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Comparative modeling of microwave and ultrasound assisted extraction of phenolics and berberine from *Coptis teeta* Wall. rhizomes†

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Coptis teeta rhizomes are a rich source of bioactive phytochemicals with significant applications in the food and nutraceutical industries. Standardized methods and solvent compositions are crucial to sustainably maximize bioactive yield while ensuring industrial feasibility. This study models and compares microwave (MAE) and ultrasound (UAE) assisted extraction of phenolics and berberine – the primary active alkaloid in *Coptis teeta* rhizomes. Previous studies on extracting phytochemicals from *Coptis teeta* have relied on the central composite design, which is limited in handling multiple independent variables. To address this limitation, a Box–Behnken design along with a response surface method was utilized, where independent variables included the solvent concentration (water : methanol), power level, extraction time, and solid–liquid ratio, and dependent variables were total phenolic content (TPC) and antioxidant activity. The results showed that for MAE, using 65% solvent concentration, 310 W power, 30 min extraction time, and 1 : 39 g mL^{-1} solid–liquid ratio resulted in a TPC of 210.04 mg GAE 100 g^{-1} and antioxidant activity of 98.57%. Whereas for UAE, 36% solvent concentration, 160 W ultrasound power, 10 min extraction time, and 1 : 78 g mL^{-1} solid–liquid ratio resulted in a TPC of 251.11 mg GAE 100 g^{-1} and 97.82% antioxidant activity. Berberine concentration in MAE extract was 212.18 ppm, whereas it was 162.96 ppm in UAE extract. While MAE yielded a higher berberine content, UAE was superior in extracting total phenolics. The findings provide a foundation for developing standardized methods and solvent compositions suitable for food and nutraceutical formulations.

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Sustainability spotlight

Coptis teeta is a medicinal plant highly valued for its bioactive phytochemicals but also recognized for ecological sensitivity due to overharvesting. This study promotes the sustainable use of *Coptis teeta* rhizomes by employing microwave and ultrasound assisted extraction – green techniques that maximize high-value bioactive yield while minimizing resource consumption. By providing standardized methods and solvent compositions, this research reduces the environmental impact of conventional methods and helps alleviate harvesting pressure on wild plant populations, thereby supporting green industrial practices and a circular bioeconomy.

1 Introduction

Plants are rich in bioactive phytochemicals and have garnered significant research and industrial attention due to their extensive health benefits and industrial applicability.[1–3] In this regard, *Coptis teeta* is a major pharmacological plant species widely utilized in Indian and Chinese traditional medicine.[4,5] The plant is a perennial herb from the Ranunculaceae family and is predominantly found in the forested regions of Sikkim and Arunachal Pradesh in India, Bhutan, and Yunnan in China. There are 15 identified species in this genus, all native to Asia.[4] The efficacy of this plant and its dried rhizomes has been documented to show various pharmacologically beneficial effects in fever, gastrointestinal disorders, malaria, detoxification, and other antibacterial, antiviral, anti-inflammatory, and anti-hyperglycemic activities.[6–12] In this regard, *Coptis teeta* Wall. is an endemic and endangered medicinal plant found in the Mishmi Hills of Arunachal Pradesh in India.[4,5,13] Locally the plant is referred to as '*Mishmi tita*'.[4] The bitter taste of the

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rhizome is associated with the word 'teeta/tita'.[4] The indigenous people of Arunachal Pradesh have traditionally used its dried rhizomes to treat various ailments such as gastrointestinal disorders, malaria, and detoxification.[4,14] *Coptis teeta* is a rich source of phytochemicals, and studies have revealed phytochemicals such as berberine, palmatine, jatrorrhizine, coptisine, columbamine, and epiberberine as the predominant phenolic constituents.[4,6,15] Among these, the major phytochemical in *Coptis teeta* is berberine, which occurs in high concentrations in the *Coptis teeta* rhizomes.[4] Berberine, often called the wonder molecule, is a benzylisoquinoline plant alkaloid.[16] Berberine demonstrates broad-spectrum pharmacological properties and recent research has highlighted its potential therapeutic applications, including anticancer, antidiabetic, and anti-inflammatory properties, and effects on the central nervous system and cardiovascular system.[11,16,17] Given these considerations, it becomes crucial to explore efficient and green extraction methods to prevent overexploitation while enabling the responsible utilization of its valuable phytochemicals for industrial use.

A crucial step in extracting phytochemicals is optimizing the extraction of compounds to promote greater extraction efficiencies. Green technologies primarily include industrially viable methods such as microwave-assisted extraction (MAE)[18] and ultrasound-assisted extraction (UAE).[19] MAE is commonly used in the food, pharmaceutical, and cosmetics industries. MAE involves the application of electromagnetic waves that penetrate plant cellular matrices and interact with polar groups, causing dipole heating primarily *via* polarization of water molecules. This generates significant heat and pressure, causing cellular membrane disassembly and release of cellular constituents into the surrounding liquid medium.[20,21] Conversely, UAE is commonly used in the chemical and food industries. UAE utilizes cavitation effects to rupture plant cell walls, enhancing the interaction between solid–liquid phases and contributing to mass diffusivity.[22,23] Recent studies on MAE and UAE methods have shown that the efficiency of phytochemical extraction depends on factors such as solvent concentration, microwave/ultrasound power, extraction time, and solid–liquid ratio.[24,25] The optimization of these extraction techniques would thereby ensure maximal phytochemical yield while minimizing solvent and material use, energy consumption, and extraction time.[26] The effectiveness of MAE and UAE has been demonstrated for extracting phytochemicals from *Coptis chinensis* Franch. – predominantly found in China[27,28] and in other plant materials such as olive leaves,[29] sesame leaves,[30] passion fruit peels,[31] and grape pomace.[22]

However, reports on the green extraction of phytochemicals from *Coptis teeta* Wall. are lacking in current literature to our knowledge. As discussed earlier, only two reports have demonstrated that MAE and UAE could improve the extraction of phytochemicals from a closely related genus, but distinct species *Coptis chinensis* Franch.[27,28] However, both past studies used a central composite design, which is limited in its capacity to model more than three independent variables. This study builds and expands on previous studies to utilize MAE and UAE techniques to extract phenolics from *Coptis teeta* Wall. rhizomes. Furthermore, a Box–Behnken experimental design is employed with the response surface method, a mathematical modeling and optimization routine frequently applied to improve the extraction of phytochemicals from natural sources. This approach offers advantages compared to the central composite design, including suitability for more than three factors, elimination of extreme factor levels, greater uniform precision, spherical design space, and lower risk of aliasing. It is hypothesized that this enhanced modeling routine will improve phenolic extraction from *Coptis teeta* Wall. rhizomes and responds to the ecological imperative of reducing overexploitation, while supporting industrial translation. The findings offer standardised methods and solvent concentrations for preparing *Coptis teeta* Wall. extracts in food and nutraceutical industries.

