Supporting Information

Ultrasound-assisted extraction of bioactive alkaloids from *Phellodendri amurensis* cortex using deep eutectic solvent aqueous solutions

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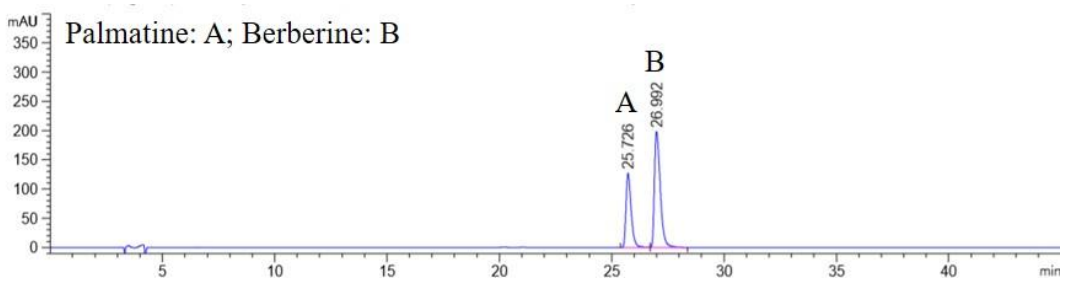

Fig. S1 HPLC profile of mixed *berberine* and *palmatine* standard solution.

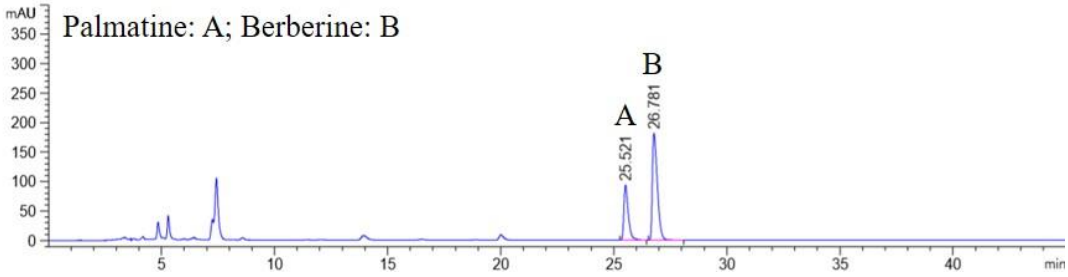

Fig. S2 HPLC profile of extract solution from PAC with water under the operating conditions of 25ºC, 30 min of ultrasonic extraction time, 20 mL/g of solvent to solid ratio.

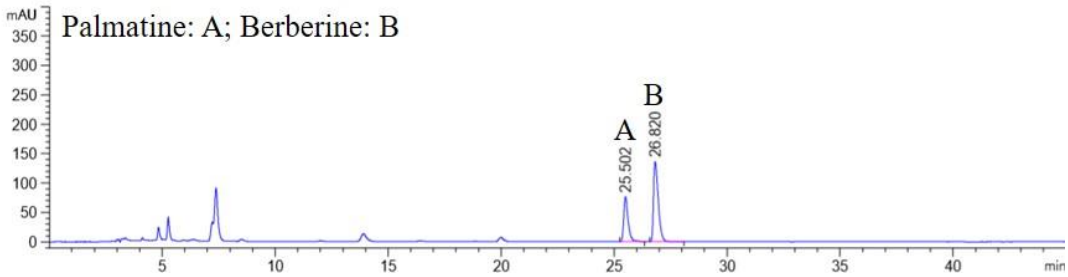

Fig. S3 HPLC profile of extract solution from PAC with ethanol under the operating conditions of 25ºC, 30 min of ultrasonic extraction time, 20 mL/g of solvent to solid ratio.

