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Optimizing Ultrasonic-Assisted and Microwave-Assisted Extraction Processes to Recover Phenolics and Flavonoids from Passion Fruit Peels

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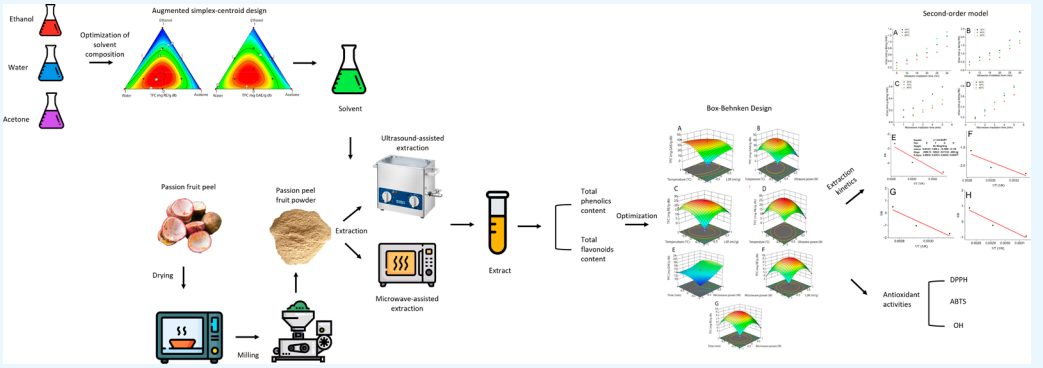

ABSTRACT: This study optimized the ultrasonic-assisted extraction (UAE) and microwave-assisted extraction (MAE) processes to acquire phenolics and flavonoids from passion fruit peels using a mixture of ethanol, acetone, and water. An augmented simplex−centroid design was employed to find the suitable volume ratio among solvent ingredients to attain the highest extraction yield of phenolics and flavonoids. One-factor experiments were conducted to investigate the influence of UAE and MAE parameters on the recovery yield of phenolics and flavonoids before the two processes were optimized using Box−Behnken Design (BBD) models. The optimal UAE conditions for recovering phenolics and flavonoids from passion fruit peel powder (PFP) were 28 mL/g of liquid-to-solid ratio (LSR), 608 W of ultrasonic power, and 63 °C for 20 min to acquire total phenolic content (TPC) and total flavonoid content (TFC) at 39.38 mg of gallic acid equivalents per gram of dried basis (mg GAE/g db) and 25.79 mg of rutin equivalents per gram of dried basis (mg RE/g db), respectively. MAE conditions for attaining phenolics and flavonoids from PFP were 26 mL/g of LSR and 606 W of microwave power for 2 min to recover TPC and TFC at 17.74 mg GAE/g db and 8.11 mg RE/g db, respectively. The second-order kinetic model was employed to determine the UAE and MAE mechanism of TPC and TFC and the thermodynamic parameters of the extraction processes. The antioxidant activities of passion fruit peel extracts at optimal conditions were examined to compare the efficiency of UAE and MAE. This study establishes an effective approach for obtaining phenolics and flavonoids from passion fruit peels.

1. INTRODUCTION

Passion fruit, widely cultivated in tropical and subtropical areas, yields an annual harvest of approximately 50 million tonnes in India.[1] Passion fruit peel comprises 53−60% of the total mass and is the main byproduct of food processing.[1] Passion fruit peels are commonly discarded into landfills, leading to treatment burdens and environmental pollution. However, passion fruit peels hold tremendous potential as a rich source of bioactive components, such as phenolic acids, flavonoids, terpenoids, and pectin.[1] Pectin is composed of poly(galacturonic acid) chains linked by α-1,4 glycosides and partially esterified with methyl alcohol.[2] Terpenoids, considered modified terpenes, are generally structured by isoprenoids.[3] The general structure of phenolic acid is C_6-C_1, while flavonoids possess a $C_6-C_3-C_6$ configuration.[3] These substances exhibit scavenging capacity against free radicals.[2,4] Free radicals damage macromolecules such as proteins, lipids, and DNA, triggering chronic diseases such as cancer and respiratory, cardiovascular, neurodegenerative, and digestive diseases.[5] These natural compounds can scavenge free radicals

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and terminate the oxidative chain reactions, which can protect organs in the human body.[5] For these functions, the development of an appropriate extraction method becomes crucial for recovering these bioactive compounds from passion fruit peels.

Microwave-assisted extraction (MAE) and ultrasonic-assisted extraction (UAE) are rapid processes that have recently attracted more attention in academic and industrial fields.[6] MAE involves microwave absorption by solvents, resulting in the dipole rotation and friction of solvent molecules.[6] This effect converts electromagnetic energy to thermal energy, thereby increasing solvent temperature.[6] The increase in solvent temperature causes water evaporation, increasing pressure within plant cells.[6] High pressure and temperature disrupt plant cell walls, creating numerous microchannels.[6] This phenomenon facilitates the release of bioactive compounds in the plant matrix into solvents, thereby improving the recovery yield of bioactive compounds.[7] The conversion degree of electromagnetic energy into heat relies on the intensity of the electromagnetic field and dielectric properties of solvents.[6] The dielectric constant is described as the ability of a solvent to absorb microwave energy, while the electric loss is the ability of a solvent to release microwave energy as heat.[6] The electric properties depend on the chemical composition and nature of solvents.[6] For instance, bulk water and dissociated salts possess a high dielectric activity, whereas bound water and associated salts show low dielectric activity. Additionally, the use of organic solvent should be obeyed by the Q3C-tables and list the guidance for industry of FDA.[8] UAE improves the extraction efficiency compared to conventional extraction methods by exploiting the acoustic cavitation effect in extraction medium.[9] When rarefaction cycles repel the medium's molecules, creating cavitation bubbles,[9] the explosion of the cavitation bubble triggers shearing force and turbulent effect on the material surface, disrupting the cell wall.[9] Destroyed cell walls allow solvent penetration into the material to enhance the extraction yield of bioactive compounds.[9] UAE is a green technology due to its high extraction yield, less energy, time, and solvent consumption.[9] For these advantages, UAE and MAE have been combined to enhance the recovery of bioactive compounds from plants, such as the[10] the extraction of phenolics from burdock leaves,[11] and the purification of antioxidant phenolics from jackfruit peels.[12] However, previous studies used the aqueous solution of ethanol or acetone, limiting their ability to solubilize various bioactive compounds from the material. Thus, there is a need to design a solvent system with improved solubility for bioactive compounds in passion fruit peels. Additionally, the extraction mechanism of the MAE and UAE processes for obtaining phenolics and flavonoids from passion fruit peels using the designed solvent system remains unexplored. The optimal conditions for simultaneously maximizing total phenolic and flavonoid content from passion fruit peels have not been elucidated.

Therefore, this work aimed to optimize the UAE and MAE of phenolics and flavonoids from passion fruit peels using the solvent mixture (ethanol, water, and acetone) as a representative model. Although the acetone toxicity is high, acetone selection as an ingredient is based on its versatility and low polarity, which can generate a suitable polarity to dissolve phenolics and flavonoids from passion fruit peels. The augmented simplex−centroid design was used to find the optimal volume ratio for attaining the highest phenolic and flavonoid content before one-factor experiments were performed to investigate the effects of UAE and MAE conditions on the extraction efficiency of phenolics and flavonoids. Response surface methodology (RSM) with a Box−Behnken design model was used to establish the optimal phenolic and flavonoid extraction conditions. The extraction mechanism and thermodynamic parameters of UAE and MAE were also investigated.

2. MATERIALS AND METHODS

2.1. Materials. Passion fruit peels were acquired from Nam Viet Company, Di An, Binh Duong, Vietnam, before dehydrating at 45 °C to reach a moisture content of 5%. Dried passion fruit peels were milled to attain passion fruit peel powder (PFP). 2-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS, purity ≥98%), 1,1-diphenyl-2-picrylhydrazyl (DPPH, purity ≥97%), Folin−Ciocalteu reagent (concentration 1.9−2.1 N), gallic acid monohydrate (purity ≥98%), Whatman Filter Paper No. 1 (WHA1001325), 6-hydroxy-2,5,7,8 tetramethyl chroman-2-carboxylic acid (Trolox, purity 98%), acetone (purity ≥99.5%), iron sulfate heptahydrate (purity 97%), hydrogen peroxide (purity 30%), salicylic acid (purity ≥99.0%), sodium carbonate (purity ≥99.5%), potassium acetate (purity ≥99.5%), aluminum chloride hexahydrate (purity 99%), and ethanol (purity ≥99.8%) were purchased from Sigma-Aldrich Chemical Co., Ltd., Singapore.

