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Research Article

Optimization of Deep Eutectic Solvents Extraction of Effective Components from *Phellodendron chinense* Schneid by Response Surface Methodology

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Taking *Phellodendron chinense* Schneid (PcS) as the raw material with ultrasonic-assisted eutectic solvent, the effects of various DESs on the extractable content of palmatine and berberine in PcS were investigated. On the basis of the single-factor test, the best DES was determined to be choline chloride and 1,3-propanediol (mole ratio 1 : 2). After optimizing by the response surface method, the optimum extraction conditions were as follows: the solid-liquid ratio was 1 : 30 (w/v), water content was 30% (v/v), vortex time was 7 min, ultrasonic time was 20 min, ultrasonic temperature was 60°C, ultrasonic power was 400 W, and the content of palmatine in PcS was 5.421 ± 0.283 mg/g, and the content of berberine in PcS was 15.573 ± 0.539 mg/g. Therefore, DES prepared from choline chloride and 1,3-propanediol can be used to extract palmatine and berberine from PcS. The optimized process conditions determined by the response surface method are reliable and can provide a reference for the green extraction of effective components from PcS.

1. Introduction

Phellodendron chinense Schneid (PcS), which is commonly known as "Sichuan Phellodendron amurense Rupr," is the dried bark of plant-*Phellodendron chinense* Schneid [1]. It is mainly distributed in Shaanxi and Sichuan provinces of China [2]. PcS has the functions of clearing heat, dryness, and dampness, purging fire, and removing steam, and detoxifying and treating pain [3]. The main chemical components are alkaloids with a content of more than 3% [4], including berberine, palmatine, jatrorrhizine, and magnoflorine [5]. These alkaloids have effects of bacteriostasis, anti-inflammation, [5] antiarrhythmia, regulation of lipid metabolism [6], and anticancer [7] in modern pharmacology. PcS is a traditional Chinese medicine commonly adopted in traditional Chinese medicine, which is widely adopted in clinical practice. It is often used in the treatment of skin diseases, [8] infantile eczema, [9, 10] enteritis [11, 12] and anal eczema. [13].

DES is a system composed of organic molecules and ionic compounds [14], which is formed by the hydrogen bond association of two or three compounds. In the meanwhile, hydrogen bonding will reduce the melting point of the system, and the final melting point of DES is lower than that of any component [15]. Due to its high surface tension, high density, and high polarity, DES has good solvent properties, such as thermal stability [16], chemical stability, and simple synthesis. In recent years, DES are more widely adopted, such as electrochemical research [17, 18], natural product analysis [19, 20], biological sample analysis [21], food analysis [22], environmental analysis [23], Chinese medicine compound extraction [24], and many other fields.

At present, the research on the extraction technology of PcS mainly focuses on the traditional extraction methods, such as water extraction [25]and alcohol extraction [26]. With palmatine and berberine as the detection indexes, the effective components of PC were extracted by DES. With assisted ultrasonic extraction technology, single factor experiments [27] were conducted to investigate the effect of DES types and other extraction factors on the extraction of

effective components of PcS. The response surface method [28, 29] was used to optimize the extraction process of PcS and to compare with traditional water extraction and alcohol extraction. This study intends to provide a more green, cost-effective, and new technological method for the extraction of PcS medicinal materials.

2. Materials and Methods

2.1. Instruments. The chromatographic analysis was performed with the use of Agilent 1260 high performance liquid chromatography system (including four-element low-pressure stirring pump, automatic injector, column incubator, 1100 diode array detector, and chemical workstation) was purchased from Agilent Technologies Co., Ltd. In addition, AB135-S electronic balance was purchased from Mettler-Toledo International Co., Ltd. QL-901 Vortex instrument was purchased from Haimen Qilinbeier Instrument Manufacturing Co., Ltd. TGL-16 freezing centrifuge was purchased from Hunan Xiangyi Laboratory Instrument Development Co., Ltd. HH-S4 digital display constant temperature water bath pot was purchased from Jiangsu Jinyi Instrument Technology Co., Ltd., and JP-300G ultrasonic extractor was purchased from Wuhan Jiapeng Electronics Co., Ltd. DFY-500 (swing type) multifunction high-speed traditional Chinese medicine grinder was purchased from Wenzhou Dingli Medical Equipment Co., Ltd. JM-A5002 Analytical balance was purchased from Zhuji Chaoze Equipment Co., Ltd.

2.2. Materials. The PcS adopted in this experiment was produced in Sichuan Province, China, which met the requirements of Chinese Pharmacopoeia (2020 edition). Chromatographic grade methanol and acetonitrile were purchased from Fisher Company of the United States, analytical pure phosphoric acid (batch number 20170408) was purchased from Tianjin Guangfu Technology Development Co., Ltd., and ultrapure water was purchased from Hangzhou Wa Co., Ltd. Choline chloride (batch number 150120) was purchased from Shanghai Zhanyun Chemical Co., Ltd. The batch numbers and manufacturers of hydrogen bond donors are shown in Table 1.

6.14 mg of palmatine hydrochloride (batch no. 110732-201611, purity ≥85.7%, China Institute for Food and Drug Control) and 10.45 mg of berberine hydrochloride (batch no. 110713-201613, purity ≥85.9%, China Institute for Food and Drug Control) were weighed precisely and diluted separately with methanol to obtain 0.614 mg/mL of palmatine hydrochloride and 2.09 mg/mL of berberine hydrochloride. Equal volumes of palmatine hydrochloride and berberine hydrochloride were mixed to obtain a mixed solution containing 0.307 mg/mL and 1.045 mg/mL of palmatine and berberine. The solution was filtered through a filter with a pore size of 0.22 μm to obtain the control solution for HPLC analysis.

2.3. HPLC Analysis Condition. High performance liquid chromatography (HPLC) detection was conducted, with chromatographic column Agilent $^{TC}C_{18}$(5 μm,4.6 × 250 mm). The mobile phase was acetonitrile-0.1% phosphoric acid aqueous solution (28 : 72, v : v). The detector wavelength was 238 nm, the injection volume was 20 μL, the flow rate was 1.0 mL/min, and the column temperature was 30°C.

2.4. Preparation of DES. In this paper, choline chloride, the most frequently used in the market, was used as hydrogen bond acceptor, and 11 kinds of hydrogen bond donor materials were selected, as shown in Table 1. Mix according to the mole ratio in Table 1, heat in 80–100°C water bath, stir continuously until transparent, and form DES. They were named in order from DES-1 to DES-11.

