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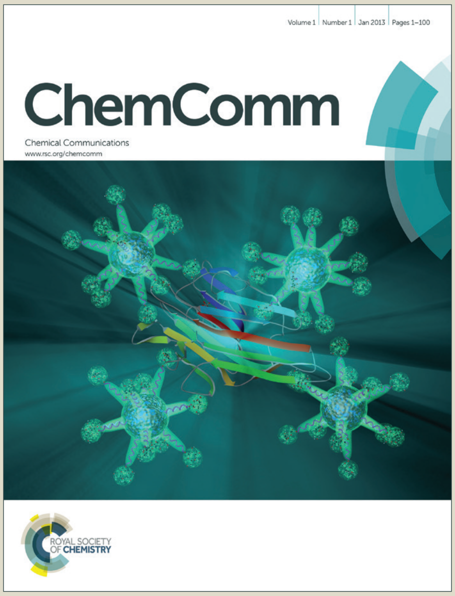

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ARTICLE TYPE

Deep eutectic solvents as novel extraction media for phenolic compounds from model oil

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Deep eutectic solvents (DES) as a new kind of green solvents were used for the first time to excellently extract phenolic compounds from model oil. It was also proved that DES can be used to extract other polar compounds from non-polar or weak-polar solvents by liquid-phase microextraction.

During the chemical analysis, sample pretreatment is usually necessary in order to extract and concentrate the trace amounts of analytes in complex sample. How to develop a faster, simpler, and more inexpensive and environmentally-friendly sample-preparation technique is very important in modern society.[1] From 1998, ionic liquids (ILs) have been frequently proposed as an alternative to organic solvents due to their low vapor pressure and their high viscosity, which allow the green and reproducible extracting process.[2] However, compared with organic solvents, most ILs are more difficult and more costly to be prepared, and ILs' eco-friendly is challenged.[3]

In 2003, deep eutectic solvents (DESs) were developed by Abbott et al., which are generally composed of two or three cheap and safe components that are capable of self-association, often through hydrogen bond interactions, to form a eutectic mixture with a melting point lower than that of each individual component.[4] Their physical properties and phase behavior are similar to ionic liquids. The ease of synthesis, availability and biodegradability of the components make these DESs versatile alternatives to ionic liquids as reviewed by the literature.[5] In recent years, DES is rapidly emerging in the different research fields.[6]

The excellent properties of DES also highlight their advantages as promising inexpensive green solvents for chemical analysis, including the extraction of desulfurization products of fuels,[6d] the determination of Cu, Fe, Ni and Zn in marine biological samples,[7] the extraction media for azeotropic mixtures[8] and a range of bioactive compounds from natural products.[9]

On the other hand, liquid phase microextraction (LPME) is normally performed to concentrate analytes into a small amount of a water-immiscible solvent from an aqueous sample.[1,10] In the past decades, ultrasonic wave has been widely used in dispersion, emulsification, activating chemical synthesis and so on, depend upon its unique properties.[11] Furthermore, in recent years, ultrasonic wave was applied to the liquid-liquid extraction to enhance the dispersion of samples and improve the interaction of targets.[12] The current DES are belong to a kind of polar and water-miscible solvents, which cannot be used to extract the analytes by immerging directly from aqueous sample. However, DES should have the potential ability to extract the analytes from non-aqueous sample. Guo et al. separated phenols effectively from model oils via a clever method by the forming of deep eutectic solvents from quaternary ammonium salts and phenol.[13]

In this work, DES was directly used as novel green and inexpensive extractant to concentrate the polar compounds including phenols, amines and acids from non-polar solvents by the proposed ultrasonic wave-assisted LPME method.

The syntheses of DESs were conducted as described elsewhere.[4,5a,14] Briefly, DESs were obtained by simply mixing the halide salts (HS) and hydrogen bond donors (HBD) together at a proper molar ratio with magnetic agitation at 80~100 ℃ until clear and colorless liquid formed, as shown in Fig. S1 (ESI). Table S1 (ESI) lists their compostions and the freezing points and the viscosities (25 ℃) of studied DESs.

The selection of the acceptor phase is important in LPME to achieve good selectivity and efficient analyte enrichment. In the direct-immersion LPME, the acceptor phase must form a liquid droplet in the sample solution.[15] According to the existing research reports,[5b,6e,16] nearly all the DESs are lipophobic and can readily form a liquid droplet in non-polar solvents. However, it is not that all the DESs are liquid at room temperature. Furthermore, the DES's physicochemical properties have significant influence on extraction efficiency of the target analytes. Therefore, four room-temperature DESs were selected as the acceptor phase. In the optimized experiments, considering the factors effecting extraction efficiency, such as the viscosity of DES, the polarity of sample compounds, π-π stacking, hydrogen bonding interaction and homologous affinity of the same atom between DES and sample compounds, DES-1 was selected as the acceptor phase for three phenols in order to obtain higher extraction efficiency.