2.2. Augmented Simplex−Centroid Design. An augmented simplex−centroid design is a powerful tool for determining components' synergetic and antagonistic impact to quantify the optimal solvent composition for attaining the highest phenolic and terpenoid recovery yield. In an augmented simplex−centroid design, three components (water, ethanol, and acetone) with different volume fractions were proposed to investigate the effect of solvent ingredients on the extraction performance of phenolics and flavonoids. The pure solvent was placed 100% at the top, and each solvent in the mixture was examined at six levels of volume fractions with 12 experiments, presented in Table S1. The special cubic model was employed to show the effect of the solvent composition on the extraction performance of phenolic and flavonoids. Two responses, total phenolic content (TPC) and total flavonoid content (TFC), were used to assess the effectiveness of the solvent composition. Analysis of variance was used to evaluate the special cubic model's regression coefficient significance, and the triangle graphics were plotted from fitted models. The special cubic models were verified by conducting experiments with the optimal solvent composition. In the augmented simplex−centroid design, the exact weight of PFP was mixed with 10 mL of the solvent mixture with different ratios of solvent ingredients (presented in Table S1). The mixture of PFP and solvent was subjected to an ultrasonic bath Rama (model RS22L, Rama Viet Nam Joint Stock Company, District 9, Ho Chi Minh City, Vietnam) with a maximal volume of 22 L (40 kHz, maximal ultrasonic power 900 W, total power 1500 W) at 20 mL/g of liquid-to-solid ratio (LSR), 300 W of ultrasonic power, 30 °C, and 10 min. Subsequently, the solid part of the samples was removed using a filter paper before quantifying TPC and TFC.

2.3. One-Factor Experiments. The fixed conditions of the UAE and MAE processes were randomly selected in the surveyed conditional ranges to ensure the randomized experimentation design. The fixed conditions of the UAE

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processes were 20 mL/g of LSR, 300 W of ultrasonic power, 30 °C, and 10 min. The samples were exactly weighed before 10 mL of solvents were added. The extraction of phenolics and flavonoids was conducted in an ultrasonic bath. The UAE of PFP was conducted at different LSRs (10, 20, 30, 40, and 50 mL/g), ultrasonic power (0−900 W, the interval of 150 W), and temperatures (30−70 °C) for different extraction time periods (5−30 min).

Regarding MAE, phenolics and flavonoids were recovered using a microwave oven (model EMM2009W, Electrolux, Stockholm, Sweden). The fixed conditions of the MAE processes were 20 mL/g of LSR, 400 W of microwave power, and 2 min. The MAE of PFP was performed under distinctive LSR (10−50 mL/g), microwave power (0, 240, 400, and 800 W), and extraction time (1, 2, 3, 4, and 5 min). After treatment, samples were separated using a filter paper before the phenolic and flavonoid extracts were measured.

2.4. Experimental Design. A BBD model, which was used to find optimal conditions and parameter interaction, was conducted based on the experimental values of one-factor experiments. Regarding UAE, four factors (LSR, ultrasonic power, temperature, and time) at three levels (−1, 0, +1) with 29 total experiments and three center points were employed to explore the linear and interactive effects on the extraction yield of phenolics and flavonoids. Regarding MAE, three factors at three levels of LSR, microwave power, and time with 17 total experiments and three center points were applied to find the factorial interaction. The dependent responses for optimizing the UAE and MAE processes were TPC and TFC. Analysis of variance (ANOVA) analyzed the significance of process parameters.

2.5. Extraction Kinetics. The liquid/solid extraction operation can be taken the reverse of an adsorption process into consideration. First-order and second-order kinetic models are widely employed to investigate the adsorption rate in the extraction operation. The first-order model is illustrated to be effective at the initial phase of the adsorption process, while the second-order model is employed to assess the experimental velocity of the extraction operation.[13] In this research, the kinetic parameters of the MAE and UAE processes were discovered by the second-order model. Various studies employed this model to comprehend the extraction kinetics of flavonoids from Terminalia by MAE and carotenoids from pomegranate by UAE.[14,15] The second-order (n = 2) model can be expressed as

$$r_e = \frac{dC_t}{t} = k(C_{ec} - C_t)^2 \quad (1)$$

where k is the constant of the second-order extraction rate (g/mg min), r_e is the rate of extraction, C_{ec} is the saturation concentration of phenolics or flavonoids in the extract (the capacity of extraction, mg/mL), and C_t is TPC or TFC (mg/g) in the extract at a given time t (min).

Integrating eq 1, using the boundary conditions C_t = 0 to C_t = C_t, t = 0 to t, the order of reaction (n), and the constant of the second-order extraction rate (k) considered as variables, the second-order (n = 2) extraction kinetic model can be shown as in eq 2:

$$C_t = \frac{C_{ec}^2 kt}{1 + C_{ec} kt} \quad (2)$$

The second-order kinetic model (eq 2) was rearranged in a linearized form to establish eq 3 that corresponded to the linear regression model $y = mt + c$, in which $m = 1/C_{ec}$ and $c = 1/C_{ec}^2 k$, enabling the quantification of k and C_{ec}. The initial extraction rate, h (mg/g min) when t is equal to 0, can be determined by eq 4

$$\frac{t}{C_t} = \frac{t}{C_{ec}} + \frac{1}{C_{ec}^2 k} \quad (3)$$

$$h = C_{ec}^2 k \quad (4)$$

The second-order extraction rate constant is extrapolated by constructing t/C_t against t using eq 3. The constant of the second-order extraction rate is calculated by building t/C_a against t using eq 3. The degree of activation energy (E_a, kJ/mol) and Arrhenius constant (A_e, g/mg min) were calculated using eq 5

$$\ln k = \ln A_e - \frac{E_a}{RT} \quad (5)$$

According to eq 5, the enthalpy, entropy, and Gibbs free energies (ΔH, ΔS, and ΔG, respectively) can be attained from eqs 6−8

$$\Delta G = -RT \ln k \quad (6)$$

$$\Delta H = E_a - RT \quad (7)$$

$$\Delta G = \Delta H - T\Delta S \quad (8)$$

2.6. Phenolic and Flavonoid Determination. The total phenolic content of diluted samples was quantified using the method of Pattrathip Rodsamran.[16] 0.25 mL of each extract was dispersed into 4 mL of distilled water, and then 0.25 mL of 10% Folin−Ciocalteu was mixed and allowed to stand still for 5 min. Next, 0.5 mL of sodium carbonate 7.5% was added, and the tested extract samples were placed in dark spots for 1 h at room temperature. A UV−vis spectrophotometer (Hach DR/2010, LabWrech, Midland, Ontario, Canada) measured the absorbance of tested extract samples at 765 nm. The total phenolic content of tested extract samples was determined through the gallic acid standard curve (0−150 mg/L) and reported as milligrams of gallic acid equivalents per gram of dried basis (mg GAE/g db).

TFC was determined using the Meilin Xu method with a slight modification.[17] The sample (0.5 mL) was mixed with 1 mL of ethanolic solution (96%) before 0.1 mL of potassium acetate solution (1 M) and aluminum trichloride solution (10%) were added. Then, 4 mL of deionized water was dispersed, and the mixture was put in a dark place for 30 min. The sample absorbance was read at 415 nm using the UV−vis spectrophotometer. Rutin was used as a standard, and the results were reported as milligrams of rutin equivalents per gram of dried materials (mg RE/g db).