2.5. Preparation of Test Solution. Take proper amount of PcS, grind it through a sieve of 100 mesh, and accurately weigh 50 mg PcS powder. DES was added on the grounds of the ratio of material to liquid at 1 : 30 (w/v); it was placed in water at 60°C for 5 min, vortex oscillation 5 min (power supply 220 V, power 40 W, speed 2800 rmp/min), ultrasonic extraction 30 min (power 300 W) at 60°C, vortex oscillation 5 min, and 3000 r/min centrifugal 5 min. Finally, PcS extract was obtained.

3. Results and Analysis

3.1. HPLC Method Verification

3.1.1. Investigation of the Linear Relation. The appropriate amount of the above mixed reference substance reserve solution was taken and it was diluted with methanol in turn to obtain a series of reference substance solutions, carrying on the HPLC analysis. Taking the peak area (A) as the ordinate (y) and the reference substance concentration (μg/mL) as the abscissa (x), the standard curve was drawn. The regression equations of palmatine and berberine were $y = 8.8248 \times -19.508$ ($r = 0.9996$), and the linear range was 6.14~307 μg/mL. $y = 10.059 \times -35.925$($r = 0.9997$), and the linear range was 20.9~1045 μg/mL.

3.1.2. Precision Test. The same PcS extract was injected continuously for 6 times according to Section 2.3. In addition, the RSD values of palmatine and berberine peak area were calculated to be 1.15% and 0.77%, respectively. According to the above method, 6 samples of PcS extract were prepared and analyzed by HPLC. The average contents of palmatine and berberine were calculated as 5.456 ± 0.097 mg/g and 16.229 ± 0.219 mg/g, respectively. Besides, the RSDs were 1.78% and 1.35%, respectively.

3.1.3. Recovery Test. Six samples of PcS with known content were taken with each about 25 mg. The palmatine reference solution (concentration 0.695 mg/mL) 0.2 mL and berberine reference solution (concentration 0.416 mg/mL) 1 mL were precisely extracted in the same centrifuge tube, steaming dry solvent in the water bath, adding PcS powder, adding DES-7 (water content 30%) 1.5 mL, extracting PcS extract according to Section 2.3, and being analyzed by HPLC. The average

Table 1: Sources of hydrogen bond donor.

Num.	Kind of hydrogen bond donor	Manufacturer	Mole ratio
1	Xylitol	Zhengzhou #Angyuan Chemical Products Co., Ltd.	1 : 1
2	Urea	Tianjin Ruijinte Chemical Co., Ltd.	1 : 2
3	Acetic acid	Xilong Science Co., Ltd.	1 : 2
4	Citric acid	Zhengzhou Kangyuan Chemical Products Co., Ltd.	1 : 2
5	Phenol	Xilong Science Co., Ltd.	1 : 3
6	Glycerol	Guangzhou Miya Cosmetics co., Ltd.	1 : 2
7	Propylene glycol	Tianjin Zhonghe Shengtai Chemical Co., Ltd.	1 : 2
8	Maltose	Zhengzhou Kangyuan Chemical Products Co., Ltd.	1 : 1
9	Malic acid	Zhengzhou Kangyuan Chemical Products Co., Ltd.	1 : 1
10	Lactic acid	Zhengzhou Kangyuan Chemical Products Co., Ltd.	1 : 2
11	Fructose	Zhengzhou Kangyuan Chemical Products Co., Ltd.	1 : 1

recoveries of palmatine and berberine were 99.31% and 98.89%, respectively. In addition, the RSDs were 1.94% and 1.12%; the results are shown in Table 2.

3.2. Screening of DES

3.2.1. DESs Type, Water Content, and Solid-Liquid Ratio. The composition and properties of DES determine the extraction rate [30]. The extraction of natural products has the disadvantage of the relatively high toxicity efficiency of organic solvents, which leads to the loss of active components and may lead to considerable waste. As a consequence, as a new green solvent, DES has attracted wide attention. The influence of 11 various DESs (Table 1) on the extraction efficiency of effective components from PcS was discussed. As shown in Figure 1(a), DES-7, the group of choline chloride and propylene glycol, had the highest extraction efficiency of effective components from PcS. At the same time, choline chloride and propylene glycol are both simple and easy to obtain products, nontoxic, nonvolatile, and not harmful to humans as extraction solvents, so DES-7 was finally chosen as the extraction solvent.

3.2.2. Water Content of DES. The viscosity of DES is usually very high. Generally speaking, adding water to DES can reduce the viscosity of DES and increase its solubility. As shown in Figure 1(b), the extraction amount of effective components in PcS improves with the increase of water content in DES. However, the continuous increase of water content will change the intermolecular hydrogen bond of DES, thus changing the structure of DES and reducing the solubility of the effective components of PCS. Consequently, increasing water content in a certain range is beneficial to the extraction of effective components from PcS. DES with 30% water content was selected as the extraction solvent of PcS [31].

3.2.3. Solid-Liquid Ratio. It can be seen from Figure 1(c) that the extraction amount of effective components in PcS improves with the increase of the ratio of material to liquid. After all, the increase of the ratio of liquid to material can enhance the solubility of the system. When the ratio of material to liquid is 1 : 30 g/mL, it reaches the highest point of extraction. Besides, when the ratio of material to liquid continues to increase, the content of palmatine and berberine is almost unchanged. This may be because when the ratio of material to liquid increases to a certain extent, the solubility reaches a certain degree, and saturation may occur, resulting in that part of the components can not be dissolved, which then affects the extraction effect. As a consequence, 1 : 30 g/mL was selected as the ratio of material to liquid for the extraction of effective components in PcS.

3.3. Investigation on Single Factors of Extraction Process

3.3.1. Vortex Time. The vortex can accelerate the full dispersion of DES into the sample solution and fully contact with the target analyte. In addition, it can improve the extraction efficiency by affecting the emulsification and two-phase equilibrium of DES. As a consequence, the choice of vortex time is very important [32]. As shown in Figure 2(a), the extraction amount of palmatine and berberine increased, reached the maximum at 5 min, and then decreased with the increase of time, which may be due to the introduction of bubbles by the continuous vortex, weakening the interaction between the extractant and the target. As a consequence, the best vortex time is 5 min.

3.3.2. Ultrasonic Power. Ultrasonic power can promote the dissolution of active substances. When the ultrasonic power is too low, the cavitation effect is weak. As a result, the local tensile stress in the liquid is not enough. When the ultrasonic power increases, the cavitation effect will increase with the increase of ultrasonic power, accelerate the molecular diffusion speed, and improve the extraction rate of palmatine and berberine. However, too high ultrasonic power not only will waste the experimental cost, but may destroy the structure of the active material. It can be seen in Figure 2(b) that when the ultrasonic power reaches 300 W, the content of palmatine and berberine in the extracted PcS is the highest, so the ultrasonic extraction power is 300 W.