The direct-immersion LPME procedure was as follows. 10 μL of DES was aspirated into a 50-μL microsyringe (Shimadzu-GL), which was added into a 1.5-mL centrifuge tube containing 1 mL of sample solution (Fig. S2A, ESI). After shaking and then balanced with ultrasonic wave for 3 min (Fig. S2B, ESI), the acceptor solvent (DES) was again aspirated into the microsyringe and injected into the HPLC system for analysis.

Hexane is of lower toxicity and could give the highest extraction efficiency for the used polar compounds, and this could be attributed to its lower polarity, among the solvents investigated. The preliminary experiment demonstrated that the effect of temperature is insignificant for extraction efficiency of polar compounds from hexane to DES under the ultrasonic wave-assisted condition at temperature lower than the boiling point of hexane (69 ℃). Thus, further experiments were conducted using hexane as the sample solvent at room temperature to minimize the sample compounds' volatilization.

It is well-known that ultrasonic wave can apply to the liquid-liquid extraction to enhance the dispersion of samples and improve the mass transfer of sample compounds. In the following study, ultrasonic wave was adopted to affect the time required for extraction equilibrium.[17] As the results demonstrated, extraction equilibrium of the polar compounds from hexane to DES was established in only 3 minutes. Fig. 1A showed the influence of extraction time on the peak area of phenols and when DES-1 was used as extractant for phenols, where it was observed that the peak area increased with enrichment time over the range of 1~3 min, and then maintained constant after 3 min (the longest tested time was 30 min), which was much different from the case of traditional LPME, which suffered decreased efficiency at longer extraction time (60 min) due to the dissolution of extractant in sample solution. The reasons may reside in that insolubility of DES in sample solution, as well as the saturation of samples in DES.

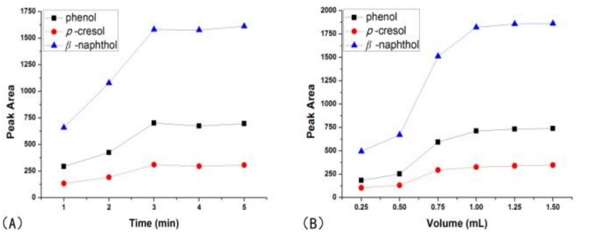

Fig. 1 The effect of ultrasonic wave-assisted extraction time (A) and the sample extraction solution volume (B) on for three phenols. Sample concentration: 10 μg/L, volume of DES: 10 μL.

The effect of the volume of sample solution on extraction efficiency, represented by HPLC peak area, was studied by exposing 10 μL of DES-1 droplet into different volumes of sample solutions for 3 min. the results showed in Fig. 1B indicated that the peak area increased with the increase of solution volume in the range of 0.25~1.00 mL and then maintained almost fixed in the range of 1.00~1.50 mL (the largest tested volume was 3.00 mL). Due to LPME's a non-equilibrium nature in consideration of varying volume of extractant, the enrichment was controlled by diffusion of analytes.[1,2b,15] LPME should not always be non-equilibrium in nature, however, for the given volume of 10 μL of DES-1 droplet under the ultrasonic wave-assisted condition, a relative equilibrium was maintained beyond the saturation point, irrespective of the increase of sample solution volume, as the volume of DES was constant and the DES was hardly dissolved in the sample solution.

In order to get insight into the DES's excellence in extraction of polar compounds from non-polar solvents, a comparative study was carried out to illustrate the enrichment efficiency of water, DES-1 and its individual components as the extractant, repectively, for the phenols. The enrichment factors were calculated according to the following equation.

$$\mathrm{EF} = {\mathrm{C}_{\mathrm{a,final}}}\Big/{\mathrm{C}_{\mathrm{s,initial}}}$$

where $C_{a,\ final}$ is the final concentration of analyte in the acceptor solvent, and $C_{s,\ initial}$ is the initial analyte concentration in the sample solution. According to above experiments, the optimized extraction condition was set as 10 μL for sampling volume, 3 min for extraction time, 1.00 mL for sample extraction solution (10 μg/L), in ultrasonic wave-assisted condition at room temperature. As displayed in Fig. 2A, DES-1 provided a much larger enrichment factor (EF) than others studied polar acceptor solvent, such as water, the mixture (W-D) of water and DES (1:1, v/v), the aqueous solution of choline chloride (1:3, molar ratio of ChCl to Water), ethylene glycol and DES. It could be perceived that any single component was dwarfed by corresponding DES of high extraction efficiency. The main reason could be DES's superior dissolving capacity for the polar compounds.

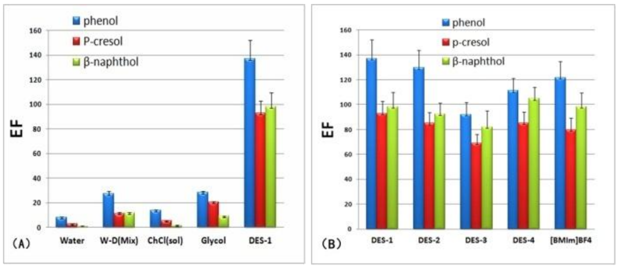

Fig. 2 (A) The effect of the different acceptor solvents for three phenols. Extractant from left to right: water, W-D (mix): the mixture of water and DES (1:1, v/v), ChCl (sol): the aqueous solution of choline chloride (1:3, molar ratio of ChCl to Water), Glycol, DES-1. (B) The effect of the different DES with IL as acceptor solvents. Extraction time: 3 min, Extractant volume: 10 μL.

