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Ionic Liquid-Based Microwave-Assisted Extraction: Fast and Green Extraction Method of Secondary Metabolites on Medicinal Plant

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ABSTRACT

Background: Ionic liquid-based microwave-assisted extraction (ILMAE) is one of the non-conventional extraction methods that has been developed and applied in recent years. Some studies have reported the success of this approach for extracting the target compound (secondary metabolites) from medicinal plants optimally. **Objective:** This review paper aimed to provide detail information about the application of the ILMAE method as a fast and green extraction of a secondary metabolite from the medicinal plant. **Materials and Methods:** The literature published on ILMAE was searched and collected using online resources from the electronic databases including Google Scholar, DOAJ, PubMed, ScienceDirect, and Scopus. **Results:** This review highlights the role of IL as a green solvent, the basic principles, mechanisms of MAE, and its utilization of natural product extraction. Furthermore, this review explained about the application of the ILMAE method to extract secondary metabolite (particularly the targeted compound) from a medicinal plant, and a brief extraction mechanism of ILMAE using Fourier-transform infrared spectroscopy and scanning electron microscopy. **Conclusion:** The application of ILMAE method has successfully performed to extract the targeted secondary metabolite from a natural product, where the extraction process to be rapid, efficient, and green.

Key words: Ionic liquid-based microwave-assisted extraction, ionic liquids, medicinal plant, microwave-assisted extraction, secondary metabolite

INTRODUCTION

Exploration of the active constituents of natural products has been done for a long time. However, the resultant products are still relatively small that can be used commercially. Scientific research on natural products (especially traditional medicine), ranging from the search for raw materials, production processes, to the test of efficacy and toxicity has been done so far. Problems in the development of raw materials from nature are still constrained by different quality depending on various conditions.

The natural products (plants, animals, and microorganisms) are a sustainable source in nature that is known to be beneficial to humans for thousands of years. The diversity of species from natural products is still a primary source of ideas for the development of new drugs, functional food, and food additives.^[1] In general, the active compound of the natural

product is a secondary metabolite produced through biological pathways of various biosynthetic pathways and is obtained using an appropriate extraction procedure.^[2,3] The active constituents of natural products can be extracted by multiple conventional and nonconventional extraction techniques.^[4,5] Most of these methods based on exploration of different solvent strengths.

Application of green chemistry principles to explore the potential of active constituents from natural products continues to rise, in this case, the use of molten salt liquid as a solvent.^[6] Ionic liquids (ILs) were selected because they are nonflammable, stable at high temperature, nonvolatile, nontoxic, and have the flexibility to adjust the physicochemical properties of the target compound.^[7] Furthermore, economic and environmental impact standpoint should even be considered in the selection of solvents.^[8]

Ionic liquid-based microwave-assisted extraction (IL-MAE) is one of the non-conventional methods of extraction that has been developed and applied in recent years. The principle of using the IL-MAE is the same as the principle of the MAE method, only differing in the principle and type of solvent used. Success in applying this technique to obtain the optimal of target constituents has been widely reported including resveratrol extraction of *Polygonum cuspidatum* Sieb.et.Zucc.,^[9] phenolic alkaloid extraction of *Nelumbo nucifera* Gaertn.,^[10] Essential oils extraction of some plant, namely *Illicium verum*, *Cuminum cyminum*,^[11] *Schisandra chinensis*,^[12] *Cinnamomum* spp.,^[13] quercetin and kaempferol extraction from *Toona sinensis* and *Rosa sinensis*,^[14] flavonoid extraction from

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Cajanus cajan and *Scutellaria baicalensis*,^[15,16] secondary metabolite and polyphenolic extraction from *Peperomia pellucida* (L) Kunth,^[17,18] and so on. This review aimed to provide detail information about the application of the IL-MAE method as a fast and green extraction of a secondary metabolite from the herbal plant.

MATERIALS AND METHODS

This article reviews about an ionic IL-MAE method for secondary metabolite extraction on the herbal plant from extensive literature. The literature was searched between January and October 2017 from the electronic databases including Google Scholar, DOAJ, PubMed, ScienceDirect, and Scopus.

RESULTS AND DISCUSSION

Ionic liquid as a green solvent for extraction

Knowledge of the solubility properties of the target constituents in the natural products is essential to know for the extraction and separation process to maximally succeed. Some potential components of natural products (especially medicinal plant) have low solubility in water then usually used organic solvents such as alcohols, ethers, ethyl acetate, alkanes, chloroalkanes, and other organic solvents. However, the selection of such solvents can be selected if the targeted or already literature constituents are known. If the information is not available, then it should follow the principle of "like dissolves like."^[19]

The widely accepted and understood polarity concept based on the polarity definition is the number of all intermolecular (specific and nonspecific interactions) between the solvent and the potential of the solute, this interaction produces a chemical reaction.^[20] It can be regarded as both a physical and chemical phenomenon consisting of Coulomb interaction, dipole-dipole interactions, hydrogen bond interactions, and acid-base donor-acceptor interactions. Associated with the polarity of ILs depends on the nature of the components, usually in the range of dipolar nonhydrogen-bond-donation solvents (DMF, DMSO, and acetonitrile) to polar hydrogen-bond-donation solvents (primary alcohols, water).^[19,20] Furthermore, other significant factors affect such as boiling point and melting point, density, viscosity, and surface tension of the solvents.^[21] The ILs can be considered as "self-assembly amphiphiles" that form an H-bonded-polymeric network becomes a common structure pattern as a solid and liquid phase.^[22,23]

The ILs or room temperature ionic liquid is a promising candidate that can meet the above requirements which consist entirely of stable organic

cations and inorganic or organic anions, can be seen in Table 1 which is liquid at room temperature and has unique properties, such as high thermal stability, nonflammability, and low chemical reactivity.^[24-27] Because of these uniqueness that has properties with the viscosity, fine-tunable density, polarity, and miscibility with common organic solvents, which are highly applicable in areas such as analytical chemistry,^[28] catalysts and synthesis,^[29,30] electrochemistry,^[31] and most importantly, ILs can be applied in the separation process (extraction) from natural products.^[27,32-34]