2.7. Antioxidant Activity Determination. DPPH was quantified using the Lingfeng Wu method with a slight modification.[18] The samples (0.5 mL) were mixed with 3.5 mL of an absolute ethanol solution of DPPH (100 μM) and placed in the dark for 30 min at 30 °C. The absorbance of each sample was measured at 515 nm using a UV−vis spectrophotometer. ABTS was determined using the described method by Pattrathip Rodsamran.[16] An equal volume of ABTS solution (7.4 mM) and potassium persulfate (2.45 mM) was allowed to react for 16 h at ambient temperature in the dark to produce $ABTS^+$. The solution of $ABTS^+$ was acquired by

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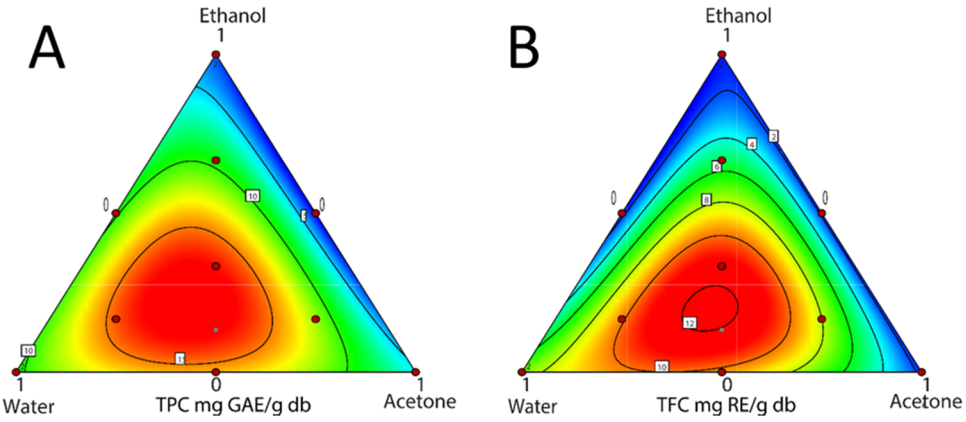

Figure 1. Effect of the solvent combination on the recovery of phenolics and flavonoids; (A) TPC and (B) TFC.

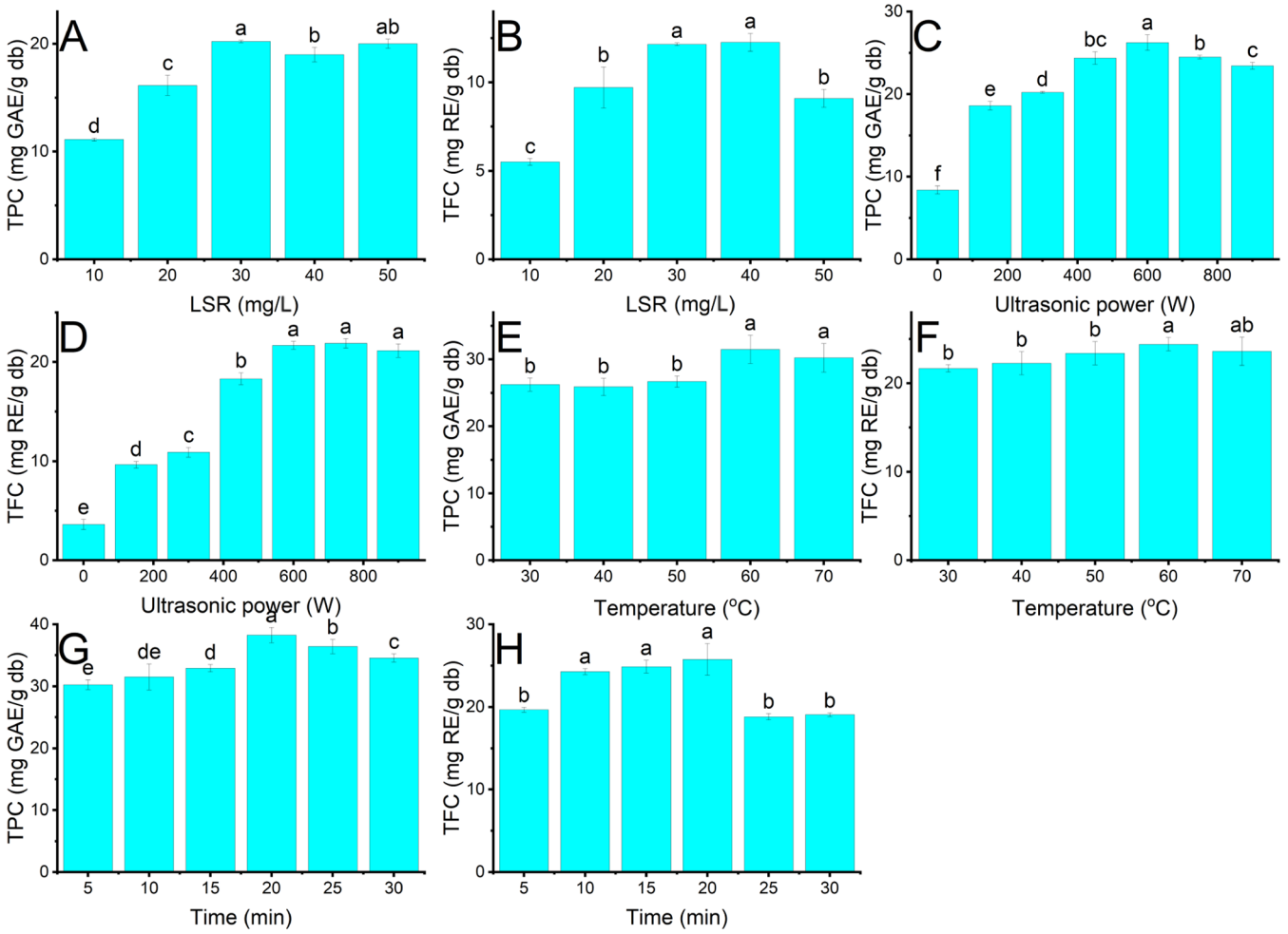

Figure 2. Effects of UAE parameters on TPC and TFC. (A, B) Influence of LSR on TPC and TFC; (C, D) influence of ultrasonic power on TPC and TFC; (E, F) influence of temperature on TPC and TFC; and (G, H) influence of time on TPC and TFC. The same characters expressed insignificantly statistical differences.

diluting it with distilled water to reach an absorbance of 1.0 at 734 nm. Then 0.1 mL of samples was mixed with 3.9 mL of $ABTS^{+}$, then incubated in the dark for 20 min, and the absorbance of tested samples was read at 734 nm. Hydroxyl radical (OH) was evaluated using the Lingfeng Wu method.[18] DPPH, ABTS, and OH were reported as micromoles of Trolox equivalent per gram of dried materials (μM TE/g db).

2.8. Statistical Analysis. All experiments were carried out three times, and the results were depicted as the mean ± standard deviation. The data were analyzed using ANOVA with a significant level of 5% ($p < 0.05$), and multiple-range tests were conducted using Minitab 19 (Minitab, Inc, Pennsylvania). Graphs were generated using Origin Pro (Origin Lab, Northampton, Massachusetts). The optimization study using the Box−Behnken Design (BBD) model was

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performed using the Design-Expert v.13 software (Stat-Ease Inc., Minneapolis, Minnesota 55413).

3. RESULTS AND DISCUSSION

3.1. Optimization of Solvent Component Ratios. The augmented simplex−centroid design was employed to determine the optimal solvent composition for achieving the highest extraction efficiency of phenolics and flavonoids from PFP. Ethanol, acetone, and water were combined in different volume ratios, and statistical analysis with a significant level of 5% (α = 5%) was conducted. The ternary diagrams of solvent compositions are presented in Figure 1, while experimental results and their statistical analysis are detailed in Tables S1 and S2. The special cubic models for TPC and TFC exhibited high determination coefficients (R^2) of 0.9952 and 0.9945, respectively, indicating good agreement between predicted and experimental results. The high *F*-values of models (195 and 151 for TPC and TFC, respectively) showed the significance of special cubic models. The analysis of the polynomial regression models revealed that water had the most significant effect on the extraction efficiency of phenolics and flavonoids, followed by acetone and ethanol for phenolics and ethanol and acetone for flavonoids. Pure ethanol and acetone were found to negatively affect the extraction efficiency of phenolics and flavonoids due to protein denaturation and pectin precipitation, hindering solvent diffusion into the plant matrix.[19,20] This trend was in agreement with our previous study, in which we used acetone to extract phenolics and flavonoids from watermelon rinds.[19] Water in the solvent mixture can improve PFP hydration and contact between solvents and materials, increasing the extraction yield of phenolics and flavonoids. Meanwhile, ethanol and acetone can break the linkages between target analytes and the plant matrix.[20] Additionally, combining solvents with distinctive polarities is proposed to effectively recover phytochemicals, probably due to improving the solubility of bioactive compounds in the employed solvent mixture.[17] Bezerra et al. presented the influence of solvent systems, including water, ethanol, methanol, and acetone, on phytochemicals' extraction efficiency from *Eugenia uniflora* Linn. The study reported that binary and quaternary solvent systems showed higher extraction yield than one solvent.[21] Furthermore, the enhanced extraction yield acquired by the solvent mixture can be ascribed to the decreased polyphenol oxidase (PPO) activity in the PFP extracts. This effect can result from inactivating PPO, which is the primary catalyst responsible for phenolic oxidation processes.[22] Therefore, the optimal solvent volume ratio of ethanol, water, and acetone for the highest recovery of phenolics and flavonoids from PFP was 0.29:0.34:0.37, respectively, to obtain TPC and TFC at 16.975 mg GAE/g db and 11.834 mg RE/g db, respectively. The experiments were conducted at an optimal ratio to validate the reliability of special cubic models. The experimental data of TPC and TFC at the optimal ratio were 16.15 ± 0.94 mg GAE/g db and 10.21 ± 1.15 mg RE/g db, respectively, which are close to the predicted results. It can be concluded that the volume ratio of 0.29:0.34:0.37, ethanol, water, and acetone, respectively, was suitable for attaining the highest TPC and TFC from PFP. This optimal ratio was used for all experiments in the study.