3.3.3. Ultrasonic Time. Extraction time is an important parameter for the extraction of natural products. Generally speaking, the content of chemical components improves with the increase of extraction time. As can be seen from

Table 2: Results of recovery test of two active constituents.

Constituent	Original amount (μg)	Added amount (μg)	Total measured amount (μg)	Recovery rate (%)	Average recovery (%)	RSD (%)
Palmatine	140.220	139.000	277.346	98.65	99.31	1.94
	142.402	139.000	278.261	97.74		
	140.766	139.000	282.002	101.61		
	127.671	139.000	269.254	101.86		
	136.401	139.000	271.942	97.51		
	143.494	139.000	280.359	98.46		
Berberine	417.103	416.000	828.205	98.82	98.89	1.12
	423.595	416.000	828.994	97.45		
	418.726	416.000	836.081	100.33		
	379.775	416.000	794.346	99.66		
	405.742	416.000	812.502	97.78		
	426.841	416.000	840.002	99.32		

The above results showed that the HPLC analysis method was accurate and reproducible.

Figure 2(c), the extraction amount of palmatine and berberine increased at first and then reduced with the extension of ultrasonic time. The reason is that ultrasonic has cavitation effect, mechanical effect, and thermal effect. In a certain range of ultrasonic time, prolonging ultrasonic time can fully destroy the plant cell wall and make the active components in plant cells effectively dissolve [33, 34]. As a consequence, with the extension of time, the extraction amount of palmatine and berberine gradually increased. However, too long ultrasonic time may lead to the destruction of alkaloid structure [35]. As a consequence, the best ultrasonic extraction time is 30 min.

3.3.4. Ultrasonic Temperature. The extraction temperature affects the mass transfer, thus affecting the chemical composition. Some studies have shown that, with the increase of temperature and the enhancement of mass transfer, the viscosity of extraction solvent decreases and the extraction efficiency increases. However, the dissolution of the active components is affected, or the decomposition of the active components is caused by the influence of high temperature when the temperature exceeds a certain range. As a consequence, it is necessary to select the appropriate ultrasonic temperature for research. The appropriate extraction temperature is one of the important parameters affecting the extraction of DES. It can be concluded from Figure 2(d) that the extraction content of effective components in PcS increases with the increase of temperature. Moreover, when the extraction temperature exceeds 70°C, the extraction amount of palmatine and berberine decreases. It can be seen that increasing the temperature to 60°C can reduce the surface tension and viscosity of DES, make the extract easier to infiltrate, and improve the extraction efficiency.

3.4. Response Surface Test Results and Analysis. Design-Expert 8.0.6 statistical software was adopted. Based on the results of single factor test and the design principle of Box–Behnken experiment, the influential factors such as ultrasonic power (A/W), ultrasonic time (B/min), ultrasonic temperature (C/°C), and vortex time (D/min) were selected as independent variables, and the comprehensive scores (CS) of palmatine (mg/g) and berberine (mg/g) contents were taken as investigation indexes. The weight coefficients were as follows: 50% of palmatine content and 50% of berberine content. The central point was selected to repeat the experiment for 5 times, and the response surface analysis model of 29 test sites with 4 factors and 3 levels was designed. The experimental design and response values are shown in Tables 3 and 4. In addition, the results of analysis of variance are shown in Table 5.

Design-Expert 8.0.6 software was adopted to analyze, and the quadratic multiple regression equation was obtained as follows: $Y = 87.37 + 2.66A + 1.53B + 4.77\,C + 0.53D - 0.98AB - 0.89AC + 0.2AD - 0.17BC - 2.29BD + 3.40CD + 1.91A^2 + 2.59B^2 - 3.94^2 + 1.57D$. The results show that when the model $P < 0.001$, the regression model was very significant; when the misfit item $P > 0.05$, the nonexperimental factors had little influence on the test results; when the determination coefficient was $0.8262 > 0.8$, the model fitting was high; when the variant was 3.64%, the test accuracy was good; when the signal-to-noise ratio S/N was $7.821 > 4$, the model can be adopted to analyze and predict the extraction of PcS. The significant analysis of the regression model showed that A was significant ($P < 0.05$), C and C^2 were very significant ($P < 0.01$ or $P < 0.001$), and the other items were not significant. The order of the four factors affecting PcS extraction was C > A > B > D.

PcS extracts the response surface 3D map and contour map of the interaction between the two factors, as shown in Figure 3. It can be seen that the interaction between ultrasonic time and vortex time was the strongest.

The optimum extraction conditions of PcS DES obtained by response surface method were as follows: ultrasonic power 399.93 W, ultrasonic time 20 min, ultrasonic temperature 58.69°C, vortex time 7 min, and the theoretical comprehensive score 102.061. Considering the actual operation, the optimum process conditions are modified 400 W, ultrasonic time 20 min, ultrasonic temperature 60°C, and vortex time 7 min. Under these conditions, the contents of palmatine and berberine in PcS were 5.421 ± 0.283 and 15.573 ± 0.539 mg/g, respectively, and the comprehensive