The selection of solvents with the approach of the principle of green chemistry in exploring the constituent target and potential of active compound from natural products continue to rise, in this case, the use of ILs as a green solvent.^[6] The ILs can be employed as a solvent because they have the flexibility of ions combinations (cations and anions) to adjust the physicochemical properties of the target constituents and can be considered possible substituents to replace volatile and toxic organic solvents whereas ILs otherwise.^[7,33] Besides to the physicochemical properties of ILs that affect the extraction results, several other considerations regarding the overall process, economic and environmental impacts standpoint should also be considered.^[8,33,35-37]

The ILs as a solvents are widely used for extracting secondary metabolite (especially polyphenols and alkaloids) from natural products such as 1-butyl-3-methyl imidazolium chloride [BMIM] Cl, 1-butyl-3-methyl imidazolium bromide [BMIM] Br, 1-butyl-3-methyl imidazolium tetrafluoroborate [BMIM] BF₄, 1-butyl-3-methyl imidazolium dihydrogen phosphate [BMIM][H₂SO₄], 1-butyl-3-methyl imidazolium hydrosulfate [BMIM][HSO₄], 1-ethyl-3-methyl imidazolium bromide [EMIM] Br, 1-hexyl-3-methyl imidazolium bromide [HMIM] Br, 1-octyl-3-methyl imidazolium bromide [OMIM] Br, and other types.^[9,16,38-45] In general, the increased ability to attract certain chemical constituents may increase with the increase in hydrophobicity of the solvents used.^[42] Furthermore, the hydrogen bonding capability of ILs is also a factor affecting extraction by considering anions.^[37,46]

Toxicity and environmental impact standpoint

Since the introduction of green chemistry, especially in this case, the use of ILs as an alternative solvent, at that time also there have been concerns related to toxicity and environmental impact by the originators of ILs solvent. In the last 10 years, research efforts have focused on increasing biodegradability and examining the toxicity reduction of ILs.^[47] Furthermore, some studies have reported on ILs, where anions have limited effects on the level of ionic biodegradation and the most

Table 1: Some ionic liquids were used as alternative solvent for extracting secondary metabolite from herbal plants

Ionic Liquids (ILs)	Abbreviation	Melting point °C	Density (g/mL)	Viscosity (cP)	BM
1-ethyl-3-methylimidazolium tetrafluoroborate	(EMIM) (BF ₄)	6	1.248	66	197.8
1-ethyl-3-methylimidazolium hexafluorophosphate	(EMIM) (PF ₆)	58-62	1.373	450	256.13
1-butyl-3-methylimidazolium tetrafluoroborate	(BMIM) (BF ₄)	-82	1.208	233	225.80
1-butyl-3-methylimidazolium hexafluorophosphate	(BMIM) (PF ₆)	10	1.373	400	284.18
1-butyl-3-methylimidazolium bromide	(BMIM) Br	60	1.134	Solid	218.9
1-butyl-3-methylimidazolium chloride	(BMIM) Cl	89	1.120	Solid	146.50
1-butyl-3-methylimidazolium trifluoromethylsulfonate	(BMIM) (CF ₃ SO ₃)	16	1.290	90	260.0
1-butyl-3-methylimidazolium bis (trifluoromethylsulfonyl) amide	(BMIM) (NtfO ₂)	-8	1.404	48	433.0
1-allyl-3-methylimidazolium tetrafluoroborate	(AMIM) (BF ₄)	-88	1.231	321	240.02
1-hexyl-3-methylimidazolium tetrafluoroborate	(HMIM) (BF ₄)	-82	1.075	211	254.08
1-butyl-3-methylimidazolium hexafluorophosphate	(HMIM) (PF ₆)	-61	1.304	800	312.0
1-octyl-3-methylimidazolium tetrafluoroborate	(OMIM) (BF ₄)	-79	1.11	440	281.2
1-octyl-3-methylimidazolium chloride	(OMIM) Cl	0	1.000	16,000	230.50
N-methylpyrrolidinium bis (trifluoromethylsulfonyl) amide	(MPPyr) (NtfO ₂)	0	1.44	39	416
Ethylammonium formate (BAF)	(NHHH ₃)(HCO ₂)	-10	0.99	11.5	91
N-butylpyrrolidinium bis (trifluoromethylsulfonyl) amide	(BMPyrrol) (NtfO ₂)	-50	1.4	71	422

ILs=Ionic liquid

important component is a cation.^[48] The toxicity of ILs is strongly influenced by its lipophilicity associated with the length of the straight chain alkyl and its branching degree and also is affected by its anionic properties.^[49-51] Peric *et al.* has undertaken toxicity assay studies of the protic ILs (derived from aliphatic and organic acid) and the aprotic ILs (imidazolium and pyridinium) groups to aquatic organisms, as well as tests on the enzyme acetylcholinesterase and mouse leukemia cell (IPC-18), with protic ILs activity >100 mg/L, and aprotic ILs weaker than protic IL.^[52]

The main reason for believing that ILs with non-toxic and non-volatile properties, make these solvents potential as a green solvent can be an alternative material or substitute for conventional organic solvents. Unfortunately, this green image is misplaced and recently awakened the consciousness of the chemists, especially those who work in the field of green chemistry. Pham *et al.* have reported that some cations and anions have toxic properties that harmful. However, the risk of harm can be reduced by combining a specific cation and anion into an IL solvent.^[47] On the other hand, combining different functional groups makes it complicated to investigate toxicity because it has functional groups that potentially cytotoxic. Although ILs may help in reducing the risk of air pollution, however, its release to the aquatic environment can cause severe water contamination due to its potential toxicity and its uncontrollable biodegradability.^[53] It has a relatively stable form of an ILs so that it can cause accumulation in the aquatic environment. Related environmental impacts and toxicities have been described in more detail in some literature.^[47,53,54] However, with nonflammable properties and reproducible, so that the utilization of ILs as a green solvent becomes more economical and eco-friendly.