3.2. One-Factor Experiment. *3.2.1. Effects of Ultrasonic-Assisted Extraction Conditions.* The UAE conditions significantly affect the extraction yield of phenolics and flavonoids from PFP, as depicted in Figure 2A−H. Figure 2A,B demonstrates the impact of varying LSR (10−50 mL/g) on the extraction yield of phenolics and flavonoids under fixed conditions (300 W ultrasonic power, 30 °C, and 10 min). There was an increase in the extraction yield of phenolics and flavonoids when LSR changed from 10 to 30 mL/g. It can be attributed to the enhanced cavitation effect, resulting from a decrease in the viscosity of the extractant.[9] The intensified cavitation effect can lead to enhanced sonoporation and fragmentation on the material surface, facilitating solvent diffusivity into the plant matrix, thereby elevating the extraction yield of phenolics and flavonoids from PFP. However, continuous increase of LSR to 50 mL/g caused a stabilization in TPC while decreasing TFC. The excessive LSR can impose more intensity of a cavitation effect on the extraction medium, causing flavonoid degradation and decreasing its recovery.[9] Moorthy et al. showed a rise in the extraction yield of pectin from pomegranate peel as LSR increased from 10 to 15 mL/g, and the continuous growth in LSR to 20 mL/g decreased the recovery yield of pectin.[23] Therefore, the optimal LSR was 30 mL/g to extract phenolics and flavonoids from PFP.

The effect of ultrasonic power on the extractability of phenolics and flavonoids from PFP was investigated over a range of 0−900 W, maintaining a constant LSR of 30 mL/g and 30 °C for 10 min. The results are illustrated in Figure 2C,D. TPC and TFC exhibited an increase of 3.1 and 6.0 times, respectively, as the ultrasonic power varied from 0 to 600 W. The increase in ultrasonic power can increase the size and intensity of collapsing cavitation bubbles, provoking more sonoporation and fragmentation on plant cell walls and tissues. This phenomenon can increase mass transfer and solvent penetration into plant tissues, accelerating the recovery of TPC and TFC.[9] However, as the ultrasonic power continued to increase to 900 W, a decrease in the extraction yield of phenolics was observed, while TFC remained unchanged. The excessive ultrasonic power can modify the structure of phenolics during the extraction process, decreasing its recovery.[9] This result was similar to that reported by Al-Dhabi et al., who studied the effect of ultrasonic power on the extraction yield of phenolics in waste spent coffee ground.[24] Therefore, ultrasonic power at 600 W was appropriate for extracting phenolics and flavonoids from PFP.

Figure 2E,F shows the impact of temperature (30−70 °C) on the recovery of phenolics and flavonoids from PFP at LSR of 30 mL/g, ultrasonic power of 600 W, and 10 min. TPC and TFC increased by 1.2 and 1.1 times, respectively, when the temperature was increased to 60 °C. The increase in TPC and TFC can be attributed to the favorable effect of high temperature on the solubility of the target analytes in the solvent mixture and an increase in desorption capacity.[25] This result was similar to that reported by Al-Dhabi et al., who investigated the recovery of phenolics from the spent coffee ground. In that study, the extraction efficiency of phenolics improved with the increase of temperature from 30 to 45 °C.[24] However, TPC and TFC remained stable as the temperature of the extraction medium increased to 70 °C. Therefore, 70 °C was suitable for phenolic and flavonoid extraction from PFP.

The impact of time on the extraction efficiency of phenolics and flavonoids was investigated under fixed conditions (LSR of 30 mL/g, ultrasonic power of 600 W, and 70 °C). As presented in Figure 2G,H, the extraction yield of phenolics and flavonoids increased to 20 min, while the continuous extension of extraction time reduced TPC and TFC. This observed

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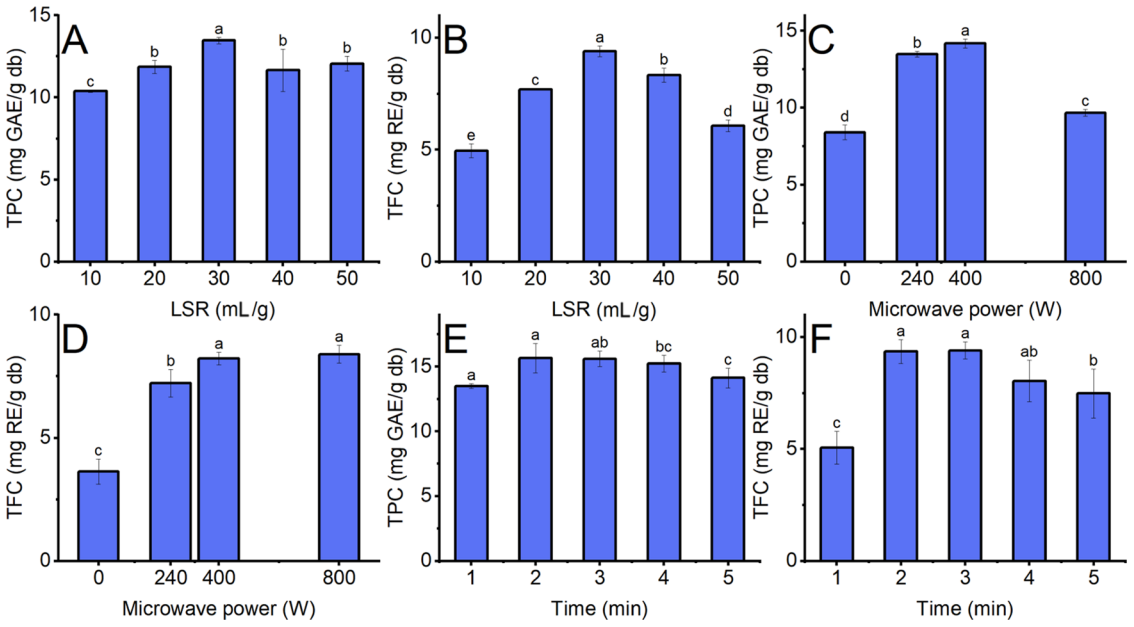

Figure 3. Effect of MAE parameters on TPC and TFC. (A, B) Influence of LSR on TPC and TFC at 240 W of microwave power for 2 min; (C, D) influence of microwave power on TPC and TFC at 30 mL/g of LSR for 2 min; and (E, F) influence of time on TPC and TFC at 400 W of microwave power and 30 mL/g of LSR. The same characters expressed insignificantly statistical differences.

pattern can be attributed to the effects of acoustic cavitation on the plant cell surface. Adequate ultrasound exposure promotes sonoporation and erosion, facilitating the diffusion of phenolics and flavonoids into the extractant and increasing their contact with the solvent, thereby improving their extraction yield.[25] However, the prolonged extraction time can generate inter-bubble collisions and structural damage of phenolics and flavonoids, thereby decreasing their extraction yield.[25] This trend has been presented by Raza et al., who recovered bioactive polysaccharides from the stem of *Trapa quadrispinosa*.[26] Therefore, 20 min of extraction time was appropriate for recovering phenolics and flavonoids from PFP.