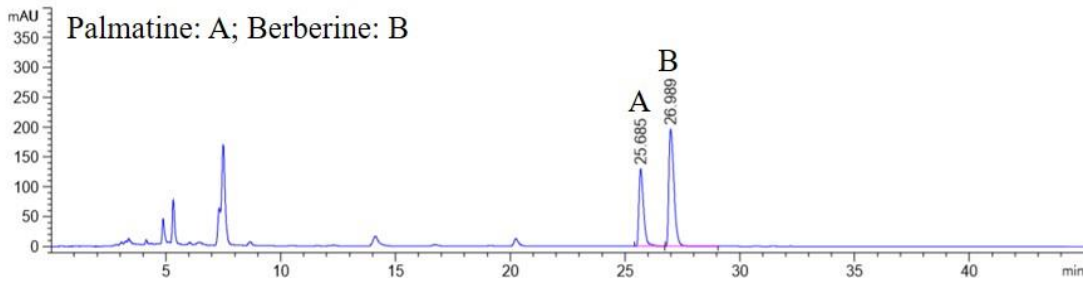

Fig. S4 HPLC profile of extract solution from PAC with 30 wt% aqueous solution of DES-1 under the operating conditions of 25°C, 30 min of ultrasonic extraction time, 20 mL/g of solvent to solid ratio.

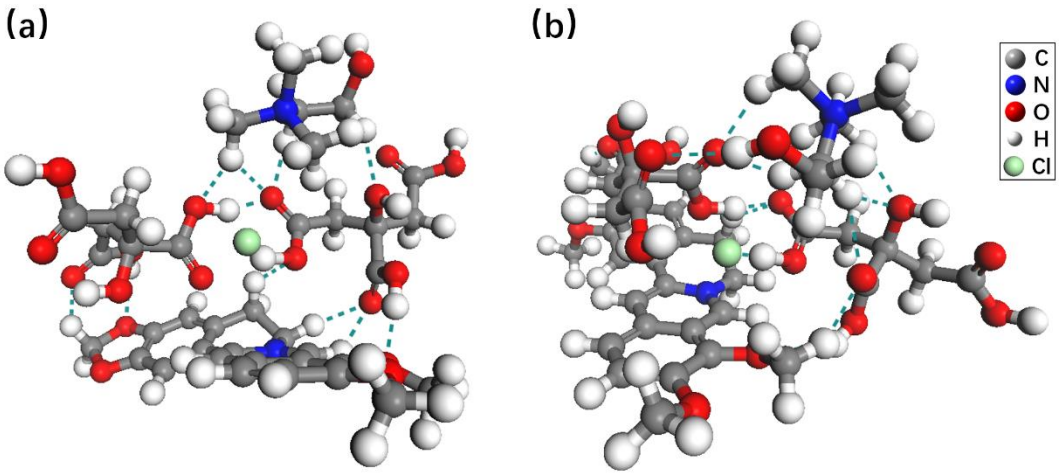

Fig. S5 Optimized geometry of (a) the complex of DES-1 with *berberine*, and (b) the complex of DES-1 with *palmatine.* The geometry optimization was completed by PM6-D3H4 method in MOPAC2016.[1] Hydrogen bonding interactions within the complexes in their optimized geometries are marked with dashed lines.

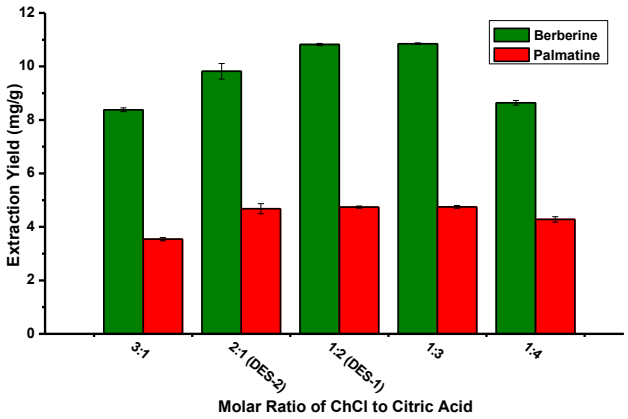

Fig. S6 Extraction yields of *berberine* and *palmatine* using DESs with different molar ratio of ChCl to citric acid. (30 wt% aqueous solution of DES, 25°C, 30 min of ultrasonic extraction time, 20 mL/g of solvent to solid ratio.)