Microwave-assisted extraction

The development of non-conventional extraction methods has been widely practiced. The MAE method is one of the non-conventional methods that is quite easy to apply to extract the target constituent from natural products.^[55-61] Fundamentally, MAE method is different from conventional extraction methods because this extraction occurs as a result of changes in cell structure caused by electromagnetic.^[58]

Kaufmann and Christen^[62] have explained the mechanism of extraction process of the MAE method in more detail and has been clarified by Mandal *et al.*,^[56] Routray and Orsat,^[58] Périno-Issartier *et al.*,^[63] Zhang, *et al.*,^[64] and Sagarika, *et al.*^[65] As can be seen in Figure 1 that has been described by Périno-Issartier *et al.*, in the MAE method involves three steps: (1) separation of solutes from the active side of the sample matrix due to increased temperature and pressure; (2) solvent diffusion across the matrix sample; and (3) the solute release of the matrix sample by the solvent.^[63] Based on these mechanisms, some advantages of MAE methods such as rapid extraction, reducing gradient thermal, and increase the extract yields. In addition, the MAE method is also recognized as a green technology because it reduces the use of solvents.^[56,58,63,64] The MAE method was first introduced and patented as an extraction method for organic compounds by Pare in 1995.^[66] However, it has begun to be applied to extract essential oils from *Cordia curassavica* by Gómez and Witte in 2001.^[67]

The principle of heating using microwave energy is based on the direct effects of microwaves on material molecules.^[62] The transformation of electromagnetic energy occurs through two mechanisms, namely, ionic conduction and dipole rotation in both solvents and samples. In many applications, these two mechanisms co-occur, which effectively convert microwave energy to thermal energy.^[56,58,62-64]

Application of MAE method to extract secondary metabolites of the natural product has been successfully reported. Some studies have been reported including essential oil extraction from *C. curassavica*,^[67]

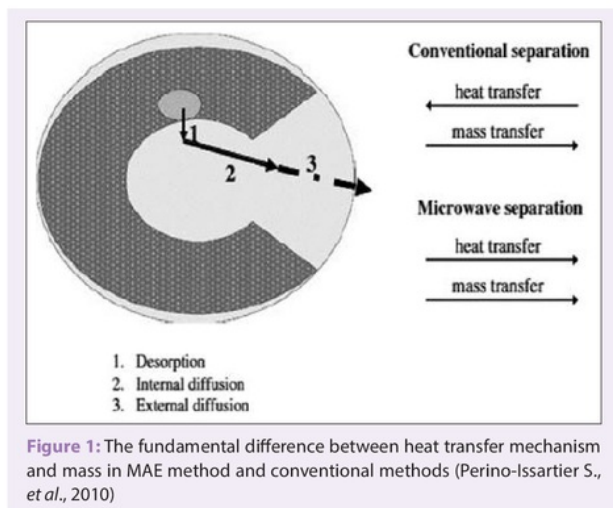


Figure 1: The fundamental difference between heat transfer mechanism and mass in MAE method and conventional methods (Perino-Issartier S., *et al.*, 2010)

26 polyphenols and caffeine extraction from green tea leaves,^[55] flavonoid extraction of *Radix Astragali* (*Astragalus mongolicus*),^[68] phenolics compound extraction of peanut skins and wine lees,^[57,69] phenolic compound extraction from *Gordonia axillaris*,^[70] bioactive alkaloid extraction of *Stephania sinica* and *N. nucifera*,^[59,71] polyphenolics compound extraction from selected medicinal herbs grown in Turkey (including *Hypericum scabrum* L., *Papaver fugax* Poir. var. *platydiscus* Cullen, and *Achillea vermicularis* Trin.),^[61] optimization of green tea waste extraction,^[72] extraction of active compound from *P. pellucida* (L.) Kunth,^[73] and others.

8 Application of ionic liquid-based microwave-assisted extraction to extract secondary metabolites from herbal plant

The use of the IL-MAE method in the development of extraction method to obtain the optimum targeted compound of natural products. As has been described by Bogdanov at chapter 7 in the book entitled "Green Chemistry and Sustainable Technology: Alternative Solvent for Natural Products Extraction,"^[8] some essential factors must be considered to obtain optimal results in the extraction process from natural materials as shown in Figure 2. One of the critical factors to think and focus on this review article is the selection of extraction methods (especially the MAE methods). The utilization of MAE method combined with ILs as a green solvent has been successful and has been done since 2007,^[9] although the use of ILs as a solution has been applied since 2003.^[74]

The IL-MAE method has advantages over other conventional means, besides provides higher yields and shorter extraction time but has also examined economics and environmental impact standpoint as a green solvent. For example, research has been conducted by Du *et al.* shows that resveratrol extraction using ILs is better than using conventional methods as well as MAE methods with conventional organic solvents (methanol),^[9] as well as in other plant species such as *Psidium guajava* and *Smilax china*.^[38] As for the other target group, compounds also successfully performed such as alkaloids,^[75-180] polyphenols,^[18,81] flavonoid,^[16] essential oils,^[11] and other. The optimum condition of IL-MAE depends on the sample matrix of plant and the type of ILs selected, but some terms that are parameters in the optimization process of the IL-MAE [Table 2] include microwave power, ILs concentration, liquid-solid ratio, extraction time, temperature, pH, particle size of samples matrix, and so on.

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Table 2: Application of ionic liquid-based microwave-assisted extraction to extraction the targeted compound from the herbal plant

