Journal of Chromatography A, 1218 (2011) 1556–1566

Contents lists available at ScienceDirect

Journal of Chromatography A

journal homepage: www.elsevier.com/locate/chroma

Selective extraction of emerging contaminants from water samples by dispersive liquid–liquid microextraction using functionalized ionic liquids

Cong Yao[a], Tianhao Li[a], Pamela Twu[a], William R. Pitner[b], Jared L. Anderson[a,*]

[a] Department of Chemistry, The University of Toledo, 2801 W. Bancroft Street, MS 602, Toledo, OH 43606, USA
[b] Merck KGaA, Frankfurter Straße 250, Darmstadt D-64293, Germany

ARTICLE INFO

Article history:
Received 10 December 2010
Received in revised form 10 January 2011
Accepted 12 January 2011
Available online 19 January 2011

Keywords:
Functionalized ionic liquid
Dispersive liquid–liquid microextraction
Emerging contaminants
High performance liquid chromatography
Tris(pentafluoroethyl)trifluorophosphate anion

ABSTRACT

Functionalized ionic liquids containing the tris(pentafluoroethyl)trifluorophosphate (FAP) anion were used as extraction solvents in dispersive liquid–liquid microextraction (DLLME) for the extraction of 14 emerging contaminants from water samples. The extraction efficiencies and selectivities were compared to those of an in situ IL DLLME method which uses an in situ metathesis reaction to exchange 1-butyl-3-methylimidazolium chloride (BMIM-Cl) to 1-butyl-3-methylimidazolium bis[(trifluoromethyl)sulfonyl]imide (BMIM-NTf_2). Compounds containing tertiary amine functionality were extracted with high selectivity and sensitivity by the 1-(6-amino-hexyl)-1-methylpyrrolidinium tris(pentafluoroethyl)trifluorophosphate (HNH_2MPL-FAP) IL compared to other FAP-based ILs and the BMIM-NTf_2 IL. On the other hand, polar or acidic compounds without amine groups exhibited higher enrichment factors using the BMIM-NTf_2 IL. The detection limits for the studied analytes varied from 0.1 to 55.1 μg/L using the traditional IL DLLME method with the HNH_2MPL-FAP IL as extraction solvent, and from 0.1 to 55.8 μg/L using in situ IL DLLME method with BMIM-Cl + $LiNTf_2$ as extraction solvent. A 93-fold decrease in the detection limit of caffeine was observed when using the HNH_2MPL-FAP IL compared to that obtained using in situ IL DLLME method. Real water samples including tap water and creek water were analyzed with both IL DLLME methods and yielded recoveries ranging from 91% to 110%.

1. Introduction

Recently, emerging contaminants, also called contaminants of emerging concern (CECs), have attracted increasing attention from both the general public and the government agencies including the United States Environmental Protection Agency (EPA) [1–3]. CECs are pollutants not currently included in routine monitoring programs but are likely the candidates of future regulation because of their potential threat to human health and the environment. CECs include a variety of compounds, such as pharmaceuticals and personal care products (PPCPs), endocrine-disrupting chemicals (EDCs), persistent organic pollutants (POPs), nanomaterials, etc. [1]. Among these compounds, PPCPs and EDCs have received considerable attention due to their wide usage and relative high toxicity [2–6]. PPCPs include a wide range of human prescribed drugs such as antidepressants, anti-inflammatory drugs, consumer products including fragrances, sunscreen, household cleaning products, as well as veterinary medicines such as antimicrobials and antibiotics. The escalation of antibiotic resistance has been a big concern due to the increasing release of antibiotics in the environment [7]. EDCs include naturally occurring or synthetic estrogens and androgens as well as some organic compounds such as alkylphenols that can modulate normal hormonal functions in aquatic organisms. It was reported that the steroid hormones of fish were affected by EDCs in environmental water even at very low concentration levels [8].