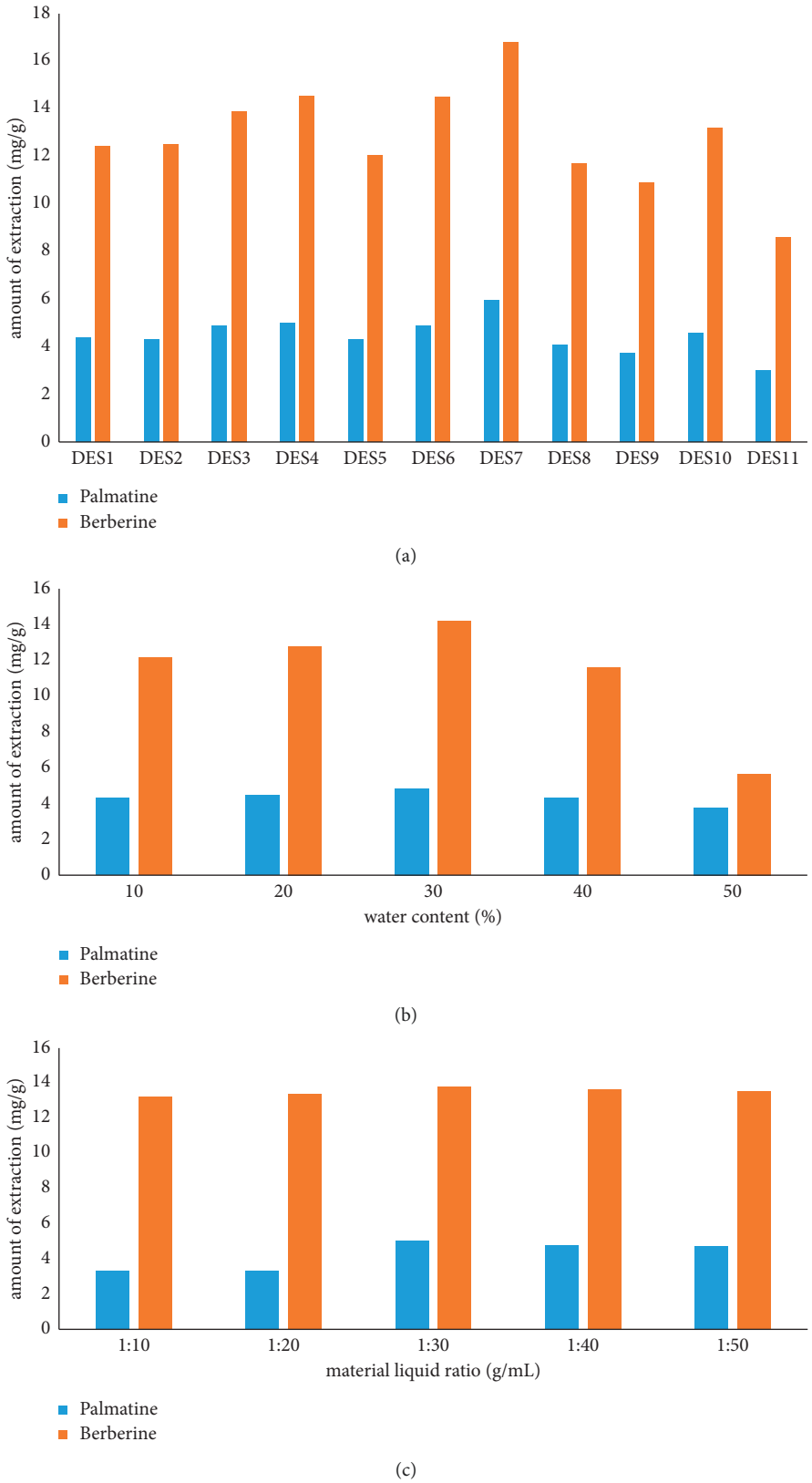
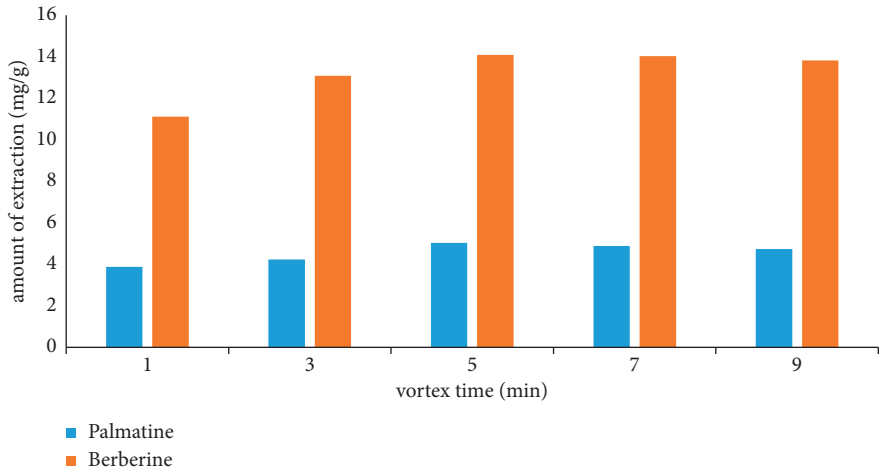
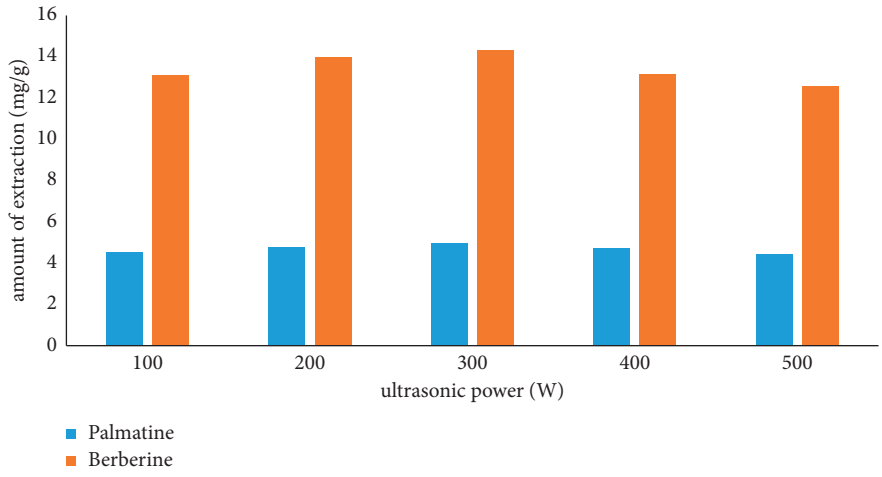


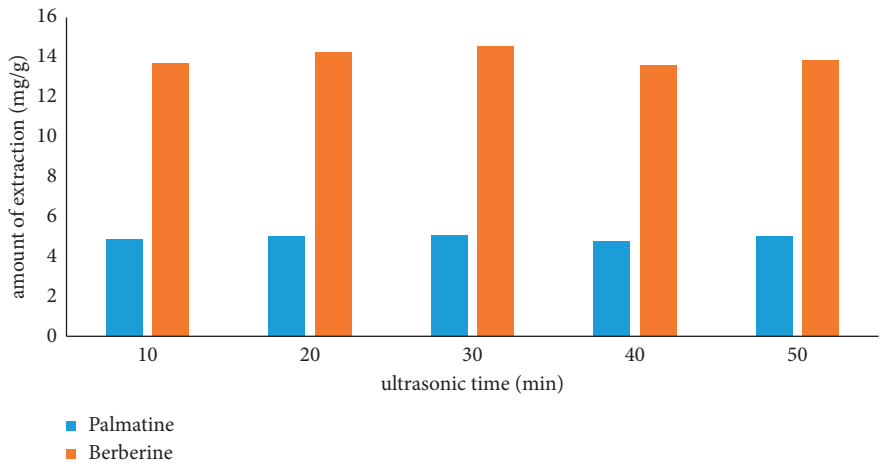
Figure 1: Effect of DES on PcS extraction efficiency: (a) effect of different types of DESs, (b) effect of DES water content, and (c) effect of solid-liquid ratio.