Herbal plant	Targeted compound	IL used	IL-MAE method and optimum condition	References
<i>Polygonum cuspidatum</i> Sieb.et.Zucc	Trans-resveratrol	[BMIM] Br	2.5 M [BMIM] Br, temperature of 60°C, extraction time of 10 min, particle size of 0.3-0.4 mm, liquid-solid ratio of 20 ml/g	[9]
<i>Illicium verum</i>	Essential oils	[BMIM][PF ₄]	[BMIM][PF ₄], microwave power of 440 W, temperature of 100°C, particle size<0.4 mm, liquid-solid ratio of 20:1.5 (ml/g)	[11]
<i>Cuminum cyminum</i>	Essential oils	[BMIM][PF ₄]	[BMIM][PF ₄], microwave power of 440 W, temperature of 100°C, extraction time of 20 min, particle size<0.4 mm, liquid-solid ratio of 20:1.5 (ml/g)	[11]
<i>Cinnamomum</i> spp.	Essential oils Proanthocyanidins	[BMIM] Br	0.5 M [BMIM] Br, microwave power of 230 W, extraction time of 15 min, and liquid-solid ratio of 10 ml/g	[13]
<i>Rosa sinensis</i>	Quercetin	[OMIM] Br	2.5 M [OMIM] Br, temperature of 70°C, extraction time of 20 min, and liquid-solid ratio of 40 ml/g	[14]
<i>Scutellaria baicalensis</i> Georgi	Flavonoids	[OMIM] Br	1.0 M [OMIM] Br, microwave power of 400 W, extraction time of 90 min, liquid-solid ratio of 6 ml/g	[16]
<i>Peperomia pellucida</i> (L) Kunth	Total polyphenolic content	[BMIM] BF ₄ , [BMIM] Cl, [BMIM] Br, [EMIM] Br	0.79 mol/L [BMIM] BF ₄ , extraction time of 18.5 min, liquid-solid ratio of 10.72 ml/g, and microwave power 270 W	[18]
<i>Radix puerariae</i>	Isoflavone	[BMIM] Br	0.8 mol/L [BMIM] Br, microwave power of 600 W, extraction time of 5 min, temperature of 80°C, and liquid-solid ratio of 20 ml/g	[41]
<i>Nelumbo nucifera</i> Gaertn	Phenolic alkaloid [liensinine, isoliensinine, and neferine)	[BMIM][BF ₄], [HMIM][BF ₄]	1,5 M [BMIM][BF ₄] and 1 M [HMIM](BF ₄), microwave power of 280 W, extraction time of 1.5 min, liquid-solid ratio of 15 and 10 (ml/g), respectively	[10]
<i>Nelumbo nucifera</i>	N-nornuciferine, O-nornuciferine, Nuciferine	[HMIM] Br	1 M [HMIM] Br, microwave power of 280 W, extraction time of 2 min, liquid-solid ratio of 30 ml/g	[76]
<i>Dyosma versipellis</i>	Podophyllotoxin	[BMIM][BF ₄]	0.6 g/mL [BMIM][BF ₄], temperature of 50°C, extraction time of 10 min, liquid-solid ratio of 10 ml/mg	[81]
<i>Sinopodophyllum hexandrum</i>	Podophyllotoxin	[DEMIM][BF ₄]	0.8 g/ml [DEMIM][BF ₄], temperature of 60°C, extraction time of 10 min, liquid-solid ratio of 10 (ml/g)	[81]
<i>Diphylleia sinensis</i>	Podophyllotoxin	[AMIM][BF ₄]	0.4 mg/mL [AMIM][BF ₄], temperature of 50°C, extraction time of 15 min, liquid-solid ratio of 10 (ml/mg)	[81]
<i>Rosmarinus officinalis</i>	Carnosic acid Rosmarinic acid	[OMIM] Br	1 M [OMIM] Br, microwave power of 700 W, extraction time of 15 min, liquid-solid ratio of 12 (ml/g)	[82]
<i>Schisandra chinensis</i>	Essential oils Lignan	[C ₁₂ MIM] Br	0.25 M [C ₁₂ MIM] Br, presoaking for 4 hours, microwave power of 385 W, extraction time of 40 min, and liquid-solid ratio of 12 ml/g	[12]
<i>Myrica rubra</i>	Myricetin Quercetin	[BMIM][HSO ₄]	2.0 M [BMIM][HSO ₄], temperature of 70°C, extraction time of 10 min, and liquid-solid ratio of 30 ml/g	[83]
<i>Bauhinia championii</i> (Benth)	Myrcetin Quercetin Kaempferol	[BMIM] Br	2.0 M [BMIM] Br with 0.8 mol/l HCl, temperature of 70°C, extraction time of 10 min, particle size of<0.30 mm, and liquid-solid ration of 30 ml/g	[84]
<i>Dryopteris fragrans</i>	Phloroglucinols	[OMIM] Br	0.75 [OMIM] Br, temperature of 50°C, microwave power of 600 W, extraction time of 7 min, and liquid-solid ratio of 12 ml/g	[85]
Lemon Peels	Pectin	[BMIM] Br	0.1 M [BMIM] Br, temperature of 60°C, extraction time of 8 min, and liquid-solid ratio 20 ml/g	[86]
<i>Cajanus cajan</i>	Glycoside Flavonoid	[BMIM] Br	1.0 M [BMIM] Br, temperature of 60°C, extraction time of 13 min, and liquid-solid ratio of 20 ml/g	[87]
<i>Pseudo-nitzschia calliantha</i> H. Andr	Phenolic compound	[BMIM] BF ₄	0.5 M [BMIM] BF ₄ , microwave power of 700 W, temperature of 40°C, extraction time of 15 min, and liquid-solid ratio 20 ml/g	[88]

Contd...

Table 2: Contd...

Herbal plant	Targeted compound	IL used	IL-MAE method and optimum condition	References
<i>Gnetum gneton</i>	Transresveratrol	[BMIM] Br	2.5 mol/l [BMIM] Br, microwave power of 90 W, extraction time of 10 min, liquid–solid ratio of 15 ml/g	[89]
Rice bran (<i>Oryza sativa</i>)	Gamma-oryzanol	[BMIM] PF ₆	1 M [BMIM] PF ₆ , microwave power of 270 W, extraction time of 10 min, liquid–solid ratio of 10 ml/g	[90]

IL-MAE=Ionic liquid based microwave-assisted extraction, IL=Ionic liquid, [OMIM] Br=1-octyl-3-methyl imidazolium bromide, [BMIM] Br=1-butyl-3-methyl imidazolium bromide, [BMIM]BF₄=1-butyl-3-methylimidazolium tetrafluoroborate, [BMIM]Cl=1-butyl-3-methylimidazolium chloride, [EMIM] Br=1-ethyl-3-methyl imidazolium bromide [HMIM] Br=1-hexyl-3-methyl imidazolium bromide, [BMIM][HSO₄]=1-butyl-3-methyl imidazolium hydrosulfate, [AMIM] [BF₄]=1-allyl-3-methylimidazolium tetrafluoroborate, [HMIM][BF₄]=1-hexyl-3-methylimidazolium tetrafluoroborate, [BMIM] PF₆=1-butyl-3-methylimidazolium hexafluorophosphate, [BMIM][PF₆]= 1-butyl-3-methylimidazolium tetrafluorophosphate, [C₁₂MIM]Br=1-dodecyl-3-methylimidazolium bromide, [DEMIM] [BF₄]= 1-decyl-3-methylimidazolium tetrafluoroborate

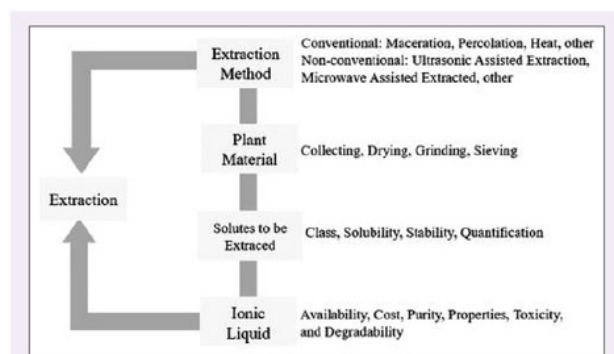


Figure 2: The main factors to be considered before extraction process

Mechanism of ionic liquid-based microwave-assisted extraction method on extraction process