3.2.2. Effects of Microwave-Assisted Extraction Conditions. Water, ethanol, and acetone are commonly employed as solvents in the MAE process due to their low viscosity, good microwave absorption capacity, and solubility of phenolics and flavonoids. Among the three solvents, ethanol and acetone exhibit the higher solubility of phenolics and flavonoids than water because they have similar polarity to these compounds. However, the high concentrations of acetone and ethanol without water can precipitate protein and polysaccharides, impairing the mass transfer and decreasing the recovery yield of phenolics and flavonoids.[19] The dielectric constants of water, ethanol, and acetone are 78.3, 24.3, and 20.7, respectively.[6] The high dielectric constant shows that these solvents can absorb microwave irradiation.[6] The dissipator factor reflects the conversion degree of microwave energy to thermal energy, in which the large value of the dissipator factor shows the high conversion capacity. The dissipator factor values of water, ethanol, and acetone are 0.15, 0.25, and 0.55, respectively.[6] These values suggest that acetone and ethanol have a higher capacity for converting microwave energy into thermal energy than water. The effect of MAE parameters on the extraction yield of phenolics and flavonoids from PFP was examined, and the data are shown in Figure 3A–F. As presented in Figure 3A,B, TPC and TFC increased as LSR increased to 30 mL/g. When a greater LSR is employed, the driving force resulting from the phenolic and flavonoid concentration difference between solvents and materials during mass transfer becomes larger. When the figure for solvent compared to materials is not adequate to achieve sufficient transfer, various equilibrium concentrations can exist, preventing mass transfer.[27] However, TPC and TFC decreased when LSR experienced a rise from 30 to 50 mL/g. A drop in TPC and TFC can be accounted for the deterioration of phenolics and flavonoids caused by high temperatures resulting from the excessive microwave power absorption of solvents.[28] These results achieved a consensus with Khadija Doldolova et al., who optimized the MAE of curcumin from turmeric using NADES.[29] Therefore, the ratio of 30:1 was suitable for the MAE extraction of phenolics and flavonoids from PFP (Figure 3).

The effect of microwave power on the extraction yield of phenolics and flavonoids from PFP was investigated from 0 to 800 W. As presented in Figure 3C,D, the extraction yield of phenolics and flavonoids initially increased with a rise in microwave power to 400 W. It can be accounted for the enhanced dipolar rotation, increasing the solvent temperature. This phenomenon can improve solute solubility in the extraction medium while decreasing surface tension and viscosity. These effects can promote the diffusivity of NADES into the plant matrix, leading to an increase in the extraction yield.[13] However, the reverse trend was observed for phenolics when microwave power was increased to 800 W. The excessive temperature generated by high microwave power can degrade phenolics, causing a decrease in the extraction yield.[13] Several studies showed that increased extraction yield positively correlated with increased extraction temperature. However, structural degradation can occur in phenolics and flavonoids at high temperatures. This finding is in agreement with Bener et al., who employed MAE to recover antioxidant components from Turkish hazelnut (*Corylus avellana* L.).[30] Therefore, the suitable microwave power for extracting phenolics and flavonoids from PFP was 400 W.

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Table 1. Experimental Data of the UAE and MAE Processes

UAE							MAE					
no.	LSR	ultrasonic power	temperature	time	TPC	TFC	no.	LSR	microwave power	time	TPC	TFC
1	0	1	1	0	27.48 ± 0.19	19.08 ± 0.82	1	0	0	0	15.66 ± 0.33	9.35 ± 0.19
2	0	1	0	1	16.69 ± 0.60	9.19 ± 0.11	2	0	0	0	15.66 ± 0.33	9.35 ± 0.19
3	0	1	−1	0	9.71 ± 0.23	6.04 ± 0.06	3	−1	0	−1	16.59 ± 0.19	4.03 ± 0.47
4	0	1	0	−1	17.06 ± 0.21	8.97 ± 0.33	4	0	−1	−1	12.17 ± 1.48	4.17 ± 0.38
5	0	0	1	−1	19.49 ± 0.62	9.21 ± 0.50	5	−1	−1	0	16.86 ± 0.76	4.50 ± 0.29
6	0	0	−1	1	13.55 ± 0.09	10.76 ± 0.14	6	0	0	0	15.66 ± 0.33	9.35 ± 0.19
7	0	0	1	1	21.10 ± 0.57	9.49 ± 0.49	7	0	0	0	15.66 ± 0.33	9.35 ± 0.19
8	0	0	−1	−1	13.16 ± 0.16	10.06 ± 0.22	8	0	1	1	16.78 ± 0.32	3.73 ± 0.51
9	0	−1	−1	0	14.64 ± 0.23	12.75 ± 0.25	9	0	1	−1	17.94 ± 1.12	4.06 ± 0.38
10	0	−1	0	−1	17.65 ± 0.23	10.89 ± 0.96	10	1	1	0	21.21 ± 1.78	3.49 ± 0.25
11	0	−1	0	1	17.77 ± 0.09	11.69 ± 0.51	11	1	0	1	16.15 ± 0.89	4.19 ± 0.11
12	0	−1	1	0	18.92 ± 2.07	11.35 ± 0.33	12	−1	1	0	22.44 ± 1.87	3.73 ± 0.49
13	−1	0	0	−1	21.29 ± 0.61	9.62 ± 0.24	13	0	−1	1	14.28 ± 1.08	4.97 ± 0.37
14	−1	0	0	1	23.54 ± 0.57	9.87 ± 0.57	14	−1	0	1	17.70 ± 0.23	4.00 ± 0.60
15	−1	0	−1	0	11.66 ± 0.32	4.34 ± 0.44	15	1	−1	0	16.09 ± 0.16	4.71 ± 0.68
16	−1	0	1	0	41.39 ± 3.60	17.77 ± 0.21	16	0	0	0	15.66 ± 0.33	9.35 ± 0.19
17	−1	−1	0	0	23.82 ± 0.69	9.16 ± 0.16	17	1	0	−1	15.78 ± 0.16	3.88 ± 0.21
18	−1	1	0	0	22.65 ± 1.08	8.82 ± 0.33						
19	1	0	0	−1	24.62 ± 0.98	8.94 ± 0.33						
20	1	0	−1	0	20.01 ± 0.07	8.39 ± 0.12						
21	1	0	1	0	25.91 ± 0.86	8.59 ± 0.19						
22	1	0	0	1	22.86 ± 0.19	8.05 ± 0.24						
23	1	−1	0	0	23.94 ± 0.21	8.85 ± 0.19						
24	1	1	0	0	26.35 ± 0.89	9.65 ± 0.23						
25	0	0	0	0	38.27 ± 2.11	25.76 ± 1.90						
26	0	0	0	0	38.27 ± 2.11	25.76 ± 1.90						
27	0	0	0	0	38.27 ± 2.11	25.76 ± 1.90						
28	0	0	0	0	38.27 ± 2.11	25.76 ± 1.90						
29	0	0	0	0	38.27 ± 2.11	25.76 ± 1.90						

The influence of microwave irradiation time on the acquired TPC and TFC from PFP was investigated from 1 to 5 min, and the results are illustrated in Figure 3E,F. TPC and TFC increased when microwave irradiation time changed from 1 to 2 min. The enhancement in extraction yield can be attributed to the efficient absorption of microwave power by the solvent during the extraction time, resulting in the increase of temperature and pressure. This effect promotes the degradation of cell walls and facilitates the solubilization of phenolics and flavonoids, leading to an enhancement in the mass transfer rate and an increase in extraction yield.[31] On the other hand, TPC and TFC showed a decrease with a further increase in extraction time. Owing to their thermally sensitive attribute, phenolics and flavonoids can deteriorate with prolonged microwave irradiation.[16] This result is in agreement with Bener et al.[30] Microwave irradiation time of 2 min was appropriate for acquiring phenolics and flavonoids from PFP.