(a)

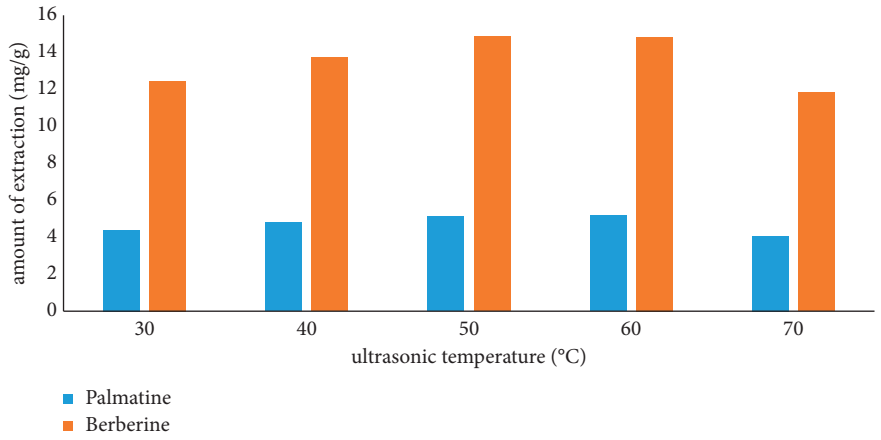


(b)



(c)

Figure 2: Continued.



(d)

Figure 2: Investigation of single factors in ultrasonic extraction process.

Table 3: Response surface test factor level of PcS extraction process.

Level	Factors			
	Ultrasonic power/W	Ultrasonic time/min	Ultrasonic temperature/°C	Vortex time/min
−1	200	20	40	3
0	300	30	50	5
1	400	40	60	7

Table 4: Response surface test design and results.

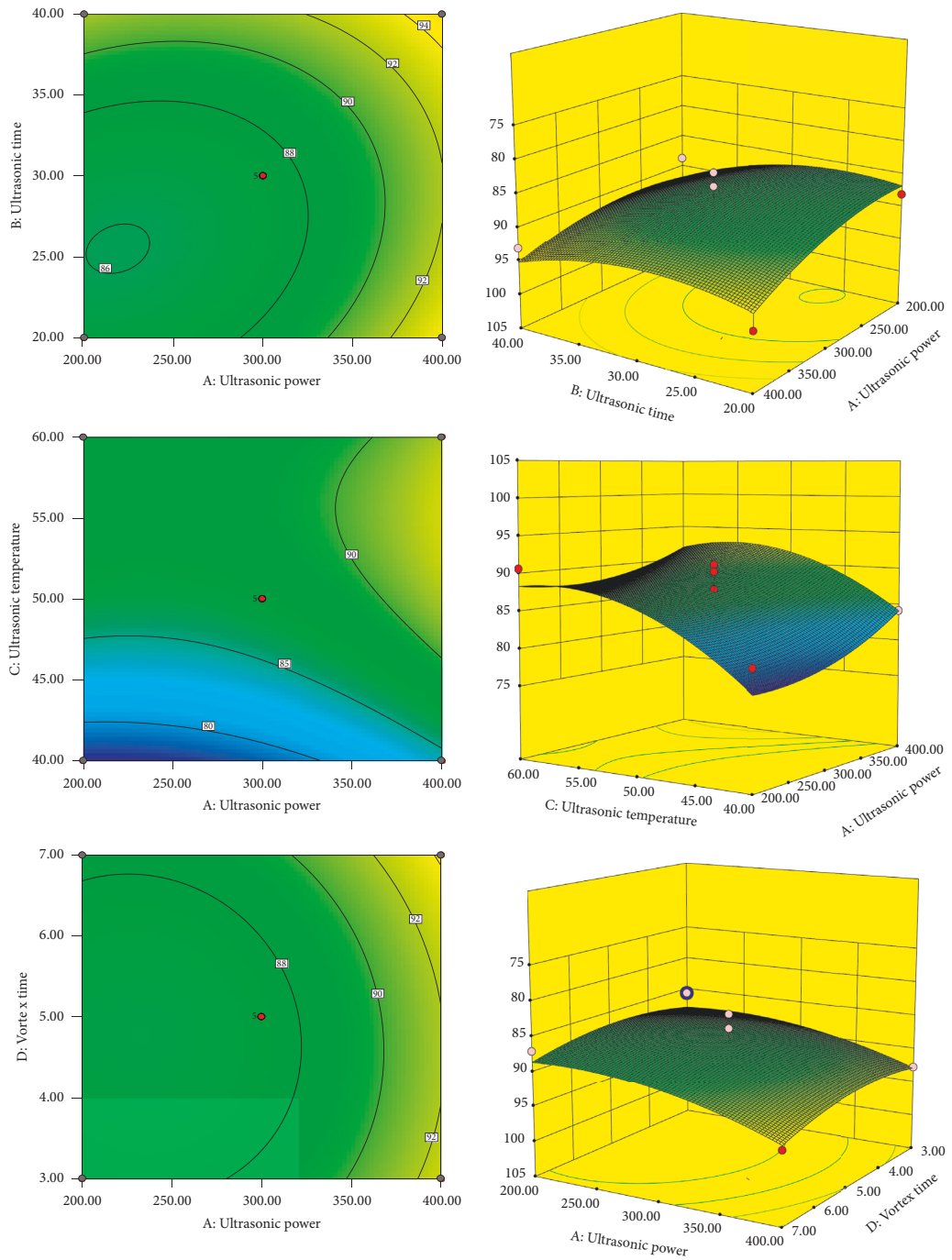
No.	A	B	C	D	CS	No.	*A*	*B*	*C*	*D*	CS
1	200	30	60	5	90.621	16	300	20	60	5	89.201
2	400	30	60	5	90.940	17	400	30	50	3	92.687
3	400	30	50	7	94.887	18	400	20	50	5	96.399
4	200	30	50	7	87.010	19	200	30	50	3	85.626
5	400	40	50	5	93.037	20	200	20	50	5	88.029
6	300	30	50	5	85.307	21	300	20	40	5	80.024
7	300	30	60	7	94.682	22	300	30	50	5	87.474
8	300	40	40	5	81.592	23	300	20	50	3	86.081
9	300	20	50	7	89.914	24	300	40	50	3	100.000
10	200	40	50	5	88.607	25	200	30	40	5	80.240
11	300	30	60	3	85.770	26	300	30	40	7	76.724
12	300	30	40	3	81.395	27	400	30	40	5	84.117
13	300	30	50	5	89.921	28	300	40	50	7	94.677
14	300	30	50	5	90.886	29	300	40	60	5	90.095
15	300	30	50	5	83.248	—	—	—	—	—	—

Table 5: Results of variance analysis of PcS extraction process response surface test.