The mechanism of the IL-MAE method was first reported by Du *et al.* with measuring the kinetic of polyphenolic constituent extraction using an ILs as a green solvent.^[38] The mechanism of extraction was conducted using Fourier-transform infrared spectroscopy and scanning electron microscopy (SEM), by observing the extent of damage to the cell surface of the sample matrix. A study carried out by Du *et al.* showed similar mechanisms for quercetin and kaempferol extraction from *T. sinensis* and *R. sinensis* using IL-MAE with (BMIM) Br and (OMIM) Br.^[38] Ahmad *et al.* demonstrated that the surface and cell wall structures of *P. pellucida* sample was visibly destroyed after IL-MAE and maceration extraction treatment [Figure 3].^[91] A synergic reaction between microwave irradiation and the penetration of ILs solvent combination causes damage to the surface of the cell wall so that the secondary metabolite constituent contained in the sample matrix can pass through the damaged cell gap. The effect of extraction condition factors using the IL-MAE method in more detail on the extent of damage to the wall of the sample matrix was described in some literature.^[38,86,87,92,93]

Based on Figure 3, the SEM analysis results show significant physical changes in the plant tissue after treatment with different solvents. It was demonstrated differences in cell wall surface changes in samples that have been extracted using the IL-MAE method compared to maceration method and the untreated sample, whereas the ratio of the rate of surface changes of the cell wall the untreated sample and after the maceration extraction is not significantly different. The result of the SEM analysis correlates with the yields value (total polyphenol content) generated by the maceration extraction and the IL-MAE extraction.^[91] Gross *et al.* (2011) have explained the reason why cellulose can be dissolved in

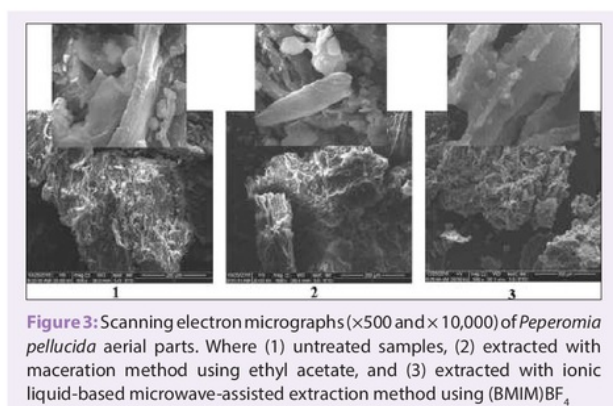


Figure 3: Scanning electron micrographs (×500 and ×10,000) of *Peperomia pellucida* aerial parts. Where (1) untreated samples, (2) extracted with maceration method using ethyl acetate, and (3) extracted with ionic liquid-based microwave-assisted extraction method using (BMIM)BF₄

ILs, but not in water, with the assumptions that anions of ILs can interact with hydroxyl protons from cellulose, and the coupling of cations to the side chain and oxygen binder strongly in peeling conditions.^[94] Payal *et al.* have also performed quantum chemical calculations on a group of solvent molecules to dissolve cellulose units, with the hypothesis that all intramolecular hydrogen bonds have been explicitly deleted on the ILs media because of the strong interaction of hydrogen bonds between cellulose and ILs.^[95] Thus, cell walls are easily damaged with ILs using heat extraction. That is the reason why extraction methods with heating or other nonconventional methods based on ILs take a short time compared to conventional organic solvent-based extraction methods. Therefore, the ILs solvent can be used as an alternative or green solvent which continues to be developed primarily for extracting the active components of medicinal plants with the aid of non-conventional extraction methods.