3.3. Optimization of Assisted Extraction Processes.

3.3.1. Optimization of the Ultrasonic-Assisted Extraction Process. Twenty-nine experiments were carried out to find the regression coefficients, and experimental results are presented in Table 1. Design-Expert v13 was employed to conduct statistical analysis on the experimental data; the statistical analysis results are shown in Table 2. The polynomial regression models showed the correlation between dependent responses and factors in UAE, which are presented in eqs 9 and 10

Table 2. Regression Coefficient of BBD Models[a]

UAE			MAE		
regression coefficients	TPC	TFC	regression coefficients	TPC	TFC
A_0	38.27*	25.76*	A_0	15.66*	9.35*
A_1	−0.05	−0.59	A_1	−0.54*	−0.001
A_2	0.26	−0.24	A_2	2.37*	−0.42*
A_3	5.96*	1.93*	A_3	0.30*	0.09*
A_4	0.19	0.11	A_{12}	−0.11	−0.11*
A_{12}	0.90	0.29	A_{13}	−0.19	0.08
A_{13}	−5.96*	−3.31*	A_{23}	−0.82*	−0.28*
A_{14}	−1.00	−0.29	A_{11}	2.38*	−2.73*
A_{23}	3.37*	3.61*	A_{22}	1.11*	−2.52*
A_{24}	−0.12	−0.15	A_{33}	−1.48*	−2.60*
A_{34}	0.30	−0.10	F values	87	1362
A_{11}	−3.76*	−8.94*	R^2	0.991	0.999
A_{22}	−10.19*	−7.14*	adjusted R^2	0.980	0.999
A_{33}	−10.14*	−6.96*	predicted R^2	0.858	0.991
A_{44}	−11.17*	−8.35*			
F values	26	23			
R^2	0.963	0.958			
adjusted R^2	0.926	0.917			
predicted R^2	0.786	0.760			

[a]* indicates statistically significant differences ($p < 0.05$).

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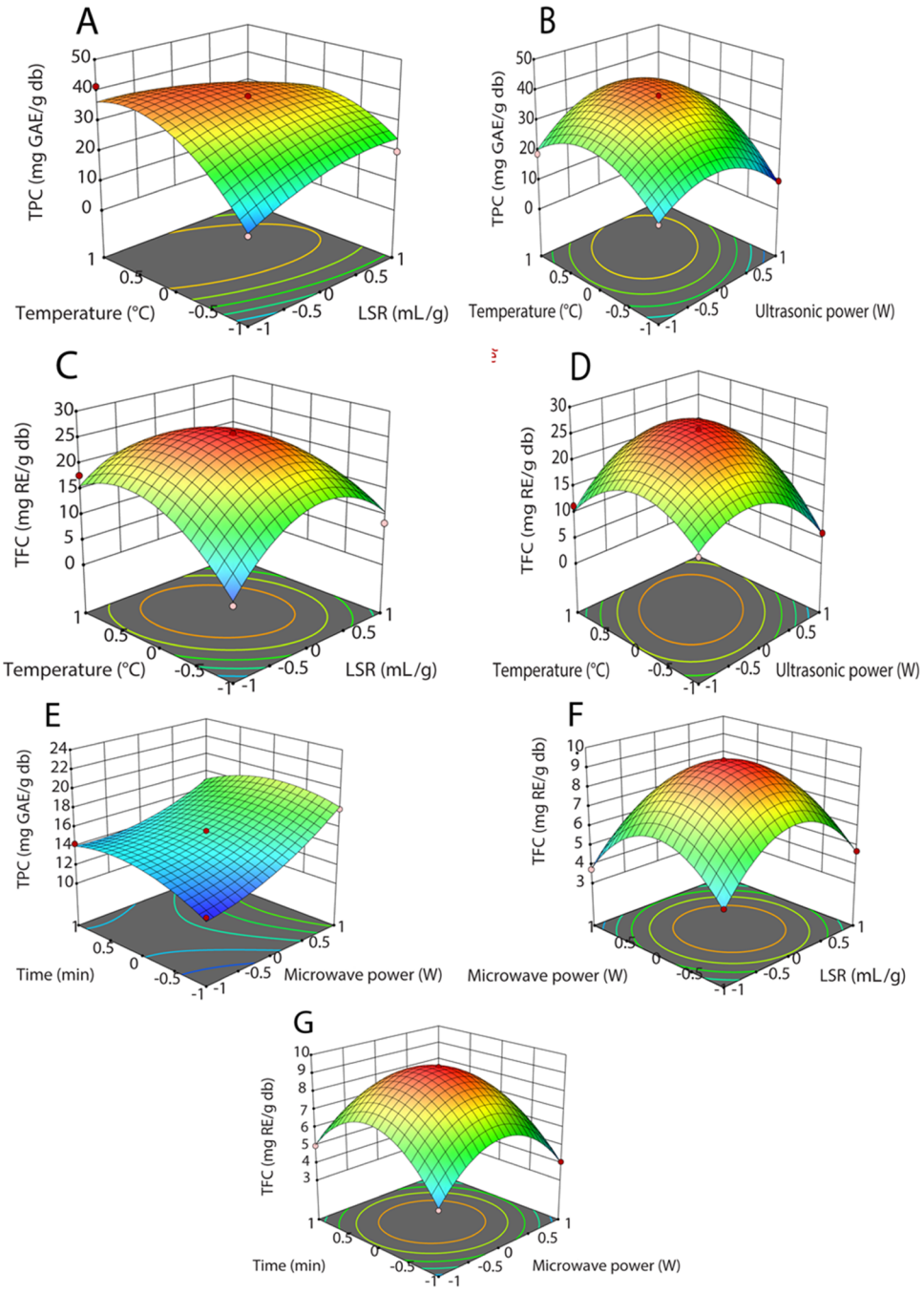

Figure 4. Three-dimensional (3D) response surface graphics illustrate the interaction among UAE and MAE parameters: the interactive effect of UAE conditions (A–D) and the interactive effect of MAE conditions (E–G).

$$Y_{\mathrm{UAE-TPC}} = 38.27 + 5.96x_3 - 5.96x_1x_3 + 3.37x_2x_3 - 3.76{x_1}^2 - 10.19{x_2}^2 - 10.14{x_3}^2 - 11.17{x_4}^2 \quad (9)$$

$$Y_{\mathrm{UAE-TFC}} = 25.76 + 1.93x_3 - 3.31x_1x_3 + 3.61x_2x_3 - 8.94{x_1}^2 - 7.14{x_2}^2 - 6.96{x_3}^2 - 8.35{x_4}^2 \quad (10)$$

The F values of TPC and TFC were 25.92 and 23.00, respectively, which proposed that the polynomial regression models were significant ($p < 0.05$). The large values of coefficient determinations and adjusted coefficient determinations (R^2 and adjusted $R^2 \geq 0.9$) revealed the well fit of the models. Table 2 also shows that x_3, x_2x_3, ${x_1}^2$, ${x_2}^2{x_3}^2$, and ${x_4}^2$ significantly affected TPC and TFC, while others were insignificant. The polynomial regression models also indicated that temperature had a major influence on the recovery of phenolics and flavonoids.

The significant interactive effects of two factors on TPC and TFC in Table 2 were employed to draw 3D response surface graphics (Figure 4A–G). 3D response surface plots were constructed by fixing one factor at the middle level, while the rest two factors were changed. Regarding the UAE process (Figure 4A–D), LSR and temperature negatively affected TPC and TFC, while a similar trend was true regarding ultrasonic power and temperature. As LSR and temperature increased,