Source	Sum of squares	Df	Mean square	*F* value	*P* value	
Model	686.04	14	49.00	4.75	0.0031	Significant
A	84.99	1	84.99	8.25	0.0123	
B	28.09	1	28.09	2.73	0.1210	
C	272.82	1	272.82	26.47	0.0001	
D	3.35	1	3.35	0.32	0.5779	
AB	3.88	1	3.88	0.38	0.5494	
AC	3.17	1	3.17	0.31	0.5882	
AD	0.17	1	0.17	0.016	0.9006	
BC	0.11	1	0.11	0.011	0.9178	
BD	20.95	1	20.95	2.03	0.1758	
CD	46.13	1	46.13	4.48	0.0528	
A^2	23.66	1	23.66	2.30	0.1520	
B^2	43.58	1	43.58	4.23	0.0589	

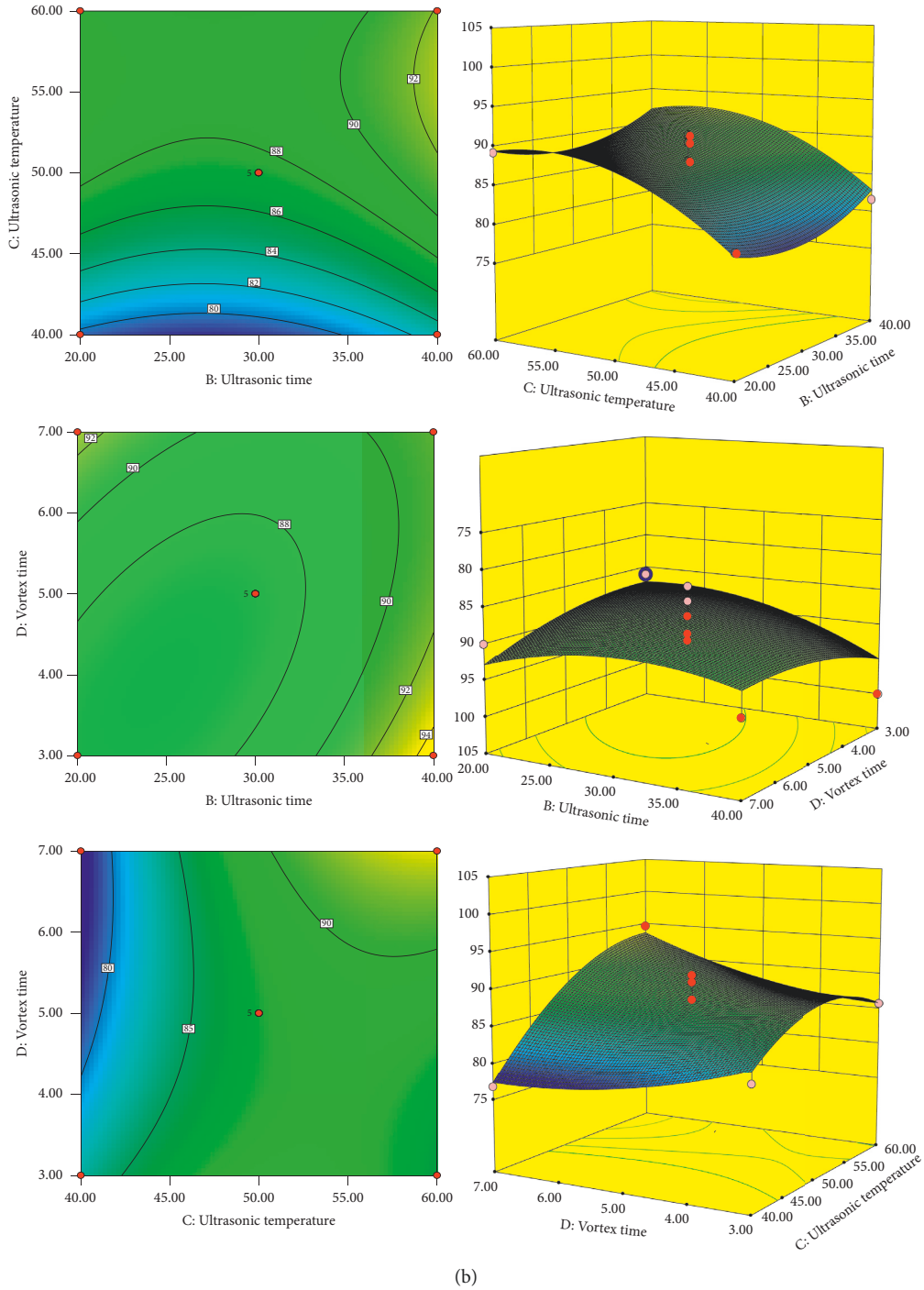
Table 5: Continued.

Source	Sum of squares	Df	Mean square	F value	P value	
C^2	100.70	1	100.70	9.77	0.0074	
D^2	15.92	1	15.92	1.54	0.2343	
Residual	144.28	14	10.31			
Lack of fit	104.15	10	10.42	1.04	0.5313	Not significant
Pure error	40.13	4	10.03			
Cor. total	830.32	28				
R-squared	0.8262					
Adj. R-squared	0.6525					
C.V.%	3.64					
Adeq. precision	7.821					



(a)

Figure 3: Continued.



(b)

Figure 3: Response surface drawings of PcS analyzed by interaction of two factors.

score was 101.111, which shows that the prediction of the model established by Design-Expert 8.0.6 has a good accuracy. As a consequence, the technological conditions of PcS DES extraction can be well optimized.