CONCLUSION

The application of IL-MAE method has been successfully performed to extract the targeted secondary metabolite from a natural product and provides higher yields and extraction rate with less solvent, short time (rapid), and energy consumption compared with conventional extraction method.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Cragg GM, Newman DJ. Natural products: A continuing source of novel drug leads. *Biochim Biophys Acta* 2013;1830:3670-95.
- Azmir J, Zaidul IS, Rahman MM, Sharif KM, Mohamed A, Saheha F, et al. Techniques for extraction of bioactive compounds from plant materials: A review. *J Food Eng* 2013;117:426-36.
- Bucar F, Wube A, Schmid M. Natural product isolation – How to get from biological material to pure compounds. *Nat Prod Rep* 2013;30:525-45.
- Sarker SD, Nahar L. *Natural Products Isolation*. 3rd ed. New York, Dordrecht, Heidelberg: London Library, Springer; 2012.
- Khoddami A, Wilkes MA, Roberts TH. Techniques for analysis of plant phenolic compounds. *Molecules* 2013;18:2328-75.
- Espino M, Fernández MD, Gomez FJ, Silva MF. Natural designer solvents for greening analytical chemistry. *Trends Anal Chem* 2016;76:126-36.
- Jessop PG, Jessop DA, Fu D, Phan L. Solvatochromic parameters for solvents of interest in green chemistry. *Green Chem* 2012;14:1245.
- Chemat F, Vian MA. *Green Chemistry and Sustainable Technology: Alternative Solvents for Natural Products Extraction*. Heidelberg, New York, Dordrecht, London: Springer, US.; 2014.
- Du FY, Xiao XH, Li GK. Application of ionic liquids in the microwave-assisted extraction of trans-resveratrol from *Rhizma Polygoni Cuspidati*. *J Chromatogr A* 2007;1140:56-62.
- Lu Y, Ma W, Hu R, Dai X, Pan Y. Ionic liquid-based microwave-assisted extraction of phenolic alkaloids from the medicinal plant *Nelumbo nucifera* Gaertn. *J Chromatogr A* 2008;1208:42-6.
- Zhai Y, Sun S, Wang Z, Cheng J, Sun Y, Wang L, et al. Microwave extraction of essential oils from dried fruits of *Illium verum* Hook. f. and *Cuminum cyminum* L. using ionic liquid as the microwave absorption medium. *J Sep Sci* 2009;32:3544-9.
- Ma CH, Liu TT, Yang L, Zu YG, Chen X, Zhang L, et al. Ionic liquid-based microwave-assisted extraction of essential oil and biphenyl cyclooctene lignans from *Schisandra chinensis* Baill fruits. *J Chromatogr A* 2011;1218:8573-80.
- Liu Y, Yang L, Zu Y, Zhao C, Zhang L, Zhang Y, et al. Development of an ionic liquid-based microwave-assisted method for simultaneous extraction and distillation for determination of proanthocyanidins and essential oil in *Cortex cinnamomi*. *Food Chem* 2012;135:2514-21.
- Liu X, Huang X, Wang Y, Huang S, Lin X. Design and performance evaluation of ionic liquid-based microwave-assisted simultaneous extraction of kaempferol and quercetin from Chinese medicinal plants. *Anal Methods* 2013;5:2591-601.
- Wei W, Fu YJ, Zu YG, Wang W, Luo M, Zhao CJ, et al. Ionic liquid-based microwave-assisted extraction for the determination of flavonoid glycosides in pigeon pea leaves by high-performance liquid chromatography-diode array detector with pentafluorophenyl column. *J Sep Sci* 2012;35:2875-83.
- Zhang Q, Zhao SH, Chen J, Zhang LW. Application of ionic liquid-based microwave-assisted extraction of flavonoids from *Scutellaria baicalensis* Georgi. *J Chromatogr B Analyt Technol Biomed Life Sci* 2015;1002:411-7.
- Ahmad I, Yanuar A, Mulia K, Mun'im A. Application of ionic liquid-based microwave-assisted extraction of the secondary metabolite from *Peperomia pellucida* (L.) Kunth. *Pharmacogn J* 2017;9:227-34.
- Ahmad I, Yanuar A, Mulia K, Mun'im A. Optimization of ionic liquid-based microwave-assisted extraction of polyphenolic content from *Peperomia pellucida* (L.) Kunth using response surface methodology. *Asian Pac J Trop Biomed* 2017;7:660-5.
- Hanani E. *Analisis Fitokimia*. Jakarta: Penerbit Buku Keokteran, EGC; 2015.
- Reichardt C. Polarity of ionic liquids determined empirically by means of solvatochromic pyridinium N-phenolate betaine dyes. *Green Chem* 2005;7:339-51.
- Jacquemin J, Husson P, Padua AA, Majer V. Density and viscosity of several pure and water-saturated ionic liquids. *Green Chem* 2006;8:172-80.
- Dupont J. On the solid, liquid, and solution structural organization of imidazolium ionic liquids. *J Braz Chem Soc* 2004;15:341-50.
- Greaves TL, Drummond CJ. Solvent nanostructure, the solvophobic effect and amphiphile self-assembly in ionic liquids. *Chem Soc Rev* 2013;42:1096-120.
- Ventura SP, e Silva FA, Gonçalves AM, Pereira JL, Gonçalves F, Coutinho JA, et al. Ecotoxicity analysis of cholinium-based ionic liquids to *Vibrio fischeri* marine bacteria. *Ecotoxicol Environ Saf* 2014;102:48-54.
- Bogdanov MG, Kantelehner W. Simple prediction of some physical properties of ionic liquids: The residual volume approach. *Z Naturforsch* 2009;64:215-22.
- Bogdanov MG, Iliev B, Kantelehner W. The residual volume approach II: Simple prediction of ionic conductivity of ionic liquids. *Z Naturforsch B* 2009;64:756-64.
- Poole CF, Poole SK. Ionic liquid stationary phases for gas chromatography. *J Sep Sci* 2011;34:888-900.
- Ho TD, Zhang C, Hantao LW, Anderson JL. Ionic liquids in analytical chemistry: Fundamentals, advances, and perspectives. *Anal Chem* 2014;86:262-85.
- Parvulescu VI, Hardacre C. Catalysis in ionic liquids. *Chem Rev* 2007;107:2615-65.
- Hallett JP, Welton T. Room-temperature ionic liquids: Solvents for synthesis and catalysis 2. *Chem Rev* 2011;111:3508-76.
- Opallo M, Lesniewski A. A review on electrodes modified with ionic liquids. *J Electroanal Chem* 2011;656:2-16.
- Poole CF, Poole SK. Extraction of organic compounds with room temperature ionic liquids. *J Chromatogr A* 2010;1217:2268-86.
- Chemat F, Vian MA, Cravotto G. Green extraction of natural products: Concept and principles. *Int J Mol Sci* 2012;13:8615-27.
- Petigny L, Périno S, Minuti M, Visinoni F, Wajsman J, Chemat F, et al. Simultaneous microwave extraction and separation of volatile and non-volatile organic compounds of boldo leaves. From lab to industrial scale. *Int J Mol Sci* 2014;15:7183-98.
- Zhang S, Lu X, Zhou Q, Li X, Zhang X, Li S. *Ionic Liquids Physicochemical Properties*. 1st ed. Amsterdam: Elsevier B.V.; 2009.
- Smiglak M, Pringle JM, Lu X, Han L, Zhang S, Gao H, et al. Ionic liquids for energy, materials, and medicine. *Chem Commun (Camb)* 2014;50:9228-50.
- Cláudio AF, Swift L, Hallett JP, Welton T, Coutinho JA, Freire MG, et al. Extended scale for the hydrogen-bond basicity of ionic liquids. *Phys Chem Chem Phys* 2014;16:6593-601.
- Du FY, Xiao XH, Luo XJ, Li GK. Application of ionic liquids in the microwave-assisted extraction of polyphenolic compounds from medicinal plants. *Talanta* 2009;78:1177-84.
- Fan JP, Cao J, Zhang XH, Huang JZ, Kong T, Tong S, et al. Optimization of ionic liquid based ultrasonic assisted extraction of puerarin from *Radix Puerariae Lobatae* by response surface methodology. *Food Chem* 2012;135:2299-306.
- Liu F, Wang D, Liu W, Wang X, Bai A, Huang L. Separation and purification technology ionic liquid-based ultrahigh pressure extraction of five tanshinones from *Salvia miltiorrhiza* Bunge. *Sep Purif Technol* 2013;110:86-92.
- Zhang Y, Liu Z, Li Y, Chi R. Optimization of ionic liquid-based microwave-assisted extraction of isoflavones from *Radix Puerariae* by response surface methodology. *Sep Purif Technol* 2014;129:71-9.
- Tan Z, Yi Y, Wang H, Zhou W, Wang C. Extraction, preconcentration and isolation of flavonoids from *Apocynum venetum* L. Leaves using ionic liquid-based ultrasonic-assisted extraction coupled with an aqueous biphasic system. *Molecules* 2016;21:262.
- Wang XH, Cai C, Li XM. Optimal extraction of gallic acid from *Suaeda glauca* Bge. Leaves and enhanced efficiency by ionic liquids. *Int J Chem Eng* 2016;2016:1-9.
- Chen F, Zhang Q, Mo K, Fei S, Gu H, Yang L. Optimization of ionic liquid-based homogenate extraction of orientin and vitexin from the flowers of *Trollius chinensis* and its application on a pilot scale. *Sep Purif Technol* 2017;175:147-57.
- Gu H, Chen F, Zhang Q, Zang J. Application of ionic liquids in vacuum microwave-assisted extraction followed by macroporous resin isolation of three flavonoids rutin, hyperoside and hesperidin from *Sorbus tianschanica* leaves. *J Chromatogr B Analyt Technol Biomed Life Sci* 2016;1014:45-55.
- Cláudio AF, Marques CF, Boal-Palheiros I, Freire MG, Coutinho JA. Development of back-extraction and recyclability routes for ionic-liquid-based aqueous two-phase systems. *Green Chem* 2014;16:259-68.
- Pham TP, Cho CW, Yun YS. Environmental fate and toxicity of ionic liquids: A review. *Water Res* 2010;44:352-72.
- Zhang C, Wang H, Malhotra SV, Dodge CJ, Francis AJ. Biodegradation of pyridinium-based ionic liquids by an axenic culture of soil *Corynebacteria*. *Green Chem* 2010;12:851-8.