2 Materials and methods

2.1. Materials

Fresh rhizomes of *Coptis teeta* Wall. plants were collected from Arunachal Pradesh in India. The samples were washed thoroughly and dried in a hot air oven at 40 °C for 72 h. The dried rhizomes were ground to a powder, sieved using mesh 60, and then stored in airtight low-density polyethylene pouches for future use. The plant herbarium specimen was also deposited at the Assam Agricultural University, India (voucher specimen number 5296).

All chemicals used in the study were procured from HiMedia, India. All solvents utilized in the study were from Merck, India, and of analytical grade. HPLC standards were purchased from Sigma, India.

2.2. Microwave (MAE) and ultrasound (UAE) assisted extraction

One gram of the dried rhizome powder was used for microwave-assisted extraction according to the Box–Behnken experimental design (Table 1) using a variable power and irradiation time microwave oven (Model: MJ3283BCG, LG Electronics, India). Intermittent cyclic heating of 30 s was utilized to prevent solvent overheating. The independent variables were power level (180–900 W), extraction time (1–30 min), solid–liquid ratio (1 : 10–40 g mL^{-1}), and methanol concentration (50–70%). After treatment, the extracts were centrifuged at 3500 rpm for 10 min and filtered through Whatman Filter paper No. #1, and stored in the dark at 4 °C for further analysis. Coded variables are shown in Fig. S1.†

The extractions of bioactive molecules were carried out in a variable ultrasonic power and ultrasound time UW 2070 ultrasonic instrument (Bandelin Sonoplus, Germany) with a frequency of 25 kHz using a titanium alloy probe (diameter, 1.5 cm). An intermittent cycle duration of 10 seconds was utilized. The entire setup was maintained in an ice bath so the temperature would not increase above 20 °C. The powdered samples were treated with various combinations of independent variables, *viz.*, solvent concentration (0–100%), extraction power (40–200 W), extraction time (10–80 min) and solid–liquid ratio (1 : 10–80 g mL^{-1}) and are

Table 1 Experimental design parameters and responses for microwave-assisted extraction (MAE) from *Coptis teeta* Wall.[a]

Run number	Solvent concentration (%)	Extraction time (min)	Solid–liquid ratio (g mL^{-1})	Microwave power (W)	TPC* (mg GAE 100 g^{-1})	Antioxidant activity (%)
1	50.00	1.00	1 : 25.00	540.00	167.95 ± 2.05	94.45 ± 1.12
2	70.00	1.00	1 : 25.00	540.00	165.53 ± 3.39	92.68 ± 2.95
3	50.00	30.00	1 : 25.00	540.00	191.22 ± 2.85	97.53 ± 3.70
4	70.00	30.00	1 : 25.00	540.00	177.62 ± 1.67	94.16 ± 4.04
5	60.00	15.50	1 : 10.00	180.00	162.23 ± 3.02	87.04 ± 2.12
6	60.00	15.50	1 : 40.00	180.00	177.21 ± 2.10	90.71 ± 3.98
7	60.00	15.50	1 : 10.00	900.00	170.90 ± 1.90	90.00 ± 2.76
8	60.00	15.50	1 : 40.00	900.00	182.38 ± 2.54	92.84 ± 3.12
9	50.00	15.50	1 : 25.00	180.00	173.76 ± 3.79	89.53 ± 1.75
10	70.00	15.50	1 : 25.00	180.00	165.75 ± 4.02	87.44 ± 3.06
11	50.00	15.50	1 : 25.00	900.00	178.18 ± 3.12	90.77 ± 1.19
12	70.00	15.50	1 : 25.00	900.00	174.16 ± 2.95	91.29 ± 2.94
13	60.00	1.00	1 : 10.00	540.00	170.44 ± 1.75	89.99 ± 1.68
14	60.00	30.00	1 : 10.00	540.00	162.94 ± 3.96	92.17 ± 4.10
15	60.00	1.00	1 : 40.00	540.00	158.99 ± 2.05	93.36 ± 3.75
16	60.00	30.00	1 : 40.00	540.00	205.85 ± 3.78	98.30 ± 2.12
17	50.00	15.50	1 : 10.00	540.00	156.77 ± 4.12	92.77 ± 2.89
18	70.00	15.50	1 : 10.00	540.00	154.57 ± 3.06	93.78 ± 1.75
19	50.00	15.50	1 : 40.00	540.00	178.31 ± 2.75	97.82 ± 2.75
20	70.00	15.50	1 : 40.00	540.00	165.49 ± 1.19	95.23 ± 1.68
21	60.00	1.00	1 : 25.00	180.00	168.93 ± 2.89	84.14 ± 2.45
22	60.00	30.00	1 : 25.00	180.00	209.61 ± 3.15	91.44 ± 3.79
23	60.00	1.00	1 : 25.00	900.00	192.35 ± 2.94	88.91 ± 1.90
24	60.00	30.00	1 : 25.00	900.00	193.03 ± 2.54	91.75 ± 2.54
25	60.00	15.50	1 : 25.00	540.00	165.09 ± 1.68	81.92 ± 2.10
26	60.00	15.50	1 : 25.00	540.00	168.59 ± 2.98	81.12 ± 3.02
27	60.00	15.50	1 : 25.00	540.00	158.23 ± 3.75	81.88 ± 2.56
28	60.00	15.50	1 : 25.00	540.00	168.55 ± 1.75	81.02 ± 2.12
29	60.00	15.50	1 : 25.00	540.00	159.32 ± 2.45	81.94 ± 2.02

[a] Experiments were performed in triplicate and the results were represented as mean ± standard deviation. Note that only mean values were used for modeling. TPC, total phenolic content; W, watt.

described in detail in Table 3. After treatment, the extracts were centrifuged at 3500 rpm for 10 min and filtered through Whatman Filter paper No. #1, and stored in the dark at 4 °C for further analysis. Coded variables are shown in Fig. S2.†

Preliminary experiments were conducted to determine the range of process variables used in microwave and ultrasound assisted extractions (data not shown). A conventional extraction of bioactive molecules was also carried out in a laboratory scale shaking incubator at 30 °C for 24 h. After shaking incubation, the extracts were centrifuged at 5000*g*, and the supernatant was collected, freeze-dried and analyzed for total phenolics.

2.3. Determination of total phenolic content

Total phenolic content (TPC) was evaluated as described previously,[30] with few modifications. Briefly, an aliquot (20 μL) of the extract was mixed with 1.58 mL of distilled water. 100 μL of Folin–Ciocalteu reagent was added to the mixture and incubated for 8 min at room temperature. 300 μL of 10% Na_2CO_3 was added to it and further incubated for 30 min in the dark at 40 °C. Absorbance was measured at 765 nm. The blank consisted of distilled water instead of extract. A gallic acid calibration curve (0–100 mg L^{-1}) was used to determine the total phenolic contents, and the results were expressed in gallic acid equivalents, mg GAE 100 g^{-1}.