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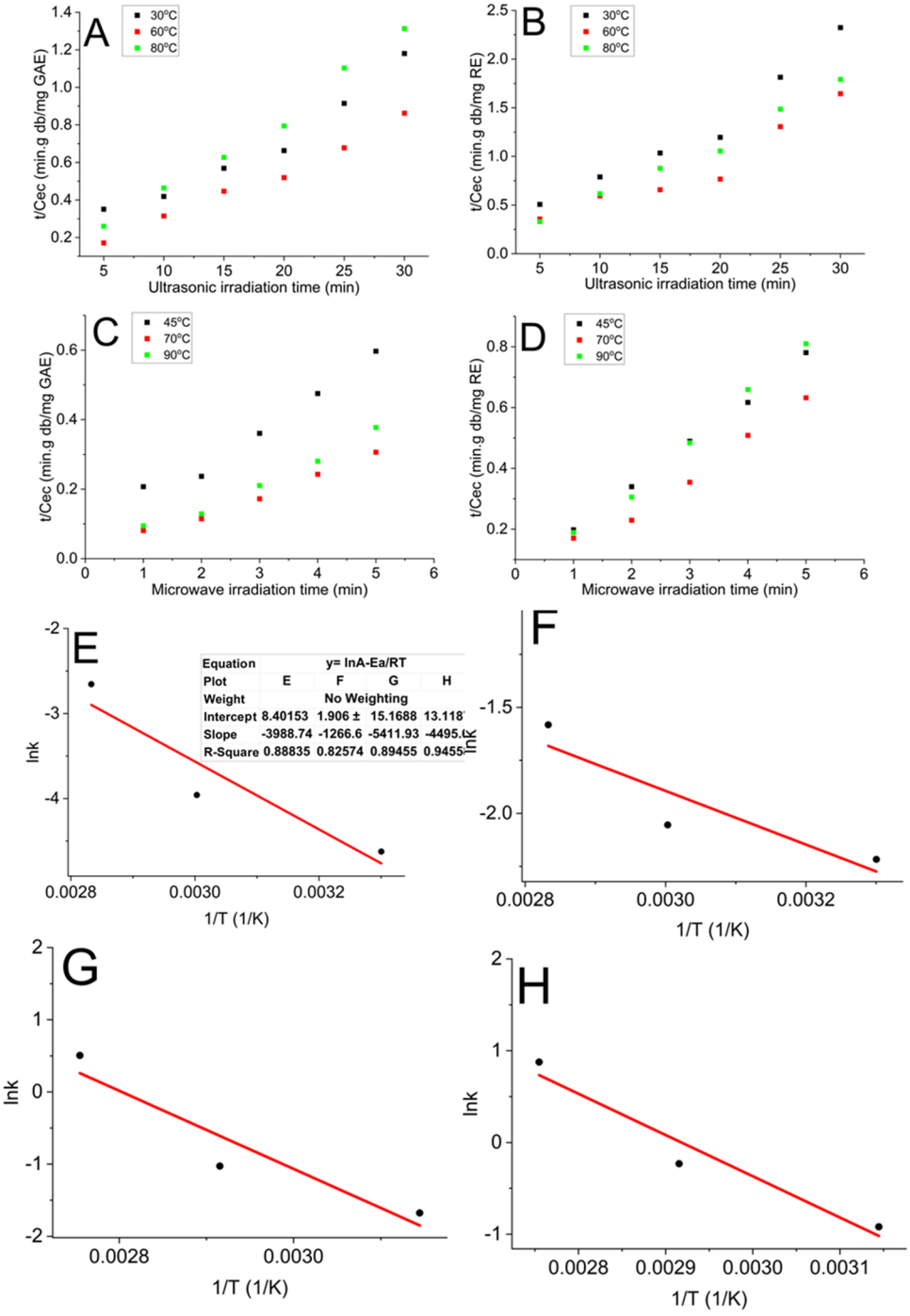

Figure 5. Second-order kinetic models (A–D) of phenolic and flavonoid recovery from PFP with the solvent mixture at different temperatures: UAE of (A) phenolics and (B) flavonoids; MAE of (C) phenolics and (D) flavonoids. Arrhenius graphics acquired from second-order kinetic models: Arrhenius plots for UAE of (E) phenolics and (F) flavonoids; Arrhenius plots for MAE of (G) phenolics and (H) flavonoids.

TPC and TPC peaked at 39.38 mg GAE/g db and 25.76 mg RE/gdb, followed by remaining stable. The high temperature and LSR can reduce viscosity and enhance the molecular interaction, sample wettability, solvent diffusion, and permeation capacity. The synergization of phenomena can improve the mass transfer rate, increasing the extraction yield of phenolics and flavonoids.[32] These findings reached a consensus with Liu et al., who simultaneously recovered organic acids and flavonoids from *Hibiscus manihot* L. flower using NADES-based UAE.[32] When ultrasonic power and temperature increased, TPC and TFC increased to the highest point, followed by a slight decrease. It can be ascribed to the combined effect of ultrasonic power and temperature. High ultrasonic power can disrupt plant cell walls, creating numerous small pores on the PFP surface. Meanwhile, high temperatures can increase the solubility and permeability of solvents. This combination can enhance the extraction yield of phenolics and flavonoids. This trend agreed with Zheng et al., who extracted phenolics from foxtail millet bran using NADES-based UAE.[33] Based on the polynomial regression models, the optimized parameters of the UAE process for extracting phenolics and flavonoids from PFP were 28 mL/g of LSR, 608

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Table 3. Kinetic Parameters Acquired from the Second-Order Extraction Models

methods−substances	temperature (°C)	C_e (mg/g)	h (mg/g min)	k (g/mg min)	R^2	E_a (kJ/mol)	ln A_e	R^2	ΔH (kJ/mol)	ΔG (kJ/mol)	ΔS (kJ/mol)
UAE−phenolics	30	30.5	9.1	0.010	0.948	33.1	8.40	0.888	30.58	11.64	0.06
	60	37.9	27.4	0.019	0.987				30.33	10.95	0.06
	80	23.8	39.8	0.070	0.989				30.17	7.79	0.06
UAE−flavonoids	30	14.2	22.0	0.109	0.951	10.5	1.96	0.826	7.98	5.58	0.01
	60	20.2	52.1	0.128	0.910				7.73	5.69	0.01
	80	17.3	61.7	0.206	0.989				7.57	4.64	0.01
MAE−phenolics	45	8.8	14.3	0.187	0.971	45.0	15.17	0.895	42.36	4.43	0.12
	70	17.2	106.4	0.358	0.982				42.15	2.93	0.11
	90	13.9	322.6	1.658	0.979				41.98	−1.53	0.12
MAE−flavonoids	45	6.9	19.2	0.399	0.999	37.4	13.12	0.946	34.76	2.43	0.10
	70	8.3	54.9	0.794	0.990				34.55	0.66	0.10
	90	6.3	94.3	2.403	0.996				34.38	−2.64	0.10

W of ultrasonic power, and 63 °C for 20 min to acquire TPC and TFC at 39.38 mg GAE/g db and 25.79 mg RE/g db, respectively.

3.3.2. Optimization of the Microwave-Assisted Extraction Process. Seventeen experiments were conducted to explore the regression coefficients, and the experimental values are shown in Table 1. The polynomial regression models expressed the relationship between dependent responses and factors in MAE, as illustrated in eqs 11 and 12

$$Y_{MAE-TPC} = 15.66 - 0.54x_1 + 2.37x_2 + 0.30x_3 - 0.82x_2x_3 + 2.38x_1^2 - 1.11x_2^2 - 1.48x_3^2 \quad (11)$$

$$Y_{MAE-TFC} = 9.35 - 0.42x_2 + 0.09x_3 - 0.11x_1x_2 - 0.28x_2x_3 - 2.73x_1^2 - 2.52x_2^2 - 2.60x_3^2 \quad (12)$$

The F values of TPC and TFC were 86 and 1361, respectively, which revealed that the polynomial regression was significant ($p < 0.05$). The R^2 and adjusted R^2 of the two dependent responses were higher than 0.97, indicating that the polynomial regression models were sufficient to describe the correlation between factors and dependent responses. The regression models demonstrated that x_1, x_2, x_3, x_2x_3, x_1^2, x_2^2, and x_3^2 considerably influenced TPC, while x_2, x_3, x_1x_2, x_2x_3, x_1^2, x_2^2, and x_3^2 significantly impacted on TFC. 3D response surface plots were drawn to imagine the interaction between dependent responses and factors (Figure 4E−G). Microwave power and time negatively impacted TPC and TFC, while LSR and microwave power also negatively influenced TFC.

As microwave power and extraction time increased, TPC reached the highest point. Increasing microwave power can generate high temperature and vapor pressure in the extraction medium, leading to the effective destruction of plant cell walls and enhancement in the dissolution capacity of phenolics in the solvent mixture. Combining these effects with the high difference in gradient concentration between the plant matrix and the extractant can contribute to the improvement in the extraction yield of phenolics and flavonoids.[29] As microwave power, LSR, and time increased, TFC increased to the highest point, followed by a fair drop. This result was consistent with Doldolova et al., who recovered curcumin from turmeric using NADES-based MAE.[29] Based on polynomial regression models, the optimized MAE conditions for obtaining phenolics and flavonoids from PFP employed 26 mL/g of LSR and 606 W of microwave power for 2 min to recover TPC and TFC at 17.74 mg GAE/g db and 8.11 mg RE/g db, respectively.

