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Swelling of herbal particles of *coptis chinensis* rhizomes in imidazolium ionic liquids

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ABSTRACT

As green solvents, a series of 1-alkyl-3-methylimidazolium ionic liquids (ILs) with different cations and anions were used in the swelling of herbal particles and their performance was evaluated and compared. The study of ILs successfully discovered some mechanisms of mass transfer in swelling and extraction for herbs. The microstructure, observed by scanning electron microscope (SEM), demonstrated the change of herbal skeleton in the process of swelling. Through the study for the effect of saturated swelling ratio, [PSMIM][H_2PO_4] was finally founded as the optimal IL for swelling. Saturated swelling ratio increased with the increase of temperature or reduction of particles size. Besides the acidic IL, the swelling ratio of neutral ILs was increased as [BMIM][Cl] > [BMIM][Br] > [BMIM][BF_4] > [BMIM][PF_6] due to the increasing hydrophilicity. Because of the viscosity and the protons, the trend of the swelling ratio of [PSMIM][H_2PO_4] is first increased and then decreased with increasing of its concentration.

KEYWORDS

Ionic liquid;
Imidazolium;
Coptis chinensis;
Swelling;
Herbal extracts.

INTRODUCTION

Ionic liquids (ILs), also known as room temperature molten salt, is liquid under or near room temperature, which is composed by the large volume of organic cation and organic or inorganic anion. Since ionic bonds are weak and have low lattice energy, ILs is not equivalent to the general electrolytes[1]. In order to prepare active pharmaceutical ingredients, the traditional extraction and catalysis processes are easy to pollute the environment when a large volume of organic solvents or inorganic solvents is used. As a new kind of green organic solvent, IL is considered as an environmentally friendly solvent and catalyst, and has the potential to replace organic and inorganic solvent[2-3]. So far imidazolium ILs have been used in extraction process for a variety of natural medicine, including microwave-assisted extraction (MAE) and ultrasound -assisted extraction (UAE). TABLE 1 summarizes some related applications.As mentioned above, there are plenty of reports that the ILs have been used in the extraction of natural medicines, while the mass-transfer details of the extraction process and mechanism of phase behavior have been rarely researched. Most raw materials of herbs have inert organic skeletons with the porous characteristics[12]. In the extraction process of the rhizomes of *Coptis chinensis* with IL, solvent can swell into the skeleton of the raw materials partially. The swelling action produces some phenomenon that solvents make some changes of the macro-and micro-structure of the solid phase, and then affect the structure of herbs and transfer characteristics of extraction process. General herbal extraction includesmixing and separation of phases[13], so that swelling of *Coptis chinensis* particles in IL has a very important significance for phase separation, which would lay a foundation for further exploration of leaching balance and prediction of equilibrium to enhancing mass transfer.

MATERIALS AND EXPERIMENTAL METHODS

Chemicals

All chemicals involved in this study were at least of analytical grade. Experimental water was obtained by the UHT-II-5L Europtronic Pure Water machine. Rhizomes of *Coptis Chinensis*, purchased from local drugstore, were crushed, sieved and dried. It is delimited that the particles, passing through 20-mesh sieve but not 40-mesh, is 20 mesh, and the particles, passing through 40-mesh sieve but not 100-mesh, is 40-mesh.

Nine kinds of 1-alkyl-3-methylimidazolium ILs (as shown in TABLE 2) were synthesized according to the literatures[14-18], and their pH values of ILs were measured by PHS-3D pH meter (REX Instrument Factory, Shanghai). The purities of ILs were checked by high performance liquid chromatography (HPLC), which were greater than 95% (w/w). All of the ILs were dried at 50°C in a vacuum oven 4h, and stored in a desiccator for use.

Experimental methods

0.5 g of dried sample was mixed and swelled completely with 10ml of different ILs aqueous solution (0~1.5 M) and then the swollen particles were obtained after centrifuged at 4500 r/min for 5 min. The mass of swollen particles was weighed and the operation was taken three times to obtain the average.

Figure 1 is a scheme of experimental devices and operating procedure. The sample was loaded into 2ml Eppendorf tube that has been perforated with 200 μm diameter microbore on the tube wall. To swell particles of herb, the EP tube was put into a small bottle with the solvent. And then the swollen particles were obtained after centrifugalization.