2.4. Determination of total antioxidant activity

The antioxidants present in the extract were measured using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay as described previously,[32] with few modifications. An aliquot of 100 μL extracts was allowed to react with 1.4 mL of DPPH radical methanolic solution (10^{-4} M), followed by 30 min incubation at room temperature. Absorbance was measured at 517 nm, and the radical scavenging activities were expressed using eqn (1):

$$\text{Free radical scavenging activity}(\%) = \frac{A_0 - A_s}{A_0} \times 100 \quad (1)$$

where A_0 and A_s is the absorbance of the control and sample extract. The control consisted of distilled water instead of extract.

2.5. Process optimization and statistical analysis

Optimization was carried out using the response surface methodology (RSM) using the Design Expert Software 7 (Stat-Ease, Inc. USA). The effects of the four independent variables *i.e.*, solvent concentration, microwave/ultrasonic power, extraction time, and solid–liquid ratio, were correlated with the responses, *i.e.*, TPC and antioxidant activity. The experiments were performed at the central value to maximize the prediction process, and randomized experimental runs were carried out to

prevent unwarranted variability in the responses. A second-order polynomial equation was fitted in each response to describe the process mathematically as in eqn (2):

$$Y = \beta_0 + \sum \beta_i X_i + \sum\sum \beta_{ij} X_i X_j + \sum \beta_{ii} X_i^2 \quad (2)$$

where β_0 is the coefficient of the constant, β_i, is the coefficient of the linear term, $\beta_{ii,}$ is the coefficient of the quadratic term, and β_{ij} is the interaction coefficient of i and j variables. X_i and X_j are the independent variables, while Y is the response variable. The second-order polynomial equation was used to build the response surfaces, and the model adequacy was assessed by using the coefficient of determination (R^2), lack of fit, and Fisher test value (F-value) obtained from the analysis of variance (ANOVA). The model and parameter significance was evaluated at $p < 0.05$, $p < 0.01$, and $p < 0.001$. The actual and coded values are listed in Tables S1 and S2.† The optimization procedure involved maximizing the responses, *i.e.*, TPC and antioxidant activity, using the response surface methodology. The predicted solution was revalidated by conducting experiments at the optimized levels.

2.6. High performance liquid chromatography (HPLC)

Berberine is the main phytochemical in *Coptis teeta*.[4] Separation and quantification of berberine was carried out in a Waters HPLC system equipped with a UV-vis detector (Waters, USA). The samples were prepared in HPLC-grade methanol and filtered through a 0.22 μm nylon filter before analysis. The separations of the samples were carried out in a Symmetry 300™ C_{18} column (4.6 mm × 250 mm) where 0.05% aqueous *ortho*-phosphoric acid and acetonitrile were used as solvents A and B, respectively. The gradient elution method of Kamal and coworkers[33] was used, the flowrate was maintained at 1 mL min^{-1}, and the sample volume used for analysis was 20 μL. Absorbance was measured at 266 nm.

3 Results and discussion

Microwave-assisted extraction of phenolics from *Coptis teeta* rhizomes will be discussed first, followed by ultrasound-assisted extraction. Particular attention is paid to the effects of extraction parameters, including solvent concentration (water : methanol), microwave/ultrasound power levels, extraction time, and solid–liquid ratio on the total phenolic content and antioxidant activity of the extracts. This is followed by the modeling and optimization of the process, along with the quantification of berberine in the optimized extracts using high-performance liquid chromatography. This sets the scene for discussing the effect of independent variables on the responses and recommending standardised methods and solvent concentrations for preparing *Coptis teeta* extracts in food and nutraceutical industry applications.

3.1. Effect of microwave extraction on total phenolics and antioxidant activity

The results obtained during microwave-assisted extraction for total phenolic content (TPC) and antioxidant activity by DPPH assay are shown in Table 1. The highest phenolic extraction was uncovered at 60% solvent concentration, an extraction time of 30 min, 1 : 25 g mL^{-1} solid–liquid ratio, and 180 W microwave power, leading to maximum extraction of total phenolics, *i.e.*, 209.61 ± 3.15 mg GAE 100 g^{-1}. The highest antioxidant activities by DPPH assay (*i.e.*, 98.30 ± 2.12%) were achieved using 60% solvent concentration, 30 min extraction time, 1 : 40 g mL^{-1} solid–liquid ratio, and a microwave power of 540 W.

The results from ANOVA show that all the independent variables were significantly responsible for the increase in TPC and antioxidant values (Table 2). Fig. 1, 2a–c show decreased phenolic content and antioxidant activity with increased solvent concentration. The difference is attributed to progressively reducing solvent polarity, where lower extraction rates were observed at higher methanol concentrations. Diluted solvents in MAE applications have proven effective for recovering phytochemicals,[34] and is an important parameter in this study as high polarity of the protoberberine alkaloids present in *Coptis teeta* has been reported earlier.[14] Water is more polar compared to methanol, *i.e.*, the latter contains a non-polar methyl group, and the C–O bond in methanol is less polar compared to the O–H bond of water. It appears that an increase in methanol concentration beyond 60% contributes negatively to the extraction of phenolics. Teng and Choi also reported that the extraction of phenolics was greater at 60% ethanol concentration from *Coptis chinensis* Franch.[27] To compare the results between methanol used in the present study, and ethanol in the study by Teng and Choi,[27] further measurements were made for phenolic extraction using the two solvents. Our results demonstrated a TPC of 422.50 ± 2.57 mg GAE 100 g^{-1}, 342.00 ± 3.65 mg GAE 100 g^{-1}, and 102.00 ± 1.58 mg GAE 100 g^{-1} for 70% aqueous methanol, 70% aqueous ethanol, and water, respectively. This demonstrates that aqueous methanol is superior to aqueous ethanol for extracting phenolics from *Coptis teeta*. It is of note that although TPC was greater for conventional solvent-based extraction, the goal of the present study was to minimize the process duration while ensuring maximum phenolic extraction for industrial suitability. Hence, the extraction time for maximized extraction of phenolics was optimized. Under the MAE conditions, phenolic and antioxidant activities in the extract were seen to increase gradually with an increase in extraction time, with maximal values at 30 min (Table 1). A further increase in extraction time was not modelled as longer durations led to plateauing followed by a reduction in TPC (data not shown). It is postulated that increased extraction time led to thermal degradation of phenolics in the extract.[35] Increased release of phenolics and antioxidants was seen with a gradual increase in extraction time, as depicted in Fig. 1, 2a, d and e. Our results highlight that the MAE process achieved comparable phenolic extraction within 30 min, which would take roughly 12–24 hours using the conventional solvent extraction method.[36]

Additionally, maximum phenolic and antioxidant activities were achieved at greater solid–liquid ratios (Table 1, Fig. 1b, d, f, 2b, d and f), consolidating the importance of the solid–

Table 2 ANOVA table for microwave-assisted extraction (MAE) from *Coptis teeta* Wall.[a]