3.3.3. Model Validation. From the regression models, the optimal UAE conditions were 28 mL/g of LSR, 608 W of ultrasonic power, and 63 °C for 20 min, while the optimized parameters of the MAE process were 26 mL/g of LSR and 606 W of microwave power for 2 min. TPC and TFC were 39.38 mg GAE/g db and 25.79 mg RE/g db, respectively, at the optimal UAE process. At the optimal MAE process, TPC and TFC were 17.74 mg GAE/g db and 8.11 mg RE/g db. The experiments were conducted at optimal conditions to verify the regression models' reliability. The TPC and TFC obtained at optimal conditions (Table 4) were 38.52 ± 1.33 mg GAE/g db and 26.08 ± 0.46 mg RE/g db in the UAE process and 17.47 ± 0.68 mg GAE/g db and 8.72 ± 0.75 mg RE/g db in the MAE process, respectively. The experimental results were statistically insignificant with predicted data obtained by regression models; thus, these models can be used to predict the variation of TPC and TFC in the surveyed conditional range.

3.4. Extraction Kinetics. The UAE and MAE extraction kinetic modeling of TFC and TFC plays an integral role in scaling these processes for industrial applications.[34] For the UAE process, kinetic investigations were conducted under different temperatures (30, 60, and 80 °C) and extraction time (5−30 min). For the MAE process, kinetic investigations were carried out under 45, 75, and 90 °C and retention time of 1−4 min, and the other conditions remained optimized. The second-order kinetic models, Arrhenius plots, and kinetic parameters of phenolic and flavonoid extraction processes are shown in Figure 5 and Table 3. The great value of determination coefficients ($R^2 \geq 0.9$) expressed the suitability of second-order kinetic models for recovering phenolics and flavonoids using UAE and MAE processes under various conditions. The h values increased with increasing temperature, which can be attributed to improved bioactive compound solubility and solvent diffusivity in the plant matrix. Hemanta Chutia and Charu Lata Mahanta reported the extraction kinetics for carotenoid extraction from PFP using UAE and conventional extraction processes and using olive oil as a solvent with different extraction time periods and temperatures. In this study, the saturation concentrations of carotenoids for the UAE and conventional extraction operations using olive oil increased with an increase in temperature, and data were discovered from 1071.81 to 1219.51 μg/100 g db for UAE and 937.21 to 1222.49 μg/100 g db for CE. The k values varied from 0.0022 to 0.0048 100 g

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db/μg in the UAE process and from 4.02×10^{-5} to 6.85×10^{-5} in the conventional extraction process.[13]

The activation energy for extracting phenolics and flavonoids from PFP using MAE and UAE processes was determined through Arrhenius plots ($1/T$ vs $\ln k$) derived from second-order kinetic models (Figure 5E–H). The activation energy expresses the minimum energy required to overcome the chemical barrier for extracting phenolics and flavonoids.[35] The higher activation energy means that a larger figure for energy is needed to solubilize phenolics and flavonoids.[35] Additionally, the activation energy determines the mechanism for extraction processes. If $E_a \geq 40$ kJ/mol, the extraction mechanism is solubilization. The diffusion mechanism governs the extraction process if the activation energy is lower than 20 kJ/mol. If E_a is between 20 and 40 kJ/mol, the extraction process combines diffusion and solubilization mechanisms.[34] The obtained activation energy values for UAE–phenolics, UAE–flavonoids, MAE–phenolics, and MAE–flavonoids are 33.1, 10.5, 45.0, and 37.4 kJ/mol, respectively. The solubilization mechanism controls the MAE–phenolics, while UAE–flavonoids are governed by diffusion. However, UAE–phenolics and UAE–flavonoids were managed by the combination of diffusion and solubilization mechanism. The higher activation energy for flavonoids compared to phenolics speculates that flavonoid extraction may initially occur, followed by phenolic extraction. Hobbi et al. modeled the extraction of polyphenols from apple pomaces using first-order and second-order kinetic models. The research demonstrated the preference of second-order kinetic models to first ones in predicting the effect of time and temperature on the recovery of polyphenols from apple pomace. The research also showed that the extraction mechanism of polyphenol using acetone solution (65%), ethanol solution (50%), and water was diffusion.[34]

Calculating thermodynamic parameters (ΔH, ΔG, ΔS) according to eqs 6–8 provides insights into the thermodynamic characteristics of the UAE and MAE processes for phenolic and flavonoid extraction from PFP. A positive value of ΔG indicates a non-spontaneous extraction process, while a negative ΔG suggests a reverse trend. The positive ΔH value demonstrates the endothermic nature of the extraction process, and ΔS indicates the reactions' chaotic level.[35] The obtained thermodynamic values reveal that energy provision should be necessary for the UAE and MAE of phenolics and flavonoids from PFP due to positive ΔG values. The MAE of flavonoids and phenolics at 90 °C was an exception because of negative ΔG values. These results confirm that MAE and UAE are essentially non-spontaneous processes because these processes are required to add external energy to reduce extraction time and enhance extraction rate.[28] The UAE and MAE of phenolics and flavonoids were endothermic and irreversible, as indicated by the positive values of ΔS and ΔH. These results are in agreement with Zhang et al., who extracted bioactive components from cinnamon waste using NADES.[35]

3.5. Method Comparison. The TPC, TFC, and antioxidant activities of extracts at optimized conditions were investigated to compare the extraction efficiency of the two methods, and the data are shown in Table 4. The UAE presented a significantly higher extraction efficiency of TPC and TFC than MAE. It can be explained that the cavitation effect of ultrasound can impose a more devastating impact on cell walls than the cell rupture resulting from the heating effect of microwaves.[16] Furthermore, the antioxidant activities of UAE-based extracts were higher than those of MAE, which can attribute to the higher TPC and TFC contents.[16] This result is in agreement with Rodsamran and Sothornvit, who extracted phenolic compounds from lime peel waste using ethanol-based UAE and MAE.[16]

Table 4. Bioactive Compound Contents and Antioxidant Activities of PFP Extracts[a]

criteria/methods	UAE	MAE
TPC (mg GAE/g db)	38.52 ± 1.33a	17.47 ± 0.68b
TFC (mg RE/g db)	26.08 ± 0.46a	8.72 ± 0.75b
DPPH (μM TE/g db)	23.11 ± 0.56a	14.87 ± 0.27b
ABTS (μM TE/g db)	213.42 ± 9.95a	155.2 ± 12.47b
OH (μM TE/g db)	9263 ± 143a	6814 ± 88b

[a]Different characters (a and b) show statistically significant distinctions between the two methods.

4. CONCLUSIONS

The optimal solvent volume ratio of ethanol, water, and acetone was determined to be 0.29:0.34:0.37, which provided a suitable polarity for recovering phenolics and flavonoids from PFP. The UAE process was optimized at 28 mL/g of LSR, 608 W of ultrasonic power, and 63 °C for 20 min to acquire TPC and TFC at 39.38 mg GAE/g db and 25.79 mg RE/g db, respectively. For the MAE process, the optimized conditions for extracting phenolics and flavonoids from PFP were 26 mL/g of LSR and 606 W of microwave power for 2 min to recover TPC and TFC at 17.74 mg GAE/g db and 8.11 mg RE/g db, respectively. The kinetics and thermodynamic parameters were analyzed based on the second-order extraction kinetic model, which elucidated the mechanism and occurrence of MAE and UAE processes in extracting phenolics and flavonoids. The diffusion mechanism governed the UAE of flavonoids, while the MAE of phenolics was driven by solubilization. The combination of solubilization and diffusion mechanism managed the UAE of phenolics and MAE of flavonoids. The UAE and MAE were endothermal and irreversible processes. TPC, TFC, and antioxidant activities obtained from UAE were higher than those obtained from MAE. Therefore, UAE is a potential and green technique for recovering bioactive compounds from PFP and achieved a greater extraction yield than MAE.

■ ASSOCIATED CONTENT

Data Availability Statement

All data generated or analyzed during this study are included in this published article.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.3c04550.

Experimental design and results of augmented simplex–centroid design; ANOVA of augmented simplex–centroid design (PDF)

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Notes

The authors declare no competing financial 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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