The ratio of the mass of the original sample to the mass of swollen particles is defined as swelling ratio. Swelling ratio is calculated as:

$$R=m/m_0$$

m is the mass of sample before swelling, and m_0 is the

TABLE 1 : Extraction active substances from natural plants with ILs

Plant origin	IL species	Active substances	Extraction Method
Bayberry leaves[4]	$[BMIM][HSO_4]$	Myricetin & Quercitin	MAE
Salvia miltiorrhiza[5]	$[C_{16}MIM][Br]$	Tanshinone I, Tanshinone IIA& Cryptotanshinone	UAE
Lycoris radiata[6]	[BMIM][Cl]	Lycorine, Dihydrogalanthamine & Galanthamine	MAE
Giant knotweed rhizome[7]	[BMIM][Br]	Trans - Resveratrol	MAE
Iris tectorum[8]	[OMIM][Br]	Isoflavones、Tectoridin、Wild tectoridin B&Wild tectoridin A	UAE
Honeysuckle[9]	$[BMIM][BF_4]$	Chlorogenic acid	UAE
White pepper[10]	$[BMIM][BF_4]$	Piperine	UAE
Szechwan lovage hizome.[11]	N,N-Dimethyl-N-(2-hydroxyethoxyethyl) ammonium propionate (DMHEEAP) & N,N- N,N-Dimethyl (cyanoethyl) ammonium propionate (DMCEAP)	Senkyunolide H Senkyunolide I & Ligustilide	MAE

TABLE 2 : The type and nature of ILs

NO.	IL	Cation	Anion	PH
A	1-Butyl-3-methylimidazolium hexafluorophosphate	$BMIM^+$	PF_6^-	Neutral
B	1-Butyl-3-methylimidazolium tetrafluoroborate	$BMIM^+$	BF_4^-	Neutral
C	1-Butyl-3-methylimidazolium bromide	$BMIM^+$	Br^-	Neutral
D	1-Butyl-3-methylimidazolium chlorides	$BMIM^+$	Cl^-	Neutral
E	1 - Butyl - 3 - methylimidazolium methanesulfonate	$BMIM^+$	$CH_3SO_3^-$	Neutral
F	1-Butyl-3-methylimidazolium hydrogen sulfate	$BMIM^+$	HSO_4^-	1.6
G	1-Butyl-3-methylimidazolium dihydrogen phosphate	$BMIM^+$	$H_2PO_4^-$	2.2
H	1-Methyl-3-(3-sulfopropyl)-imidazolium hydrogen sulfate	$PSMIM^+$	HSO_4^-	1.0
I	1-Methyl-3-(3-sulfopropyl)-imidazolium dihydrogen phosphate	$PSMIM^+$	H_2PO	1.5

***The pH values of the acidic ILs were measured in the 10 mmol/100ml aqueous solution at 30°C by pH meter**

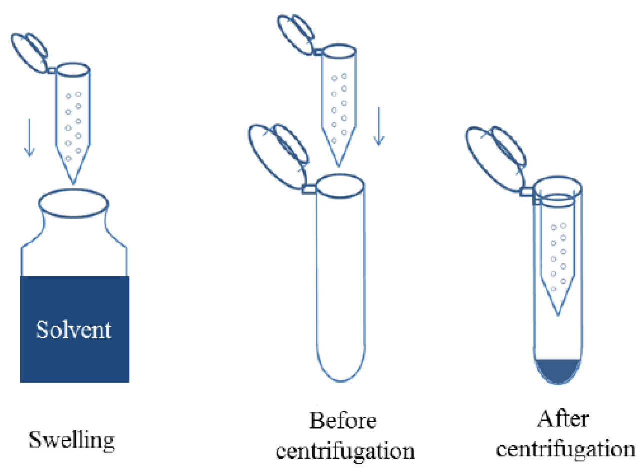


Figure 1 : Experimental device and operation procedure

mass of sample after swelling

RESULTS AND DISCUSSION

The effect of saturated swelling ratio

Solvents and particle size

The structures of the nine kinds of ILs were analyzed to discuss the mechanism of swelling. Luo has studied that ionic liquid-based ultrasonic-assisted extraction of berberine from rhizome of *Coptis chinensis*[19]. In this context, the relationship between the swelling and extraction had been discussed. The saturated swelling ratio is summarized in TABLE 3.