The molar ratio of HBA to HBD commonly shows important influence on extraction capacity of DESs. Hence, extraction using DESs with different molar ratio of ChCl to citric acid was explored (Fig. S6). When the molar ratio of ChCl to citric acid was 3:1 or 1:4, the yields of *berberine* and *palmatine* were relatively low. When the molar ratio of ChCl to citric acid was 1:2 or 1:3, both DESs gave relatively high yields of *berberine* and *palmatine*. DES-1 was selected to optimize extraction conditions by RSM.

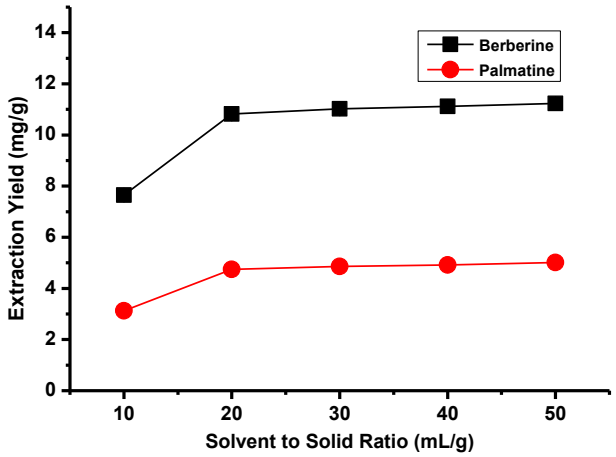

Fig. S7 Extraction yields of *berberine* and *palmatine* under different solvent to solid ratio. (30 wt% aqueous solution of DES-1, 25°C, 30 min of ultrasonic extraction time.)

The solvent to solid ratio is also an important factor which influences the economy of

extraction process. Extraction under different solvent (30 wt% aqueous solution of DES-1) to solid (PAC sample) was carried out. As shown in Fig. S7, the yields of *berberine* and *palmatine* increased dramatically with increasing solvent to solid ratio from 10 to 20 mL/g. With further increase of solvent to solid ratio, the yields improved slightly. At the solvent to solid ratio of 50 mL/g, the highest yields of *berberine* (11.23 mg/g) and *palmatine* (5.01 mg/g) were obtained. However, considering economic efficiency, the solvent to solid ratio of 20 mL/g was used to optimize extraction conditions by RSM.

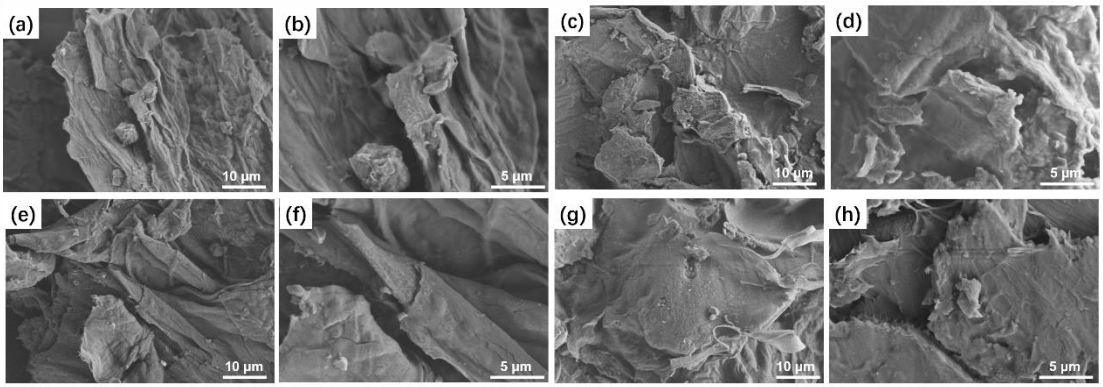

Fig. S8 SEM images of PAC samples: (a, b) treated with 30 wt% ethanol, (c, d) treated with 30 wt% methanol, (e, f) treated with 8 wt% ChCl aqueous solution, (g, h) treated with 22 wt% citric acid aqueous solution.