		Estimated variables		*F* value	
Variables	Degree of freedom	TPC	Antioxidant activity	TPC	Antioxidant activity
Model	14	163.95	81.57	29.72***	59.29***
X_1	1	−3.58	−0.77	12.20*	8.27*
X_2	1	9.67	1.90	88.62***	49.94***
X_3	1	7.53	1.87	53.72***	48.60***
X_4	1	2.79	1.27	7.38*	22.33
X_1^2	1	−2.79	−0.65	2.46	1.94***
X_2^2	1	−2.65	−0.9	2.22***	3.72***
X_3^2	1	0.99	0.65	0.31	1.96***
X_4^2	1	13.59	0.69	58.30***	2.19**
X_1X_2	1	−10	−1.11	31.57	5.72
X_1X_3	1	−0.87	−0.20	0.24	0.19
X_1X_4	1	−0.98	6.97	0.49	362.94
X_2X_3	1	13.40	5.90	92.00***	259.98
X_2X_4	1	−1.39	6.41	0.99***	307.46*
X_3X_4	1	11.40	1.64	66.64	20.29
Lack of fit	10				
R^2		0.96	0.98		
Adjusted R^2		0.93	0.96		

[a] X_1 – solvent concentration; X_2 – extraction time; X_3 – solid–liquid ratio; X_4 – microwave power. Significant differences at different levels of $*p < 0.05$; $**p < 0.01$; $***p < 0.001$, respectively.

liquid ratio in phenolic extraction. Initially, lower extraction rates were observed at a lower solid–liquid ratio, followed by maximal extraction at higher values of the solid–liquid ratio, as shown in Fig. 1, 2b, d–f. The lower extraction rates at low solid–liquid ratios might be attributed to the intermittent distribution of microwave heating in a partially soaked sample, as also suggested in previous studies.[37,38] Our results are concurrent with those on *Pistacia lentiscus* L. where the researchers reported maximal phenolic release (185.69 ± 18.35 mg GAE g^{-1} dry weight) at a higher solid–liquid-ratio of 1 : 28 g mL^{-1}.[39] Microwave power was also observed to affect the phenolic extraction (Table 1). At a short extraction time, phenolic extraction increased proportionally to microwave power (Fig. 1, 2c, e and f). The opposite was observed when a longer extraction time was used (Fig. 1, 2c, e and f) and could be attributed to thermal degradation of phytochemicals resulting from higher microwave power in tandem with extraction time, and has been reported earlier.[34] Teng and

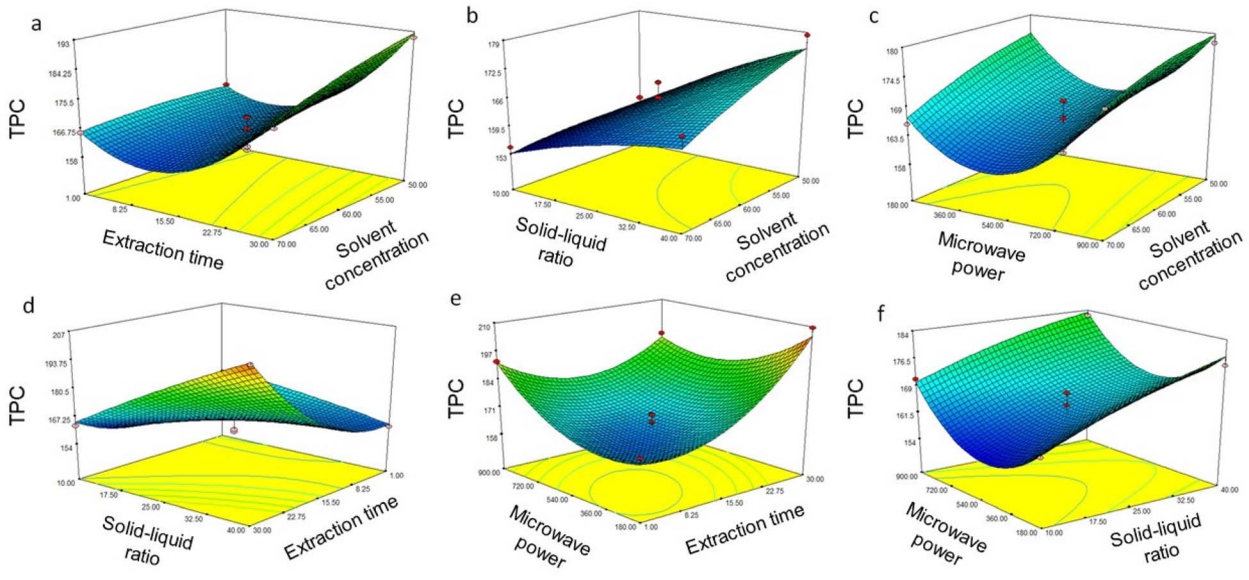

Fig. 1 Response surface for TPC yield from *Coptis teeta* rhizomes against various parameters using microwave extraction: (a) solvent concentration and extraction time; (b) solvent concentration and solid–liquid ratio; (c) solvent concentration and microwave power; (d) extraction time and solid–liquid ratio; (e) extraction time and microwave power; (f) microwave power and solid–liquid ratio. TPC: total phenolic content.