From the TABLE, the saturated swelling ratio of [PSMIM][HSO_4] is maximum. The swelling ratio of neutral IL is increased as [BMIM][Cl] > [BMIM][Br] > [BMIM][BF_4] > [BMIM][PF_6] due to increasing hydrophilicity of these five anions, which is the same as pure IL. HSO_4^- IL solution is more acidic than with the same action, but under the same conditions $H_2PO_4^-$ IL got greater swelling ratio. It can be explained by the fact that $H_2PO_4^-$ afford more protons at the same concentration level, and more acidity can effect more on the skeleton of herb. Compared with reference, ionic liquid-based ultrasonic-assisted extraction of berberine from rhizome of *Coptis chinensis*, it can be seen that swelling and extraction are closely related.

From TABLE 3, the swelling ratios of the particles with 40 mesh are larger than that of those with 20 mesh. Specific surface area would increase with the increase of particle size. And large specific surface area is benefit to solvent adsorption.

Temperature

Since the herbs are soaked at room temperature and refluxed with slightly boiling, 30°C and 70°C were selected to be studied in swelling process. It can be seen in the TABLE 4, the saturated swelling ratio at 70°C was larger the ratio at 30°C. High temperature is conducive that solvents penetrate into skeleton and interact with the alkaloids.

Concentrations of solvents

The saturated swelling ratios of the 20 mesh size particles in the IL of [PSMIM][H_2PO_4] at 30°C were shown in Figure 2.

The trend of the ratios was first increased and then decreased with the increasing of the concentrations. As the increasing of the concentrations from 0.1 M to 0.5 M, the effect makes skeleton tight and is stronger, so that it makes solvents penetrate into skeleton easily. However, when it further increased, the swelling ratio

TABLE 3 : Saturated swelling ratio of different size particle

Type of solvent	Saturated swelling ratio of 20mesh	Saturated swelling ratio of 40mes
[BMIM][PF_6]	1.60	1.71
[BMIM][BF_4]	1.63	1.74
[BMIM][Br]	1.67	1.74
[BMIM][Cl]	1.66	1.73
[BMIM][CH_3SO_3H]	1.62	1.71
[BMIM][HSO_4]	1.61	1.68
[BMIM][H_2PO_4]	1.65	1.74
[PSMIM][HSO_4]	1.66	1.69
[PSMIM][H_2PO_4]	1.70	1.75
5%HCl	1.68	1.74
0.4%H_2SO_4	1.58	1.68
CH_3OH	1.11	1.12
C_2H_5OH	1.06	1.09

***The concentration of IL is 0.5M at 30°C**

TABLE 4 : Saturated swelling ratio of different temperature

Type of solvent	Saturated swelling ratio at 30℃	Saturated swelling ratio at 70℃
[BMIM][Br]	1.67	1.76
[PSMIM][HSO_4]	1.66	1.73
[PSMIM][H_2PO_4]	1.70	1.78
5%HCl	1.68	1.72
0.4%H_2SO_4	1.59	1.71
CH_3OH	1.11	1.16
C_2H_5OH	1.06	1.16

***The concentration of IL is 0.5M and the particle size is 20 mesh**

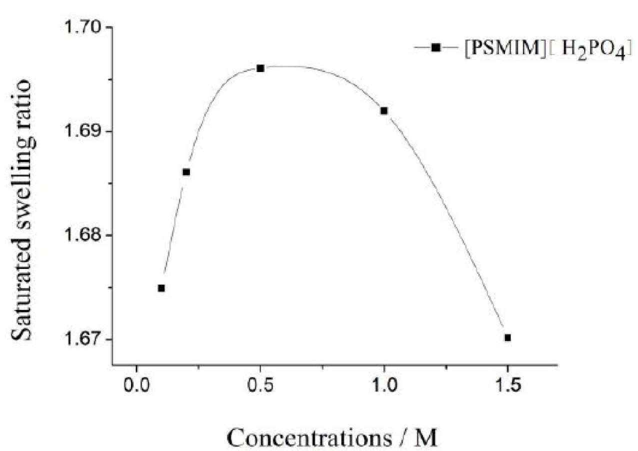


Figure 2 : The saturated swelling ratio in IL of different concentrations

decreased. The reason is that, when the concentration of IL increased, the viscosity increased significantly so that mass transfer was interrupted.