In LPME，the obtained enrichment factor is a complex result of various parameters including partition coefficient, the diffusion coefficient of the solute, the viscosity of both sample solution and acceptor solvent, in addition to the outer conditions. Thus, the influences of the different halide salts and hydrogen bond donors were investigated. As Fig. 2B showed, comparing the enrichment factors of DES-1 and DES-2 at the equal HS/HBD molar ratio, it was intuitive that the effect of hydrogen bond donors was insignificant on extraction efficiency of three phenols. However, it was clear that the enrichment factors of DES-1, DES-2 and DES-3 for three phenols slighted declined. This may be ascribed to the viscosity of the DESs varied in the sequence DES-1 < DES-2 < DES-3, and it was observed in our experiments that the enrichment factor decreased significantly with the uplift of viscosity. Among the enrichment factors of DES-1 and DES-4 at the equal HS/HBD molar ratio, it was noticeable that the halide salts hardly exerted influence on the extraction efficiency of three phenols. Morever, the experiment demonstrated that the DESs gave matchable or superior enrichment factors to that given by the respresent of commonly used ionic liquid ([BMIm]BF_4), highlighting DES can be used as a relatively inexpensive, effective and novel green extraction media.

To evaluate the proposed DES-based direct-immersion LPME method, some relevant parameters such as enrichment factor, linearity correlation coefficient (R^2), reproducibility, limit of detection (LOD) for the phenols from model oil (hexane) were determined in the optimized condition. The reproducibility was determined by five-time repetition. The linearity was investigated in a concentration range of 0.025~10000 μg/L for phenol and

0.05~10000 μg/L for the other two phenols. The LOD was 0.025 μg/L for phenol and 0.05 μg/L for the other used phenols. Results as listed in Table S2 (ESI) exhibited that acceptable linearity correlation coefficient (R^2) for the LPME was obtained, ranging from 0.9373 to 0.9899. The relative standard deviations (RSD, n=5) were between 6.7~10.6%. The enrichment factors were in the range of 92~137 in 3 min with ultrasonic wave assistance.

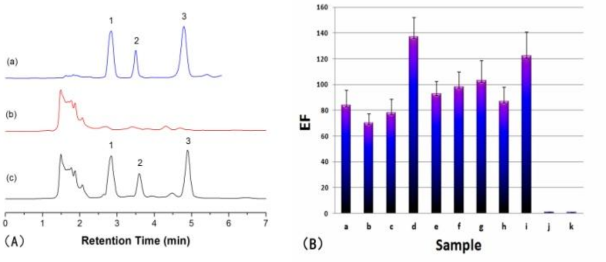

Fig. 3 (A) The chromatogram of 1000 μg/L phenol, *p*-cresol and β-naphthol without extraction (a); the extraction of safflower oil (b); enrichment of three phenols from spiked safflower oil (10 μg/L) (c). (B) Enrichment factors of different samples: a-k in order: aniline, *p*-toluidine, *α*-naphthylamine, phenol, *p*-cresol, *β*-naphthol, benzoic acid, *p*-hydroxy benzoic acid, *α*-naphthaleneacetic acid, toluene, biphenyl.

As shown in Fig. 3A, DES was successfully uesd to enrich three phenols including phenol, *p*-cresol, *β*-naphthol from spiked safflower oil (10 μg/L). The different compounds were also measured to determinate the range of applicability of the proposed novel extraction media. The results as shown in Fig. 3B indicate that DES-1 offered the satisfied enrichment factor for all the selected polar compounds, such as phenols, anilines, benzoic acids. But for the non-polar hydrophobic compounds (for example, toluene and biphenyl in the figure), the results were negligible, because of too low distribution coefficient of non-polar compounds between solution and acceptor solvent, which was in compliance with “like dissolves like” theory. As shown in Fig. S3 (ESI), it seems that DES-1 can be used to successfully extract many kinds of polar compounds from the real oils. DES can not only effectively extact the polar analytes from hexane, good results were also obtained when other non-polar or weak polar solvents such as toluene and chloroform used as the sample solvents. The activity of the regenerated DES was also examined as shown in the Fig. S4 (ESI).

In conclusion, an effective LPME method based on DES as new extractant was developed for the enrichment of phenols from model oil. With the use of ultrasonic wave, the studies successfully shortened the long extraction time needed for traditional LPME. Above all, DES was proved as a novel high-efficiency extraction media, comparing with different polar solvents, and successfully applied to the LPME. Their physicochemical properties and phase behaviors are similar to ionic liquids. Notably, not only is DES relatively inexpensive and eco-friendly, but also is able to match the ionic liquid in the extraction analysis for polar compounds from non-polar solvents, and it has the prospect of being an alternative to ionic liquid as a high-efficiency extraction media. It is foreseeable that DES is very promising in the analytical science field outside of extraction applications.

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Notes and references

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