The low concentration of CECs in environmental water makes them difficult to be directly determined by chromatographic methods such as high performance liquid chromatography (HPLC) or gas chromatography (GC). Various sample preparation techniques have been applied to preconcentrate CECs from water before subjecting them to HPLC or GC. Among those, liquid–liquid extraction (LLE) and solid phase extraction (SPE) are the most widely used [9–12]. Recently, various microextraction methods have been developed which simplify the extraction procedure, save time and labor, as well as greatly reduce the amount of organic solvent used. Solid-phase microextraction (SPME) is a solvent free, simple, and convenient method which combines extraction, preconcentration, and sample introduction in one step [13]. The determination of pharmaceutical residues in environmental water or wastewater utilizing SPME coupled with HPLC or GC have been previously reported [14,15]. Stir-bar sorptive extraction (SBSE) is considered as an alternative microextraction method and consists of an increased acceptor phase compared to SPME. SBSE-GC–MS was successfully applied to analyze 46 acidic and polar organic

* Corresponding author. Tel.: +1 419 530 1508; fax: +1 419 530 4033.
E-mail address: Jared.Anderson@UToledo.edu (J.L. Anderson).

0021-9673/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.chroma.2011.01.035

pollutants in water samples [16]. Other microextraction techniques widely used for the extraction of pharmaceutical drugs from liquid matrices include single drop microextraction (SDME) [17], dispersive liquid–liquid microextraction (DLLME) [18], and hollow-fiber liquid phase microextraction (HF-LPME) [19]. Among all of these microextraction techniques, DLLME is considered to be the most rapid while exhibiting relatively high extraction efficiency. This technique is based on the formation of a cloudy solution after quickly adding a mixture of a hydrophobic extraction solvent and a dispersive solvent to the aqueous sample solution [20]. The turbid solutions result in a large contact area between the extraction solvent and sample solution, which dramatically reduces the extraction time while enhancing the extraction efficiency. This efficient and convenient method has been used to extract and analyze various pharmaceuticals including antibiotics [21], anti-inflammatory drugs [18], and psychotropic drugs [22].

Ionic liquids (ILs) are a class of non-molecular ionic solvents with low melting points resulting from combinations of organic cations and various anions. ILs have many unique properties including wide viscosity ranges, almost no measurable vapor pressure, high thermal stability, and a multitude of varying solvation interactions. These paramount properties make them useful in various sample preparation techniques including LLE [23,24], SPME [25–27], HF-LPME [28,29], SDME [30,31], and DLLME [32–37]. The selectivity and sensitivity of IL-based microextraction techniques can be controlled and improved by introducing desired functional groups into the structure of ILs. Recently, a group of ILs containing the tris(perfluoroalkyl)trifluorophosphate anion (FAP^-) have been developed. Their unique properties including excellent hydrolytic, thermal, and electrochemical stabilities offer great application in various fields of science and engineering [38–41]. Our group has shown that FAP-based ILs are ideal extraction solvents for direct immersion-SDME due to their strong hydrophobic nature [31].

IL-based DLLME has received much attention recently [32–37]. Three types of IL-based DLLME are widely used. The first is based on traditional DLLME and involves a small amount of organic solvent that plays the role as the dispersive solvent [32,33]. A hydrophobic IL is often used as the extraction solvent and is dissolved in the dispersive solvent before being added to the sample solution. The extraction process is initiated by the formation of a cloudy solution. The analyte enriched IL phase is then sedimented by centrifugation. The determination of the analytes is performed by dissolving the analyte enriched IL phase into a small amount of organic solvent followed by injection into HPLC. Another approach of IL DLLME utilizes ultrasound or heat to disperse the IL phase [34–36]. The analyte enriched IL is sedimented by rapidly cooling the solution with ice water followed by centrifugation. More recently, our group introduced an IL DLLME method that involves an in situ metathesis reaction (in situ IL DLLME) [37]. In this approach, a hydrophilic IL is dissolved completely in the aqueous sample solution to promote interaction between the IL and analytes. An ion-exchange reagent is then introduced to carry out the in situ metathesis reaction. A turbid solution with fine IL microdroplets is formed and produces a hydrophobic IL. This phase separates from the aqueous sample and can be directly analyzed by HPLC. A significant advantage of this method lies in that the metathesis reaction and extraction are accomplished in one step making it very rapid and amendable to high-throughput analysis.