Process rate of swelling

The swelling rate of the 20 mesh size particles at 30°C was shown in Figure 4.

It can be seen in the Figure 3 that the swelling ratios of 5%HCl and ILs show an upward trend from 1 to 5 min. And then the trend slowly rose to reach balance at 15 min. The rates of 5%HCl and ILs are probably unified, while the rate of CH_3OH is fairly quickly.

ILs effect on the microstructure of coptis chinensis

The particles of *Coptis chinensis* rhizomes of 40 mesh were swollen in neutral IL [BMIM][Cl] and acidic IL [PSMIM] [HSO_4]. Reference sample was those par-

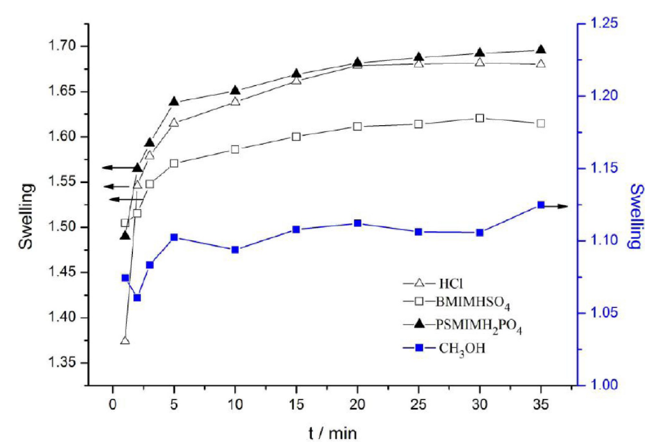
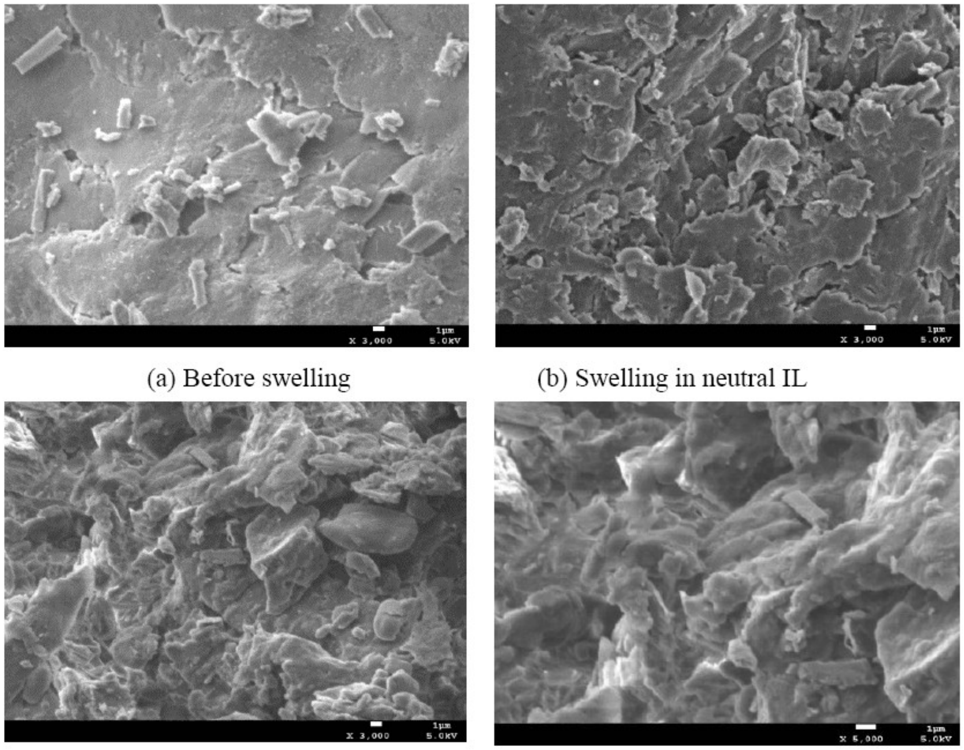


Figure 3 : The relationship of swelling rate and solvents



(a) Before swelling (b) Swelling in neutral IL

(c) Swelling in acidic IL (d) Swelling in acidic IL

Figure 4 : SEM photos of 40 mesh of *Coptis chinensis* particles

ticles without swelling. All the sample passed through 100 mesh after grinding down, and dried in vacuum oven at 30°C. Powders are placed under JSM-7500F scanning electron microscope (SEM, JEOL, Japan) to take 3000 times magnification photographs (See 4(a), (b), (c),(d)).

