 10^{12}$ (m^2/s)
35	2.507	1.089
60	2.821	1.569
85	4.387	3.320

and the HBA:HBD molar ratio of 1 (ChCl): 7 (1,6 hexanediol), achieving 19.19 ± 0.20 mg GAE/g CS for TPC, 24.06 ± 1.77 mg TE/g CS for DPPH radical scavenging capacity, and 59.13 ± 4.55 mg Fe (II)/g CS for FRAP. The experimental results were in good agreement with the BBD-based predicted results. The kinetics modeling results indicated that the two-site kinetics model best fitted the experimental data, with R^2 of 0.991–0.999. Unlike previous studies, this current research investigated the effects of water content in DES on the extraction efficiency and antioxidant capacity; and the interaction between water content in DES and other extraction parameters (*i.e.*, liquid to solid ratio, extraction time, extraction temperature). Furthermore, since the kinetics of the phenolics extraction from CS in DES using UAE are little researched, this current research thus conducted a kinetics study to investigate the complex diffusion and mass transfer of phenolic compounds.

Author contribution statement

Supawat Taweekayujan, Supitcha Somngam: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data.

Tanawan Pinnarat: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data included in article/supp. material/referenced in article.

Declaration of competing 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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