In this study, FAP-based ILs with a variety of functional groups were utilized as extraction solvents for DLLME in the analysis of pharmaceutical compounds including analgesics, antipyretics, carbonic anhydrase inhibitors, stimulants, sulfonamide antibiotics, anticonvulsants, antilipemics, and anti-inflammatory drugs, as well as endocrine disruptors and disinfectants. The effects of different IL functional groups on the extraction of emerging contaminants were investigated in an attempt to identify unique functional groups that can be imparted to the IL in order to increase extraction efficiency and selectivity. Extractions using FAP-based ILs were also compared to those performed by the in situ IL DLLME method involving the metathesis reaction of 1-butyl-3-methylimidazolium chloride (BMIM-Cl) to form the 1-butyl-3-methylimidazolium bis[(trifluoromethyl)sulfonyl]imide (BMIM-NTf_2) extraction solvent. Extraction conditions including varying sample pH, type and volume of dispersive solvent as well as the addition of salt were also examined.

2. Experimental

2.1. Reagents

The FAP-based ILs used as extraction solvents in this study were: 1-(6-amino-hexyl)-1-methylpyrrolidinium tris(pentafluoroethyl)trifluorophosphate (HNH_2MPL-FAP), 1-ethoxycarbonylmethyl-1-methylpyrrolidinium tris(pentafluoroethyl)trifluorophosphate (ECMMPL-FAP), methoxyethyl-dimethyl-ethylammonium tris(pentafluoroethyl)trifluorophosphate (MOEDEA-FAP), 1-methoxyethyl-3-methylimidazolium tris(pentafluoroethyl)trifluorophosphate (MOEMIM-FAP), 1-methoxyethyl-1-methylmorpholinium tris(pentafluoroethyl)trifluorophosphate (MOEMMO-FAP), 1-methoxyethyl-1-methylpyrrolidinium tris (pentafluoroethyl)trifluorophosphate (MOEMPL-FAP), 1-methoxypropyl-1-methylpiperidinum tris(pentafluoroethyl)trifluorophosphate (MOPMPP-FAP), and 1-butyl-3-methylpyrrolidium tris(pentafluoroethyl)trifluorophosphate (BMPL-FAP). These ILs were supplied by Merck KGaA (Darmstadt, Germany). The structures of the evaluated ILs are shown in Fig. 1. The two other ILs used in this study were 1-butyl-3-methylimidazolium chloride (BMIM-Cl) and 1-butyl-3-methylimidazolium bis[(trifluoromethyl)sulfonyl] imide (BMIM-NTf_2), which were synthesized according to previous work [37]. Sodium chloride, HPLC-grade methanol, acetone, and acetonitrile were supplied by Fisher Scientific (Fair Lawn, NJ, USA). 1-Methylimidazole, 1-chlorobutane, dodecylamine, sodium dodecyl sulfate (SDS), and acetic acid were purchased from Sigma–Aldrich (St. Louis, MO, USA). Lithium bis[(trifluoromethane)sulfonyl]imide ($LiNTf_2$) was purchased from SynQuest Labs, Inc. (Alachua, FL, USA).