Extraction of herb is based internal phase of on mass transfer. From the Figure 2, it can be seen that the surface of reference particles is loose and lack porosity. The number of porosity and the diameter of aperture surface were increased since ILs make the skeleton tight. And the effect of acidic ILs on skeleton of herb is more obvious than that of neutral ILs.

CONCLUSION

Solvent swelling of *Coptis chinensis* particles is an infiltration process. Related degree and speed of swelling have a great impact on mass transfer and extraction. Saturated swelling ratio increased with increase of temperature and reduction of particle size. The swelling ratio of neutral ILs was increased as [BMIM][Cl] > [BMIM][Br] > [BMIM][BF_4] > [BMIM][PF_6] due to increasing hydrophilicity. The more protons acidic ILs can provide, the larger swelling ratios ILs make. Swelling effect of [PSMIM][H_2PO_4] was significantly better than other ILs and inorganic acids. Above results were expected to be meaningful for the application of green organic solvent ILs in extraction process for natural medicnes.

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REFERENCES

[1] T.Welton; Chem.Rev., **99**, 2071-2084 **(1999)**.
[2] J.S.Wilkes; J.Mol.Catal.A: Chem., **214**, 11-17 **(2004)**.
[3] C.F.Poole, S.K.Poole; J.Chromatogr.A., **1217**, 2268–2286 **(2010)**.
[4] F.Y.Du, X.H.Xiao, G.K.Li; Biomed.Chromatogr., **25**, 472–478 **(2011)**.
[5] K.Wu, Q.Zhang, Q.Liu, F.Tang; J.Sep.Sci., **32**, 4220–4226 **(2009)**.

[6] F.Y.Du, X.H.Xiao; J.Chromatogr.A., **1140**, 56–62 **(2007)**.

[7] F.Y.Du, X.H.Xiao, G.K.Li; Chinese.J.Anal.Chem., **35**, 1570-1574 **(2007)**.

[8] Y.Sun, W.Li, J.Wang; J.Chromatogr.A., **879**, 975-980 **(2011)**.

[9] L.Longqing, Q.Youle; Journal of Zhejiang Ocean University, **6**, 29-1 **(2010)**.

[10] X.Cao, X.Ye, Y.Lu, Y.Yu; Anal.Chim.Acta., **640**, 47–51 **(2009)**.

[11] Y.Chi, Z.Zhang, C.Li, Q.Liu; Green.Chem., **13**, 666-670 **(2011)**.

[12] E.Simeonov, I.Tsibranska, A.Minchev; Chem.Eng.J., **73**, 255-259 **(1999)**.

[13] J.Shi; Chemical Engineering Handbook, Chemical Industry Press, Beijing, **40**, **(1996)**.

[14] Y.Y.Wang, W.Li, L.Y.Dai; Chem.Pap., **3**, 313-317 **(2008)**.

[15] P.Bonhote, A.P.Dias, N.Papageorgiou; Inorg.Chem., **35**, 1168-1178 **(1996)**.

[16] Y.Chu, H.Deng, J.P.Cheng; J.Org.Chem., **72**, 7790-7793 **(2007)**.

[17] D.Fang, H.Cheng, K.Gong; J.Fluorine.Chem., **129**, 108-111 **(2008)**.

[18] L.Li, S.T.Yu, C.X.Xie, F.S.Liu; J.Chem.Technol.Biot., **84**, 1649-1652 **(2009)**.

[19] J.Luo, H.Song, Y.W.Zhang; Nat.Prod.A.Indian.J., **8**, 41-49 **(2012)**.

[20] D.D.Ming, C.X.Hua, W.Ting; Chinese.J.Org.Chem., **23**, 331 **(2003).**