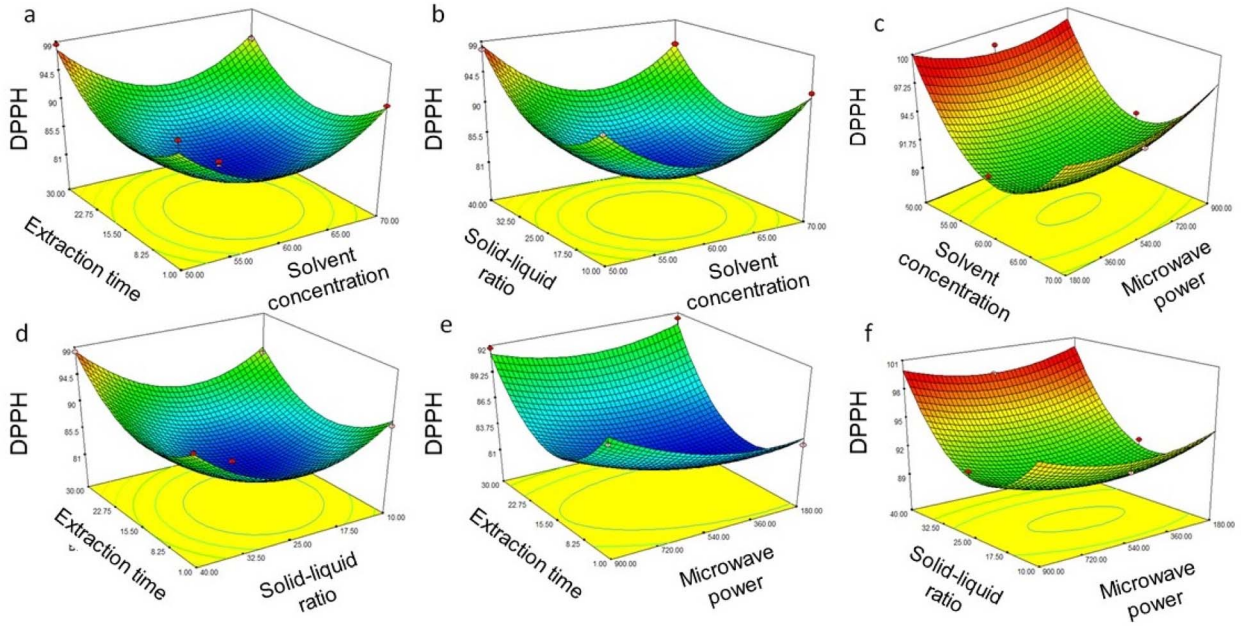

Fig. 2 Response surface for DPPH radical scavenging activity from *Coptis teeta* rhizomes against various parameters using microwave extraction: (a) solvent concentration and extraction time; (b) solvent concentration and solid–liquid ratio; (c) solvent concentration and microwave power; (d) extraction time and solid–liquid ratio; (e) extraction time and microwave power; (f) microwave power and solid–liquid ratio. DPPH: 2,2-diphenyl-1-picrylhydrazyl free radical scavenging activity.

Choi also reported that 180 W microwave power in combination with 5 min irradiation time was optimal for maximizing the extraction of alkaloids from *Coptis chinensis* Franch.[27]

The linear and quadratic terms, and their interaction terms were calculated to describe the response variables (Table 2). The developed models for dependent variables (*i.e.*, TPC, antioxidant activity; eqn (3) and (4)) were evaluated for their significance using ANOVA. The model was found to be significant, and the lack of fit was not significant. R^2 values were 0.96 and 0.98. The final equations for TPC and antioxidant activity in terms of coded factors are depicted below:

$$\begin{aligned}\text{TPC} = {} & 163.96 - 3.59 \times X_1 + 9.67 \times X_2 + 7.53 \times X_3 \\ & + 2.79 \times X_4 - 0.99 \times X_1^2 + 13.41 \times X_2^2 \\ & - 1.39 \times X_3^2 + 11.41 \times X_4^2 - 2.79 \times X_1 \\ & \times X_2 - 2.65 \times X_1 \times X_3 + 1.00 \times X_1 \times X_4 + 13.59 \\ & \times X_2 \times X_3 - 10.00 \times X_2 \times X_4 - 0.88 \times X_3 \times X_4 \end{aligned} \quad (3)$$

$$\begin{aligned}\text{Antioxidant activity} = {} & 81.58 - 0.77 \times X_1 + 1.90 \times X_2 \\ & + 1.88 \times X_3 + 1.27 \times X_4 + 6.97 \times X_1^2 \\ & + 5.90 \times X_2^2 + 6.42 \times X_3^2 + 1.65 \times X_4^2 \\ & - 0.65 \times X_1 \times X_2 - 0.90 \times X_1 \times X_3 + 0.65 \\ & \times X_1 \times X_4 + 0.69 \times X_2 \times X_3 - 1.11 \times X_2 \\ & \times X_4 - 0.21 \times X_3 \times X_4. \end{aligned} \quad (4)$$

where X_1, X_2, X_3, and X_4 represent solvent concentration, extraction time, solid–liquid ratio, and microwave power. The coefficient determines the intensity of the response. Note that the positive coefficient depicts an increase in response with an increase in the variable, whereas the negative coefficient depicts a decrease in response with an increase in the variable. For microwave-assisted extraction (MAE), the optimal conditions were 65% solvent concentration, 310 W power, 30 min extraction time, and 1 : 39 g mL^{-1} solid–liquid ratio, resulting in a TPC of 210.04 mg GAE 100 g^{-1} and antioxidant activity of 98.57%.

3.2. Effect of ultrasound extraction on total phenolics and antioxidant activity

The TPC and antioxidant activity from *Coptis teeta* rhizomes varied from 66.18 ± 3.12 to 276.20 ± 2.54 mg GAE 100 g^{-1} and 70.06 ± 1.75 to 97.68 ± 3.09%, respectively, during the ultrasound-assisted extraction process (Table 3). The highest phenolic content was observed for the extracts using 50% aqueous methanol as the extraction solvent with 80 min sonication time, 1 : 10 g mL^{-1} solid–liquid ratio, and 120 W ultrasound power. Meanwhile, antioxidant activity by DPPH scavenging assay was highest when 50% aqueous methanol was used in a 1 : 80 g mL^{-1} solid–liquid ratio at 120 W ultrasound power for a period of 10 min.

Solvent concentration is an important parameter on which the extraction of phenolic compounds depends. An investigation of the effect of methanol in water at various percentages (0–100%) was conducted to extract phenolics, as depicted in Table 3. First, 50% solvent concentration, *i.e.*, 50% aqueous methanol, was observed to maximize the extraction of phenolics (276.20 ± 2.54 mg GAE 100 g^{-1}) as revealed by TPC assay and antioxidant activity (97.68 ± 3.09%), while phenolic extraction suffered at higher solvent concentrations (Fig. 3 and 4a–c). Our results agree with recent reports showing that phytochemical extraction from *Coptis chinensis* Franch. increased with an increase in ethanol concentration, reaching a peak at an ethanol concentration of 50%.[27,28] Dilute solvents in UAE applications have also proven

Table 3 Experimental design parameters and responses for ultrasound-assisted extraction (UAE) from *Coptis teeta* Wall.[a]

Run number	Solvent concentration (%)	Extraction time (min)	Ultrasound power (W)	Solid–liquid ratio (g mL^{-1})	TPC* (mg GAE 100 g^{-1})	Antioxidant activity (%)
1	0	10	120	1 : 45	155.28 ± 2.54	75.17 ± 3.62
2	100	10	120	1 : 45	195.35 ± 3.09	86.48 ± 1.89
3	0	80	120	1 : 45	163.78 ± 1.75	75.43 ± 1.95
4	100	80	120	1 : 45	191.29 ± 1.89	86.72 ± 2.34
5	50	45	40	1 : 10	200.14 ± 2.34	95.62 ± 3.12
6	50	45	200	1 : 10	193.66 ± 3.12	86.65 ± 2.45
7	50	45	40	1 : 80	107.19 ± 2.45	73.98 ± 1.95
8	50	45	200	1 : 80	156.59 ± 1.95	70.19 ± 3.50
9	0	45	120	1 : 10	72.40 ± 3.50	71.82 ± 2.75
10	100	45	120	1 : 10	213.90 ± 2.75	95.65 ± 3.12
11	0	45	120	1 : 80	160.10 ± 3.78	75.30 ± 2.25
12	100	45	120	1 : 80	66.18 ± 3.12	70.06 ± 1.75
13	50	10	40	1 : 45	212.22 ± 2.25	97.18 ± 1.89
14	50	80	40	1 : 45	191.68 ± 1.75	86.91 ± 3.10
15	50	10	200	1 : 45	195.92 ± 2.56	87.28 ± 3.50
16	50	80	200	1 : 45	230.90 ± 1.89	95.04 ± 3.12
17	0	45	40	1 : 45	95.03 ± 3.09	84.23 ± 2.20
18	100	45	40	1 : 45	171.50 ± 2.54	80.30 ± 3.12
19	0	45	200	1 : 45	154.17 ± 1.95	72.62 ± 3.52
20	100	45	200	1 : 45	165.28 ± 3.50	87.14 ± 2.75
21	50	10	120	1 : 10	137.46 ± 1.56	89.05 ± 1.75
22	50	80	120	1 : 10	276.20 ± 2.54	90.98 ± 2.34
23	50	10	120	1 : 80	258.98 ± 3.12	97.68 ± 3.09
24	50	80	120	1 : 80	99.68 ± 3.20	94.24 ± 3.50
25	50	45	120	1 : 45	252.54 ± 3.12	95.97 ± 3.10
26	50	45	120	1 : 45	246.74 ± 3.52	91.97 ± 2.12
27	50	45	120	1 : 45	253.64 ± 2.75	90.97 ± 3.45
28	50	45	120	1 : 45	248.54 ± 2.12	90.97 ± 2.02
29	50	45	120	1 : 45	241.54 ± 2.05	92.97 ± 3.12