The analytes examined in this study included acetaminophen (AMP), acetazolamide (AZM), caffeine (CAF), sulfisomidine (SID), sulfamethoxypyridazine (SMPZ), sulfamethoxazole (SMZO), sulfamethazine (SMZI), carbamazepine (CMZ), bisphenol-A (BP-A), naproxen (NX), 17α-ethynylestradiol (17EE), ibuprofen (IB), gemfibrozil (GFZ), irgasan (IRG), 5-(4-formylphenyl)pyrimidine (FPP), biphenyl-4-carboxaldehyde (BPCA), and biphenyl (BiPh). These analytes were obtained from Sigma–Aldrich. The structures, classifications, and properties of the studied analytes are shown in Table 1. These pure compounds were dissolved in acetonitrile of HPLC grade to prepare stock standard solutions with concentrations ranging from 1000 to 10,000 mg L^{-1}. These stock standard solutions were stored at 4 °C and used in the preparation of two stock mixture solutions. The first stock mixture solution was prepared in acetonitrile and contained 100 mg L^{-1} of SID, SMPZ, FPP, BPCA, and BiPh, as well as 500 mg L^{-1} of AZM. The second stock mixture solution contained 60 mg L^{-1} of AMP, 302 mg L^{-1} of CAF, 15 mg L^{-1} of SMZI, 20 mg L^{-1} of SMZO, 10 mg L^{-1} of CMZ, 81 mg L^{-1} of BP-A, 42 mg L^{-1} of NX, 60 mg L^{-1} of 17EE, 207 mg L^{-1} of IB, 102 mg L^{-1} of GFZ, and 67 mg L^{-1} of IRG in acetonitrile. These solutions were used in the daily preparation of aqueous working standard solutions with deionized water (18.2 MΩ cm) obtained from a Milli-Q water purification system (Millipore, Bedford, MA,

Table 1
Structure and properties of studied analytes.

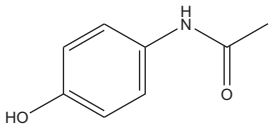
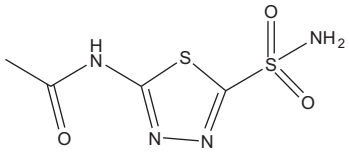
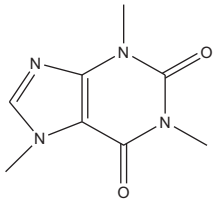
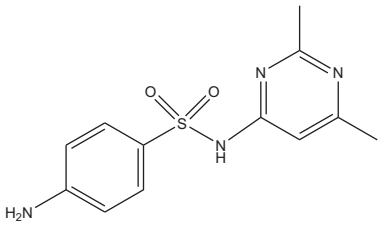
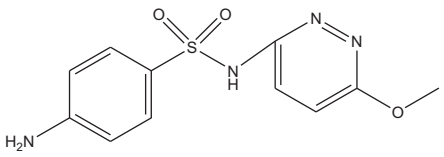
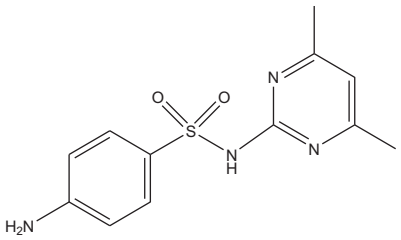
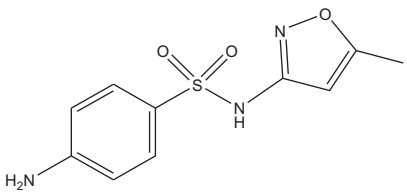
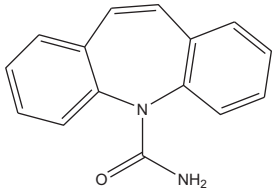
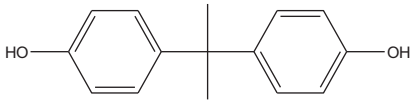
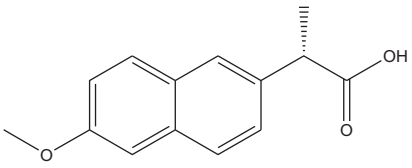
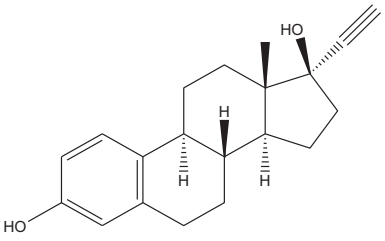
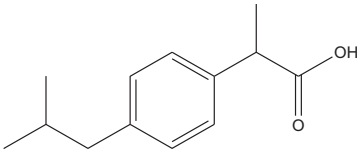
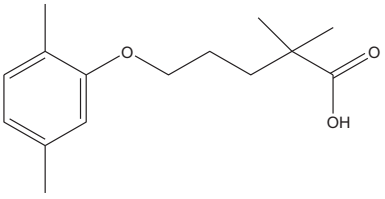
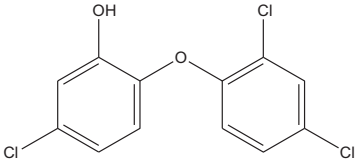
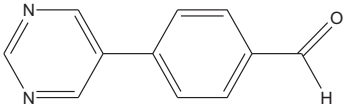
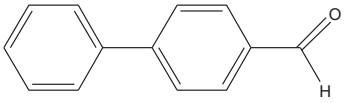
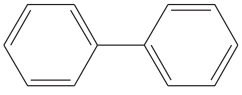
Name	Structure	Classification	Log *P*	Log *D*[a] (pH = 3)	pK_a
Acetaminophen (AMP)		Analgesic, antipyretic	0.49 [42]	0.47	9.38 [43]
Acetazolamide (AZM)		Carbonic anhydrase inhibitor	−0.26 [44]	−0.26	6.50 [44]
Caffeine (CAF)		Stimulant	−0.08 [45]	−0.63	0.52[a]
Sulfisomidine (SID)		Sulfonamide antibiotic	−0.35 [46]	−1.16	7.40 [46]
Sulfamethoxypyridazine (SMPZ)		Sulfonamide antibiotic	0.32 [47]	0.13	6.70 [47]
Sulfamethazine (SMZI)		Sulfonamide antibiotic	0.89 [47]	0.27	7.59 [47]
Sulfamethoxazole (SMZO)		Sulfonamide antibiotic	0.90 [47]	0.64	5.70 [47]
Carbamazepine (CMZ)		Anticonvulsant	2.50 [48]	1.87	14.00 [49]
Bisphenol A (BP-A)		Endocrine disruptor	3.64 [50]	3.64	9.73 [51]