3.5. Comparison with Traditional Extraction Solvents in Ultrasound-Assisted Process. Palmatine and berberine of PcS were extracted by ultrasonic-assisted DES method. In addition, the extraction results of the DES were in comparison with those of the traditional extraction solvents water, methanol, and ethanol under the same extraction method. As shown in Figure 4, the extraction effect of the optimized ultrasonic-assisted DES extraction method was slightly better than that of conventional extraction solvents. In view of the problems of traditional extraction methods, such as long cycle, complex operation, high cost and difficult recovery, volatile organic reagents, and toxicity, ultrasonic-assisted low-melting solvent extraction has the advantages of short time, high efficiency, low cost, simple operation, and

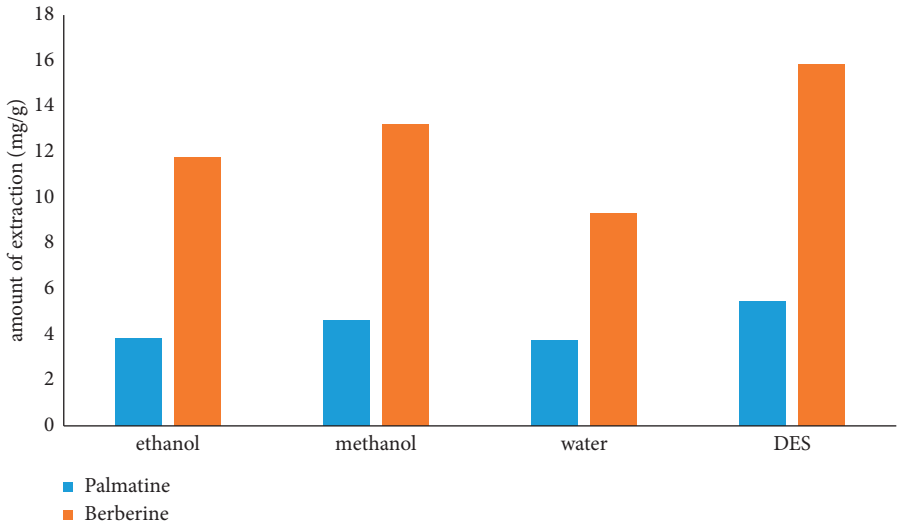


Figure 4: Comparison with traditional extraction solvents in ultrasound-assisted process.

reagent saving and greatly shortens the extraction time and saves the steps of solvent concentration, and the DES has the advantage of being green and nonpolluting and nonoxic.

4. Conclusion

Response surface methodology was used to optimize the extraction of effective components from Phellodendron phellodendri with low eutectic solvent, and compared with traditional extraction methods, it reflected the advantages of high efficiency and fast extraction of DES and nontoxic, green, and environmental protection. A new type of DES was adopted to extract the effective components of PcS, combined with ultrasonic extraction technology. Compared with the traditional Chinese medicine extraction technology, it is proved that the extraction effect of DES is better than other extraction methods, which reflects the advantages of high yield and high speed of DES extraction. The extraction effect of DES formed by choline chloride and 1,3-propanediol (molar ratio 1 : 2) was the best. Combined with single factor experiment and response surface optimization experiment, it was confirmed that the optimum extraction conditions of PcS were as follows: DES water content was 30% (v/v), ratio of material to liquid was 1 : 30 g/ml, vortex time was 7 min, ultrasonic time was 20 min, ultrasonic temperature was 60°C, and ultrasonic power was 400 W. At this time, the content of palmatine in PcS was 5.421 ± 0.283 mg/g, the content of berberine is 15.573 ± 0.539 mg/g, and the comprehensive score was 101.111. It was 0.95 different from the comprehensive score predicted by the model, which proved the effectiveness and feasibility of the model. Compared with the traditional water extraction, the extraction rate of PcS effective components extracted by DES was efficient and feasible. This study not only provides some data support for the green extraction of natural plant active components, but also provides a new idea for the further development of alkaloids in PcS.

Data Availability

The main table and figure data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare no conflicts of interest.

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References

[1] Z. M. Zhu, X. X. Lai, and M. X. Su, "Determinations of active compositions in cortex phellodendri chinensis and cortex phellodendri amurensis from different areas by HPLC," *Clinical Medicine & Engineering*, vol. 18, no. 1, pp. 106–108, 2011.

[2] J. C. Li, L. Wu, and T. K. Cai, "Research progress of Cortex Phellodendri in the chemical constituents and their pharmacological effects," *Journal of Pharmacy Practice*, vol. 36, no. 5, 2018.

[3] National Pharmacopoeia Commission, *Pharmacopoeia of the People's Republic of China Chinese Pharmacopoeia . One*, China Medical Science and Technology Press, Beijing, China, 2015.

[4] W. Gao, H. F. Zhou, D. Liu, and F. Qian, "Chemical composition analysis and pharmacological research progress of cortex phellodendri," *Asia-Pacific Traditional Medicine*, vol. 15, no. 4, pp. 207–209, 2019.

[5] Q. Dai, Y. Hu, L. Lei, and X. Luo, "Research progress on literature research, chemical constituents and pharmacological effects of cortex phellodendri processed products," *Asia-Pacific Traditional Medicine*, vol. 16, no. 10, pp. 205–208, 2020.

[6] Y. F. Chen and X. H. Zhong, "Pharmacological effects of cortex phellodendri and its active ingredient extraction," *Crop Research*, vol. 29, no. 5, pp. 564–568, 2015.

[7] E. Z. Liao J, T. Ning, and Y. X. Nie, "Photosensitive anticancer studies on Chinese medicine cortex phellodendri," *Journal of Capital University of Medical Sciences*, no. 3, pp. 153–155, 1999.

[8] J. W. Tan, H. Y. Li, and J. Liang, "Clinical application of compound Phellodendron liquid in dermatology," *Chinese Journal of Dermatology Integrated Traditional and Western Medicine*, vol. 19, no. 6, pp. 617–619, 2020.

[9] F. H. Xu, "Clinical application of compound huangbo liquid combined with compound flumethasone ointment in the treatment of children with spleen deficiency and dampness type eczema," *Maternity Child Health Care China*, vol. 34, no. 2, pp. 375–377, 2019.

[10] X. D. Sun and C. X. Qin, "Pharmacological action of compound huangbai liquid paint and its clinical application in pediatrics," *World Latest Medicine Information*, vol. 19, no. 2, pp. 31–33, 2019.

[11] C. C. Zhang and X. A. Zhang, "Clinical observation on treating 45 cases of ulcerative colitis by retention enema with the compound Huangbo decoction," *Journal of Chinese Clinical Medicine*, vol. 7, no. 25, pp. 107-108, 2015.

[12] Z. M. Zhou, "The clinical effect of compound Huangbo liquid plus Xilei powder retention enema in the treatment of chronic ulcerative proctitis," *Jiangsu Medical Journal*, vol. 42, no. 3, pp. 338-339, 2016.

[13] C. J. Yu, X. Q. Li, and C. Y. Wang, "Observation on effect of compound cortex phellodendri chinensis fluid in treatment of patients with acute anal eczema," *Chinese Nursing Research*, vol. 30, no. 31, pp. 3964-3965, 2016.