49. Landry TD, Brooks K, Poche D, Woolhiser M. Acute toxicity profile of 1-butyl-3-methylimidazolium chloride. *Bull Environ Contam Toxicol* 2005;74:559-65.
50. Petkovic M, Ferguson JL, Gunaratne HQ, Ferreira R, Leitão MC, Seddon KR, et al. Novel biocompatible cholinium-based ionic liquids-toxicity and biodegradability. *Green Chem* 2010;12:643.
51. Garcia H, Ferreira R, Petkovic M, Ferguson JL, Leitao MC, Gunaratne HQ, et al. Dissolution of cork biopolymers in biocompatible ionic liquids. *Green Chem* 2010;12:367.
52. Peric B, Sierra J, Martí E, Cruañas R, Garau MA, Arning J, et al. (Eco) toxicity and biodegradability of selected protic and aprotic ionic liquids. *J Hazard Mater* 2013;261:99-105.
53. Bubalo MC, Radošević K, Redovniković IR, Halambek J, Srček VG. A brief overview of the potential environmental hazards of ionic liquids. *Ecotoxicol Environ Saf* 2014;99:1-2.
54. Olivier-Bourbigou H, Magna L, Morvan D. Ionic liquids and catalysis: Recent progress from knowledge to applications. *Appl Catal A Gen J* 2010;373:1-56.
55. Pan X, Niu G, Liu H. Microwave-assisted extraction of tea polyphenols and tea caffeine from green tea leaves. *Chem Eng Process* 2003;42:129-33.
56. Mandal V, Mohan Y, Hemalatha S. Microwave-assisted extraction – An innovative and promising extraction tool for medicinal plant research. *Pharmacogn Rev* 2007;1:7-18.
57. Ballard TS, Mallikarjunan P, Zhou K, Keefe SO. Microwave-assisted extraction of phenolic antioxidant compounds from peanut skins. *Food Chem* 2010;120:1185-92.
58. Routray W, Orsat V. Microwave-assisted extraction of flavonoids: A review. *Food Bioprocess Technol* 2012;5:409-24.
59. Xie DT, Wang YQ, Kang Y, Hu QF, Su NY, Huang JM, et al. Microwave-assisted extraction of bioactive alkaloids from *Stephania sinica*. *Sep Purif Technol* 2014;130:173-81.
60. Rodríguez-Pérez C, Gilbert-López B, Mendiola JA, Quirantes-Piné R, Segura-Carretero A, Ibáñez E. Optimization of microwave-assisted extraction and pressurized liquid extraction of phenolic compounds from *Moringa oleifera* leaves by multiresponse surface methodology. *Electrophoresis* 2016;37:1938-46.
61. Baki S, Tufan AN, Altun M, Özgökçe F, Güçlü K, Özyürek M. Microwave-assisted extraction of polyphenolics from some selected medicinal herbs grown in Turkey. *Rec Nat Prod* 2018;12:29-39.
62. Kaufmann B, Christen P. Recent extraction techniques for natural products: Microwave-assisted extraction and pressurized solvent extraction. *Phytochem Anal* 2002;13:105-13.
63. Périno-Issartier S, Zill-e-Huma Z, Abert-Vian M, Chemat F. Solvent free microwave-assisted extraction of antioxidants from Sea Buckthorn (*Hippophae rhamnoides*) food by-products. *Food Bioprocess Technol* 2011;4:1020-8.
64. Zhang HF, Yang XH, Wang Y. Microwave-assisted extraction of secondary metabolites from plants: Current status and future directions. *Trends Food Sci Technol* 2011;22:672-88.
65. Sagarika N, Prince M, Sreeja R. Review on microwave-assisted extraction technique. *Int J Pure Appl Biosci* 2017;5:1065-74.
66. Pare J. Microwave-Assisted Extraction from Materials Containing Organic Matter. United State Patent; Patent Number: 5,458,897; 1995.
67. Gómez NE, Witte L. A simple method to extract essential oils from tissue samples by using microwave radiation. *J Chem Ecol* 2001;27:2351-9.
68. Xiao W, Han L, Shi B. Microwave-assisted extraction of flavonoids from *Radix Astragalii*. *Sep Purif Technol* 2008;62:614-8.
69. Pérez-Serradilla J, Castro M. Microwave-assisted extraction of phenolic compounds from wine lees and spray-drying of the extract. *Food Chem* 2011;124:1652-9.
70. Li Y, Li S, Lin SJ, Zhang JJ, Zhao CN, Li HB, et al. Microwave-assisted extraction of natural antioxidants from the exotic *Gordonia axillaris* fruit: Optimization and identification of phenolic compounds. *Molecules* 2017;22. pii: E1481.
71. Xiong W, Chen X, Lv G, Hu D, Zhao J, Li S. Optimization of microwave-assisted extraction of bioactive alkaloids from lotus plumule using response surface methodology. *J Pharm Anal* 2016;6:382-8.
72. Handayani D, Mun'im A, Ranti AS. Optimization of green tea waste extraction using microwave-assisted extraction to yield green tea extract. *Tradit Med J* 2014;19:29-35.
73. Mun'im A, Nurpriantia S, Setyaningsih R, Syahdi RR. Optimization of microwave-assisted extraction of active compounds, antioxidant activity and angiotensin-converting enzyme (ACE) inhibitory activity from *Peperomia pellucida* (L.) Kunth. *J Young Pharm* 2017;9:168-71.
74. Cláudio AF, Ferreira AM, Freire MG, Coutinho JA. Enhanced extraction of caffeine from Guarana seeds using aqueous solutions of ionic liquids. *Green Chem* 2013;15:2002-10.