[a] The experiments were performed in triplicate and the results were represented as mean ± standard deviation. Note that only mean values were used for modeling. *TPC, total phenolic content; W, watt.

effective for recovering phytochemicals from other plant materials, such as *Hancornia speciosa*.[34] Additionally, extraction time had little effect on total phenolic extraction or the antioxidant activity of the extracts (Table 3) and agrees with previous reports.[27,28] However, when comparing the effect of solid–liquid ratios with extraction time, the latter was observed to lead to a decline in total phenolics and antioxidant activity of the extracts (Fig. 3 and 4a, d and e). Here, an increase in the solid–liquid ratio from 1 : 10 to 1 : 80 g mL^{-1} resulted in increased total phenolics from 72.40 ± 3.50 mg GAE 100 g^{-1} to 258.98 ± 3.12 mg GAE 100 g^{-1}, and antioxidant activity from 71.82 ± 2.75% to 97.68 ± 3.09%, respectively (Table 3). Response surface graphs illustrate the effects of the interaction of independent variables and are shown in Fig. 3, 4c, e and f. It can be seen from the figures that an increase in the solid–liquid ratio decreased phenolic content and antioxidant activity. Additionally, up to 120 W microwave power, total phenolics and antioxidant activity increased (Table 3). However, above 120 W power, a sharp decline in phenolics and antioxidant activity was seen (Fig. 3, 4b, d – f). The correlation between sonochemical effects of ultrasonic fields, phenolic extraction, and phenolic degradation has been reported previously.[40] Free radical scavengers have been reported to greatly inhibit the degradation of phenolics during such extraction processes[40] and could be an area for further research, but is beyond the scope of the present study.

To describe the response variables, the linear and quadratic terms, along with their interaction terms, were calculated (Table 4). The developed models for dependent variables (*i.e.*, TPC, antioxidant activity; eqn (5) and (6)) were evaluated for their significance using ANOVA. The quadratic model was found to be significant. R^2 were 0.98 and 0.97, and the lack of fit was not significant. The predicted equations for TPC and antioxidant activity are shown below:

$$\begin{aligned}\text{TPC} = {} & 248.60 + 16.90 \times X_1 - 0.14 \times X_2 + 9.90 \\ & \times X_3 - 20.42 \times X_4 - 68.14 \times X_1^2 - 5.07 \times X_2^2 - 34.38 \\ & \times X_3^2 - 50.86 \times X_4^2 - 3.14 \times X_1 \times X_2 - 16.34 \times X_1 \\ & \times X_3 - 58.85 \times X_1 \times X_4 + 13.88 \times X_2 \times X_3 - 74.51 \times X_2 \\ & \times X_4 + 13.97 \times X_3 \times X_4 \end{aligned} \quad (5)$$

$$\begin{aligned}\text{Antioxidant activity} = {} & 92.65 + 2.90 \times X_1 - 1.63 \times X_2 \\ & + 0.81 \times X_3 + 1.47 \times X_4 - 12.41 \times X_1^2 \\ & + 0.87 \times X_2^2 + 1.12 \times X_3^2 - 0.24 \times X_4^2 \\ & + 4.24 \times X_1 \times X_2 + 4.61 \times X_1 \times X_3 + 1.74 \\ & \times X_1 \times X_4 - 0.74 \times X_2 \times X_3 - 1.34 \times X_2 \\ & \times X_4 + 1.29 \times X_3 \times X_4 \end{aligned} \quad (6)$$

where X_1, X_2, X_3, and X_4 represent solvent concentration, extraction time, ultrasound power, and solid–liquid ratio. The results showed that for ultrasound-assisted extraction (UAE),