The PAC samples treated with 30 wt% ethanol and 30 wt% methanol (Fig. S8a-d) showed more protuberances and folds compared with the samples treated with 8 wt% ChCl aqueous solution and 22 wt% citric acid aqueous solution (Fig. S8e-h). This is consistent with 30 wt% ethanol and 30 wt% methanol giving higher yields of *berberine* and *palmatine* than that of 8 wt% ChCl aqueous solution and 22 wt% citric acid aqueous solution. However, the morphologies of samples treated with 30 wt% ethanol and 30 wt% methanol seems to be different from those treated with 30 wt% aqueous solution of DES-1. It is probably because ethanol and methanol lack the ability to dissolve and/or hydrolyze cellulose like DES.

Table S1 ANOVA of the fitted second-order polynomial model for *berberine* yield, *palmatine* yield, FRAP value, and ABTS value

	Sum of Squares	d*f*	Mean Square	F Value	p-value Prob > F	Significance
Berberine yield[a]						
Model	40.56	9	4.51	42.13	< 0.0001	significant
Residual	1.07	10	0.11			
Lack of Fit	0.89	5	0.18	5.03	0.0504	not significant
Pure Error	0.18	5	0.035			
Total	41.63	19				
Palmatine yield[b]						
Model	9.02	9	1	23.43	< 0.0001	significant
Residual	0.43	10	0.043			
Lack of Fit	0.35	5	0.07	4.67	0.0581	not significant
Pure Error	0.075	5	0.015			
Total	9.45	19				
FRAP value[c]						
Model	574.23	9	63.80	9.40	0.0008	significant
Residual	67.86	10	6.79			
Lack of Fit	56.28	5	11.26	4.86	0.0538	not significant
Pure Error	11.58	5	2.315			
Total	642.10	19				
ABTS value[d]						
Model	355.53	9	39.5	51	< 0.0001	significant
Residual	7.75	10	0.77			
Lack of Fit	6.44	5	1.29	4.91	0.0527	not significant
Pure Error	1.31	5	0.26			
Total	363.28	19				

[a]The R^2 and Adj R^2 of the model were 0.9743 and 0.9521, respectively. [b]The R^2 and Adj R^2 of the model were 0.9547 and 0.9140, respectively. [c]The R^2 and Adj R^2 of the model were 0.8943 and 0.7992, respectively. [d]The R^2 and Adj R^2 of the model were 0.9787 and 0.9596, respectively.

Table S2 Second-order polynomial equations for investigated response variables

Response	Second-order polynomial model equation
Berberine yield	$Y_1=2.80-0.13X_1+0.27X_2+0.43X_3-0.083X_1X_2+0.06X_1X_3+0.068X_2X_3+0.031X_1^2+0.29X_2^2+0.53X_3^2$
Palmatine yield	$Y_2=6.30+0.10X_1+0.72X_2+1.21X_3-0.33X_1X_2+0.00583X_1X_3+0.11X_2X_3+0.054X_1^2+0.46X_2^2+0.97X_3^2$
FRAP value	$Y_3=32.08+5.58X_1+2.36X_2+3.43X_3-0.62X_1X_2-0.57X_1X_3-1.77X_2X_3-1.54X_1^2-1.38X_2^2-1.22X_3^2$
ABTS value	$Y_4=17.62-0.75X_1+3.83X_2+2.97X_3-1.12X_1X_2+0.49X_1X_3+0.61X_2X_3+0.10X_1^2+1.23X_2^2+1.6X_3^2$

References

(1) MOPAC2016, Version: 19.059W, James J. P. Stewart, Stewart Computational Chemistry, web: HTTP://OpenMOPAC.net.