Table 1 (*Continued*)

Name	Structure	Classification	Log *P*	Log *D*[a] (pH = 3)	pK_a
Naproxen (NX)		Analgesic, anti-inflammatory	3.18 [52]	2.87	4.20 [52]
17α-Ethynylestradiol (17EE)		Sex hormone	4.15 [53]	4.11	10.21 [53]
Ibuprofen (IB)		Analgesic	3.97 [54]	3.49	4.91 [54]
Gemfibrozil (GFZ)		Antilipemic	4.77 [55]	4.29	4.45 [55]
Irgasan (IRG)		Antimicrobial, disinfectant	4.80 [56]	5.34	7.90 [56]
5-(4-Formylphenyl)pyrimidine (FPP)		–	0.94[a]	0.93	0.58[a]
Biphenyl-4-carboxaldehyde (BPCA)		–	3.38[a]	3.38	–
Biphenyl (BiPh)		–	4.06 [57]	4.09	–

[a] Values were obtained from SciFinder and calculated using Advanced Chemistry Development Software.

USA). The total acetonitrile content in the daily aqueous solution was kept at a constant value of 2% (v/v).

2.2. Instrumentation

High-performance liquid chromatographic analysis was carried out using a LC-20A liquid chromatograph (Shimadzu, Japan) with two LC-20AT pumps, a SPD-20 UV/VIS detector, and a DGU-20A_3 degasser. All separations were performed using a C_{18} column (250 × 4.6 mm i.d., 5-μm particle size) from Alltech (Deerfield, IL, USA) with a guard column (Kromasil^{TM} C_{18}, 5-μm particle size) from Supelco (Bellefonte, PA, USA). Data acquisition and processing were accomplished with Shimadzu LC solution software.