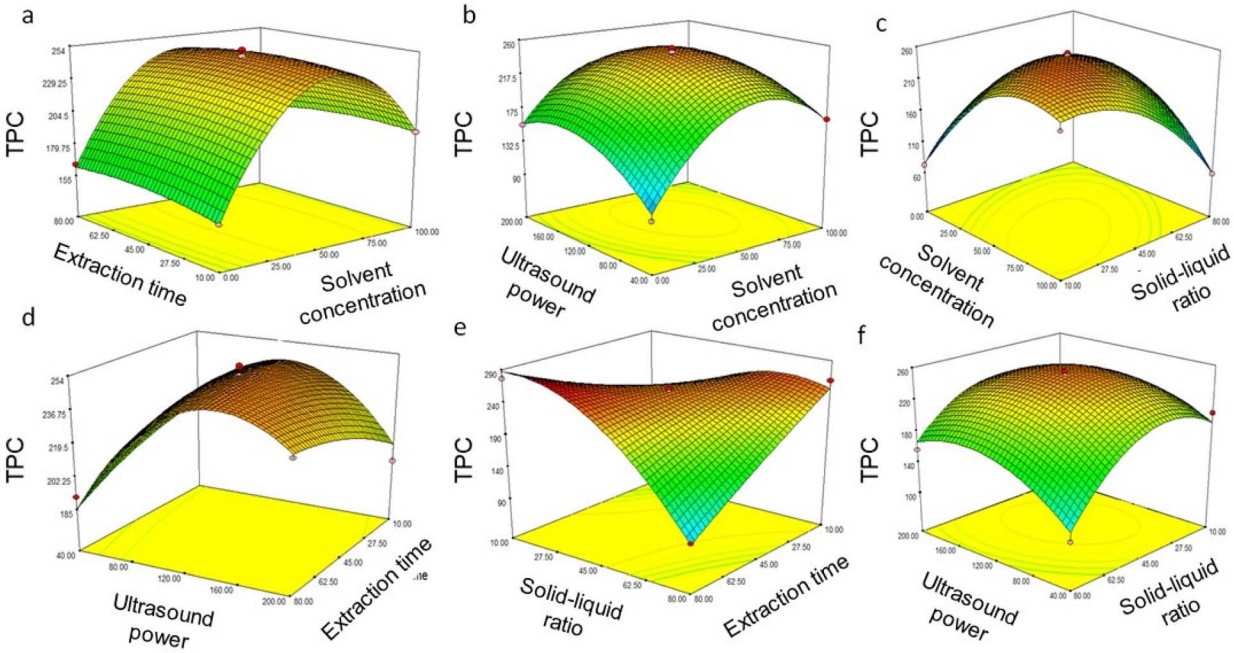

Fig. 3 Response surface for TPC yield from *Coptis teeta* rhizomes against various parameters using ultrasound extraction: (a) solvent concentration and extraction time; (b) solvent concentration and ultrasound power; (c) solvent concentration and solid–liquid ratio; (d) extraction time and ultrasound power; (e) extraction time and solid–liquid ratio; (f) ultrasound power and solid–liquid ratio. TPC: total phenolic content.

36% solvent concentration, 160 W ultrasound power, 10 min extraction time, and 1 : 78 g mL^{-1} solid–liquid ratio resulted in a TPC of 251.11 mg GAE 100 g^{-1} and 97.82% antioxidant activity.

3.3. Model validation and comparison between microwave and ultrasound assisted methods

The models developed using the response surface methodology were revalidated by using mean variation and percentage

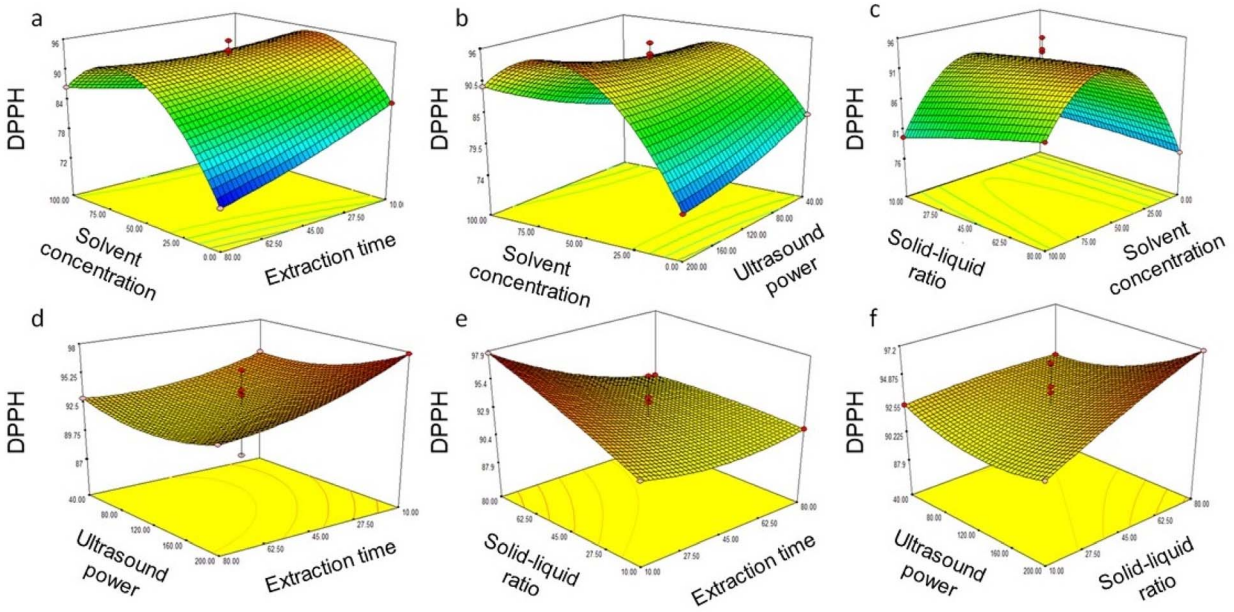

Fig. 4 Response surface for DPPH radical scavenging activity from *Coptis teeta* rhizomes against various parameters using ultrasound extraction: (a) solvent concentration and extraction time; (b) solvent concentration and ultrasound power; (c) solvent concentration and solid–liquid ratio; (d) extraction time and ultrasound power; (e) extraction time and solid–liquid ratio; (f) ultrasound power and solid–liquid ratio. DPPH: 2,2-diphenyl-1-picrylhydrazyl free radical scavenging activity.

Table 4 ANOVA table for ultrasound extraction[a]

Variables	Degree of freedom	Estimated variables		*F* value	
		TPC	Antioxidant activity	TPC	Antioxidant activity
Model	14	248.60	92.65	61.89***	39.65***
X_1	1	16.89	2.89	32.41***	37.55***
X_2	1	−0.13	−1.62	0.002	11.82*
X_3	1	9.89	0.80	11.12**	2.92
X_4	1	−20.42	1.47	47.34***	9.69*
X_1^2	1	−3.14	4.24	0.37***	26.85***
X_2^2	1	−16.34	4.61	10.10	31.67
X_3^2	1	−58.85	1.73	131.08***	4.48
X_4^2	1	13.88	−0.74	7.29***	0.82
X_1X_2	1	−74.50	−1.34	210.11	2.68***
X_1X_3	1	13.96	1.29	7.38**	2.49***
X_1X_4	1	−68.13	−12.40	284.92***	371.90
X_2X_3	1	−5.07	0.87	1.58*	1.84
X_2X_4	1	−34.38	1.12	72.55***	3.04
X_3X_4	1	−50.85	−0.24	158.75*	0.14
Lack of fit	10				
R^2		0.98	0.97		
Adjusted R^2		0.96	0.95		

[a] X_1 – solvent concentration; X_2 – extraction time; X_3 – ultrasound power; X_4 – solid–liquid ratio. Significant differences at different levels of $*p < 0.05$; $**p < 0.01$; $***p < 0.001$, respectively.

variation among the total phenol and antioxidant activity values. For validation, rhizomes of *Coptis teeta* were extracted under the optimal microwave and ultrasound-assisted extraction conditions, and are shown in Table 5. Extraction yields were greater for recovery of phenolics and antioxidant activity in the case of ultrasound-assisted extraction, compared to microwave-assisted extraction. Our results contradict the reports on MAE and UAE of *Coptis chinense* Franch., where MAE treatment was found to be superior for the extraction of alkaloids, compared to UAE.[27,28] The authors reported 33.394 and 16.57 g BCE 100 g^{-1} for MAE and UAE, respectively.[27,28] The observed differences may be attributed to variations in the plant genus, specifically *Coptis chinense* Franch. *versus Coptis teeta* Wall., as well as differences in analysis design *i.e.*, total phenolics *versus* total alkaloids. Further study is necessary to elucidate the structural changes occurring in the plant cellular matrix during the application of MAE and/or UAE and streamline experimental and analysis designs for further conclusions.