[14] J. J. Zhao, B. Y. Liu, and F. X. Wei, "Property and application of eutectic ionic liquid," *Hebei Journal of Industrial Science and Technology*, vol. 29, no. 3, pp. 184–189, 2012.

[15] J. M. Liu, H. Wang, H. Zhang, Q. Chen, and B. Kong, "Research progress on extraction of active ingredients and pretreatment of food analysis by ultrasound-assisted deep eutectic solvent method," *Science and Technology of Food Industry*, vol. 42, no. 7, pp. 399–407, 2021.

[16] J. Huang, X. Y. Guo, T. Y. Xu, L. Fan, X. Zhou, and S. Wu, "Ionic deep eutectic solvents for the extraction and separation of natural products," *Journal of Chromatography A*, vol. 1598, no. 2, pp. 1–19, 2019.

[17] L. Wang, Y. J. Fan, and L. Wei, "Study on electrodeposition of lanthanum in eutectic solvent," *Journal of the Electrochemical Society*, vol. 21, no. 6, pp. 543–547, 2015.

[18] L. Chen, Y. Y. Yang, R. R. Zhou et al., "The extraction of phenolic acids and polysaccharides from Lilium lancifolium Thunb. using a deep eutectic solvent," *Analytical Methods*, vol. 13, no. 10, pp. 1226–1231, 2021.

[19] L. F. Wu, Z. N. Chen, S. J. Li, L. Wang, and J. Zhang, "Eco-friendly and high-efficient extraction of natural antioxidants from Polygonum aviculare leaves using tailor-made deep eutectic solvents as extractants," *Separation and Purification Technology*, vol. 262, 2021.

[20] M. Panić, M. Radović, I. Maros, A. Jurinjak Tusek, M. Cvjetko Bubalo, and I. Radojcic Redovnikovic, "Development of environmentally friendly lipase-catalysed kinetic resolution of (R, S)-1-phenylethyl acetate using aqueous natural deep eutectic solvents," *Process Biochemistry*, vol. 102, pp. 1–9, 2021.

[21] R. Maryam, G. Nooshin, H. Maryam, and A. Alireza, "Highly effective and safe intermediate based on deep eutectic medium for carrier less-three phase hollow fiber microextraction of antiarrhythmic agents in complex matrices," *Journal of Chromatography B*, vol. 1104, 2018.

[22] W. W. Deng, A. Q. Huang, Q. T. Zheng et al., "A density-tunable liquid-phase microextraction system based on deep eutectic solvents for the determination of polycyclic aromatic hydrocarbons in tea, medicinal herbs and liquid foods," *Food Chemistry*, vol. 352, Article ID 129331, 2021.

[23] M. A. Farajzadeh, M. R. Afshar Mogaddam, and B. Feriduni, "Simultaneous synthesis of a deep eutectic solvent and its application in liquid–liquid microextraction of polycyclic aromatic hydrocarbons from aqueous samples," *RSC Advances*, vol. 6, no. 53, pp. 47990–47996, 2016.

[24] L. J. Li, Y. J. Wang, F. X. Liu, Y. Xu, and H. Bao, "Study on the effect of deep eutectic solvent liquid phase microextraction on quality standard, antitussive, and expectorant of sangbaipi decoction," *Journal of Analytical Methods in Chemistry*, vol. 1, p. 11, 2021.

[25] Y. L. Xu, N. X. Wu, and P. C. Li, "Study on quality evaluation for cortex phellodendri from different habitats based on the clinical dosage of chemical composition," *China Measurement and Test*, vol. 42, no. 12, pp. 45–48, 2016.

[26] L. L. Hu, "Optimization of berberine hydrochloride extracted from cortex phellodendri by box-behnken response surface method," *Guizhou Agricultural Sciences*, vol. 48, no. 7, pp. 90–93, 2020.

[27] G. Li, F. Chuanhua, H. Guo et al., "Efficient extraction of plantamajoside and acteoside from plantago asiatica L. By deep eutectic solvent," *China Pharmacist*, vol. 24, no. 9, pp. 1–11, 2021.

[28] H. Bao, Y. Xu, Y. Wang et al., "Optimization of extraction process of methyl eugenol and asarinin in asarum with deep eutectic solvent based on the response surface methodology," *Journal of Chemistry*, vol. 2021, Article ID 2069986, 11 pages, 2021.

[29] L. Li, Y. Wang, F. Liu, Y. Xu, and H. Bao, "Study on the effect of deep eutectic solvent liquid phase microextraction on quality standard, antitussive, and expectorant of sangbaipi decoction," *Journal of Analytical Methods in Chemistry*, vol. 2021, pp. 1–11, Article ID 9999406, 2021.

[30] H. W. Bao, J. H. Chi, H. L. Yang, F. Liu, K. Fang, and Y. Xu, "Simultaneous determination of six active components in danggui kushen pills via quantitative analysis of multicomponents by single marker," *Journal of Analytical Methods in Chemistry*, vol. 2019, Article ID 9620571, 11 pages, 2019.

[31] Z. Chen, J. Zhang, and F. Yang, "Deep eutectic solvents (DESs)-Ultrasonic-Assisted extraction of paeoniflflorin and paeonol from moutan cortex," *Journal of Chemistry*, vol. 2022, Article ID 5904038, 11 pages, 2022.

[32] Y. L Zhou, Y. Wu, M. Chen, and X. Y. Liu, "High density hydrophobic deep eutectic solvent based vortex-av ssisted dispersive liquid-liquid micro-extraction for the determination of aflatoxins in rice wine," *Chinese Journal Analytical Labaratory*, pp. 1–10, 2021.

[33] Y. C. Yang, M. C. Wei, T. C. Huang, S. Z. Lee, and S. S. Lin, "Comparison of modified u ltrasound-assisted and traditional extraction methods for the extraction of baicalin and baicalein from Radix Scutellariae," *Industrial Crops and Products*, vol. 45, pp. 182–190, 2013.

[34] M. Cvjetko Bubalo, N. Curko, M. Tomasevic, K. Kovacevic Ganic, and I. Radojcic Redovnikovic, "Green extraction of grape skin phenolics by using deep eutectic solvents," *Food Chemistry*, vol. 200, pp. 159–166, 2016.

[35] D. N. Xu, K. L. Nong, Y. Z. Liang, and M. X. Ma, "Study on the technology of ultrasonic-assisted extraction of alkaloids from the Dicliptera chinensis (L.) Juss," *Journal of Guangxi Normal University Nationalities*, vol. 36, no. 3, pp. 93–96, 2019.