75. Sun C, Liu H. Application of non-ionic surfactant in the microwave-assisted extraction of alkaloids from *Rhizoma Coptidis*. *Anal Chim Acta* 2008;612:160-4.
76. Ma W, Lu Y, Hu R, Chen J, Zhang Z, Pan Y, et al. Application of ionic liquids based microwave-assisted extraction of three alkaloids N-nornuciferine, O-nornuciferine, and nuciferine from lotus leaf. *Talanta* 2010;80:1292-7.
77. Bogdanov MG, Svinjarov I. Ionic liquid-supported solid-liquid extraction of bioactive alkaloids. II. Kinetics, modeling and mechanism of glaucine extraction from *Glaucium flavum* Cr. (Papaveraceae). *Sep Purif Technol* 2013;103:279-88.
78. Bogdanov MG, Svinjarov I, Keremedchieva R, Sidjimov A. Ionic liquid-supported solid-liquid extraction of bioactive alkaloids. I. New HPLC method for quantitative determination of glaucine in *Glaucium flavum*. *Sep Purif Technol* 2012;97:221-7.
79. Bogdanov MG, Keremedchieva R, Svinjarov I. Ionic liquid-supported solid-liquid extraction of bioactive alkaloids. III. Ionic liquid regeneration and glaucine recovery from ionic liquid-aqueous crude extract of *Glaucium flavum* Cr. (Papaveraceae). *Sep Purif Technol* 2015;2015:13-9.
80. Sixt M, Koudous I, Strube J. Process design for integration of extraction, purification and formulation with alternative solvent concepts. *Comptes Rendus Chim* 2016;19:733-48.
81. Yuan Y, Wang Y, Xu R, Huang M, Zeng H. Application of ionic liquids in the microwave-assisted extraction of podophyllotoxin from Chinese herbal medicine. *Analyst* 2011;136:2294-305.
82. Liu T, Sui X, Zhang R, Yang L, Zu Y, Zhang L, et al. Application of ionic liquids based microwave-assisted simultaneous extraction of carnosic acid, rosmarinic acid and essential oil from *Rosmarinus officinalis*. *J Chromatogr A* 2011;1218:8480-9.
83. Du FY, Xiao XH, Li GK. Ionic liquid aqueous solvent-based microwave-assisted hydrolysis for the extraction and HPLC determination of myricetin and quercetin from *Myrica rubra* leaves. *Biomed Chromatogr* 2011;25:472-8.
84. Xu W, Chu K, Li H, Zhang Y, Zheng H, Chen R, et al. Ionic liquid-based microwave-assisted extraction of flavonoids from *Bauhinia championii* (Benth.) benth. *Molecules* 2012;17:14323-35.
85. Li XJ, Yu HM, Gao C, Zu YG, Wang W, Luo M, et al. Application of ionic liquid-based surfactants in the microwave-assisted extraction for the determination of four main phloroglucinols from *Dryopteris fragrans*. *J Sep Sci* 2012;35:3600-8.
86. Guolin H, Jeffrey S, Kai Z, Xiaolan H. Application of ionic liquids in the microwave-assisted extraction of pectin from lemon peels. *Anal Methods* 2012;4:1012-8.
87. Wei Z, Qi X, Li T, Luo M, Wang W, Zu Y, et al. Application of natural deep eutectic solvents for extraction and determination of phenolics in *Cajanus cajan* leaves by ultra performance liquid chromatography. *Sep Purif Technol* 2015;149:237-44.
88. Zhang DY, Yao XH, Duan MH, Luo M, Wang W, Fu YJ, et al. An effective negative pressure cavitation-microwave assisted extraction for determination of phenolic compounds in *P. calliantha* H. Andr. *Analyst* 2013;138:4631-41.
89. Ayuningtyas IN, Rahmawati M, Sutriyo S, Mun'im A. Optimization of ionic liquid-based microwave assisted extraction to obtain trans-resveratrol from *Gnetum gnetum* L. Seeds. *J Young Pharm* 2017;9:168-71.
90. Trinovita E, Sutriyo S, Saputri FC, Mun'im A. Enrichment of the gamma oryzanol level from rice bran by addition of inorganic salts on ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate ([BMIM] PF6) extraction. *J Young Pharm* 2017;9:555-8.
91. Ahmad I, Yanuar A, Mulia K, Mun'im A. Application of ionic liquid as a green solvent for polyphenolics content extraction of *Peperomia pellucida* (L) Kunth herb. *J Young Pharm* 2017;9:S1-4.
92. Cláudio AF, Ferreira AM, Freire MG, Coutinho JA. Enhanced extraction of caffeine from Guarana seeds using aqueous solutions of ionic liquids. *Green Chem* 2010;12:1481-675.
93. Yansheng C, Zhida Z, Changping L, Qingshan L, Peifang Y, Welz-Biermann U. Microwave-assisted extraction of lactones from *Ligusticum chuanxiang* Hort. using protic ionic liquids. *Green Chem* 2011;13:666-70.
94. Gross AS, Bell AT, Chu JW. Thermodynamics of cellulose solvation in water and the ionic liquid 1-butyl-3-methylimidazolium chloride. *J Phys Chem B* 2011;115:13433-40.
95. Payal RS, Bharath R, Periyasamy G, Balasubramanian S. Density functional theory investigations on the structure and dissolution mechanisms for cellobiose and xylan in an ionic liquid: Gas phase and cluster calculations. *J Phys Chem B* 2012;116:833-40.

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