Berberine content in the phenolic extracts was also quantified using high-performance liquid chromatography under optimized conditions for MAE and UAE, and is shown in Fig. 5a and b. As described in the Introduction section, berberine is known to be the main phytochemical constituent in *Coptis teeta*, and one of our goals was to ascertain if the increase in phenolic content after the MAE and/or UAE treatments tandemly increased berberine content in the extracts. Fig. 5a and b show that berberine was the most abundant phytochemical in both extracts. The standard curve for berberine used in the quantification is shown in Fig. 5c. The highest concentration of berberine was observed in extracts obtained using the microwave-assisted extraction technique (212.18 ppm) followed by the ultrasound-assisted extraction technique (162.96 ppm). Ultrasound treatment led to lower berberine content, although overall, higher phenolic extraction was achieved. Teng and Choi reported higher berberine extraction using UAE treatment; however, longer extraction times were employed (*i.e.*, 60 min sonication time compared to 10 min in this study). However, the lower amount of berberine in the extracts prepared using our UAE method corroborates the lower antioxidant activity of the UAE extract, although the total phenolic content was higher

Table 5 Validation of optimized MAE and UAE methods[a]

	MAE		UAE	
	TPC (mg GAE 100 g^{-1})	Antioxidant activity (%)	TPC (mg GAE 100 g^{-1})	Antioxidant activity (%)
Predicted value	210.04 ± 4.72	98.57 ± 3.20	251.11 ± 2.29	97.82 ± 4.05
Actual value	206.74 ± 3.56	96.02 ± 4.02	248.27 ± 4.15	95.22 ± 3.06
Percentage variation	1.57	2.58	1.13	2.65
Mean difference	3.30	2.55	2.84	2.60

[a] MAE, microwave-assisted extraction; UAE, ultrasound-assisted extraction; GAE, gallic acid equivalent. $n = 5$.

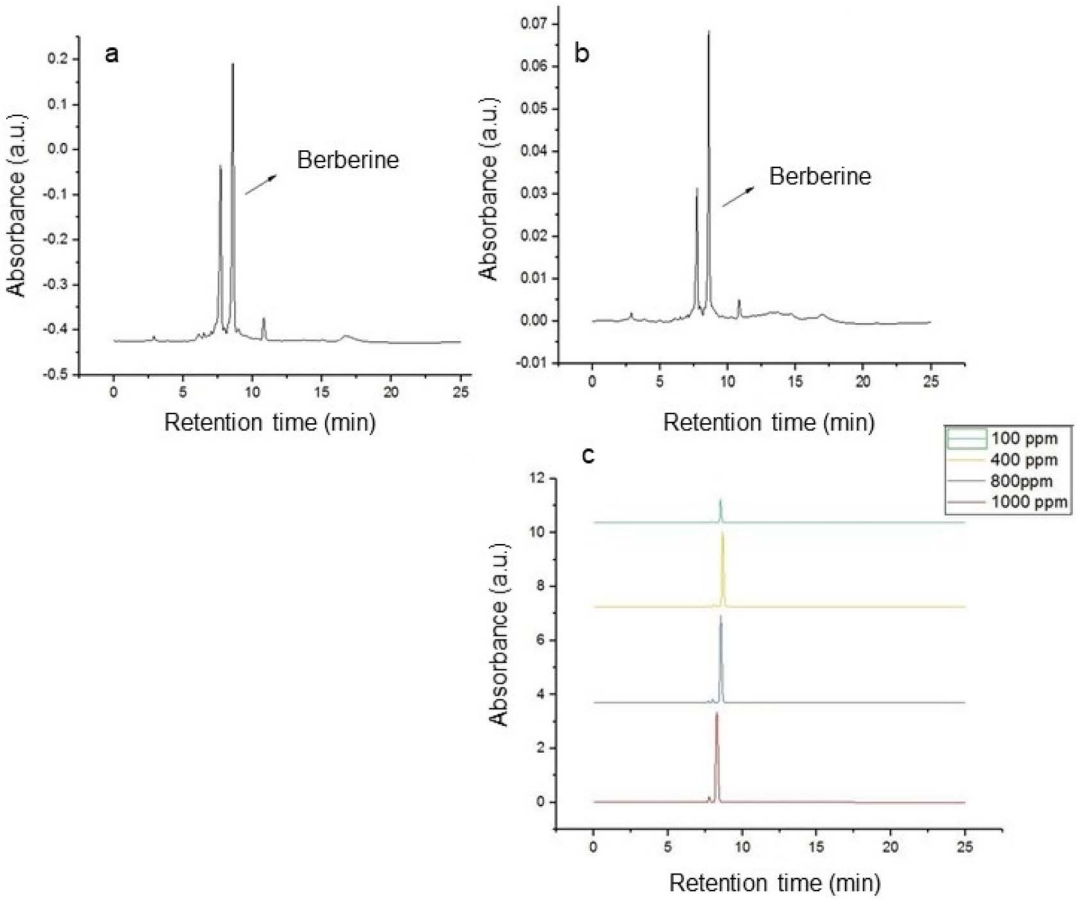

Fig. 5 HPLC chromatogram of the optimized sample using (a) microwave-assisted extraction, (b) ultrasound-assisted extraction, and (c) offset concentration series for standard berberine.

when compared to that of the MAE extract. Further work is necessary to elucidate the effects of MAE and UAE methods on berberine extraction.

4 Conclusion

In conclusion, using microwave (MAE) and ultrasound (UAE) assisted extraction in combination with the Box–Behnken design-based modeling and response surface optimization routine effectively increased the total phenolic yield and antioxidant activity of *Coptis teeta* Wall. extracts. The study statistically optimized the effects of independent variables (solvent concentration, microwave/ultrasound power, extraction time, and solid–liquid ratio) on the resulting responses, *i.e.*, total phenolic content and antioxidant activity, and is an improvement on existing literature. Notably, UAE proved superior in recovering total phenolics, whereas MAE yielded higher berberine content. The findings underscore the importance of selecting an extraction technique based on targeted phytochemicals and end-use requirements. Further work is necessary to elucidate the effects of MAE and UAE methods on berberine extraction, as well as other valuable phytochemicals which are known to be present in the *Coptis* species, such as palmatine, jatrorrhizine, coptisine, columbamine, and epiberberine. The current findings from this study provide a platform for future industrialization of standardized methods and solvent concentration for tailored phytochemical extraction from *Coptis teeta*, as well as guide further studies in other plant materials.

Data availability

Data are available on request from the authors.

Author contributions

Lopamudra Sarma: conceptualization, methodology, validation, data curation, formal analysis, investigation, visualization, writing – original draft; Falguni Patra: formal analysis, investigation, writing – review & editing; Pallab Kumar Borah: formal analysis, visualization, writing – review & editing; Sunil Meena: formal analysis, writing – review & editing; Raj Kumar Duary: conceptualization, methodology, formal analysis, resources, supervision, project administration, funding acquisition, writing – review & editing.

Conflicts of interest

The authors declare no competing interest.

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