All separations were performed utilizing acetonitrile and water as mobile phases with the addition of 0.1% acetic acid (v/v) and a flow rate of 1.0 mL min^{-1}. For the separation of AZM, SID, SMPZ, FPP, BPCA and BiPh, the separation gradient started with 20% acetonitrile, held for 5 min, and then gradually increased to 50% over 5 min. A quick linear increase to 100% over 5 min was then employed. Acetonitrile was maintained at 100% for 10 min to elute FPP, BPCA, BiPh, and all remaining IL. For the separation of the other 11 compounds, the gradient was initiated at 40% acetonitrile and gradually increased to 70% in 45 min. For all compounds

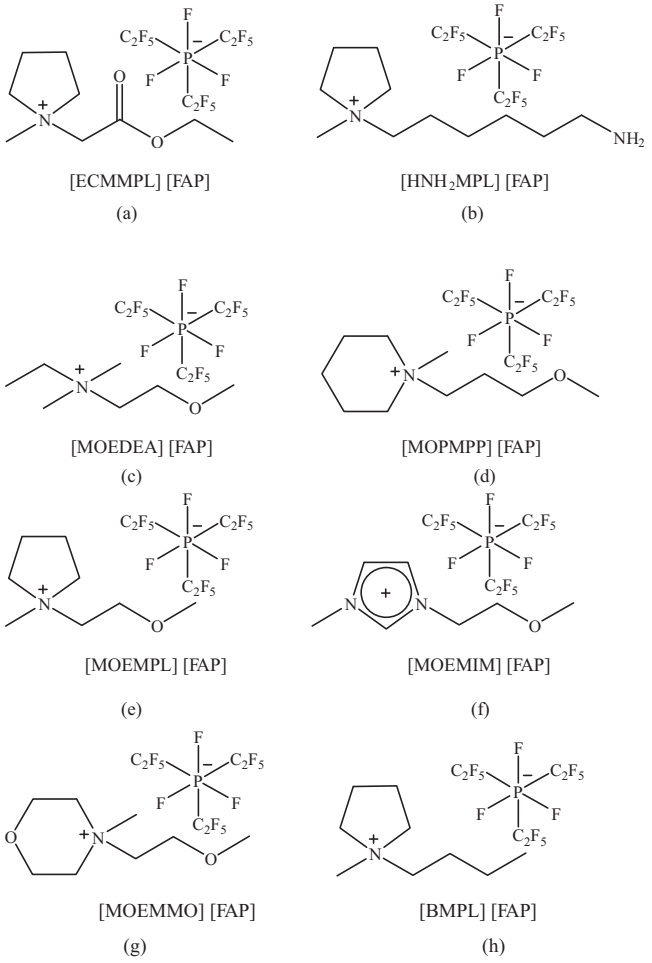


Fig. 1. Structures of studied FAP-based ILs. (a) 1-Ethoxycarbonylmethyl-1-methylpyrrolidinium tris(pentafluoroethyl)trifluorophosphate, (b) 1-(6-aminohexyl)-1-methylpyrrolidinium tris(pentafluoroethyl)trifluorophosphate, (c) 1-methoxyethyl-dimethyl-ethylammonium tris(pentafluoroethyl)trifluorophosphate, (d) 1-methoxypropyl-1-methylpiperidinium tris(pentafluoroethyl)trifluorophosphate, (e) 1-methoxyethyl-1-methylpyrrolidium tris(pentafluoroethyl) trifluorophosphate, (f) 1-methoxyethyl-3-methylimidazolium tris(pentafluoroethyl)trifluorophosphate, (g) 1-methoxyethyl-1-methylmorpholinium tris (pentafluoroethyl)trifluorophosphate, (h) 1-butyl-3-methylpyrrolidium tris (pentafluoroethyl)trifluorophosphate.

evaluated in this study, UV detection was accomplished at 254 nm.

Extractions were performed using a 15-mL polypropylene conical tube from Becton Dickinson Labware (Franklin Lakes, NJ, USA). Shaking for all extractions was performed using a mixer from Barnstead/Thermolyne (Dubuque, IA, USA). Centrifugation at 3400 rpm was accomplished using a model 228 centrifuge from Fisher Scientific.

2.3. Extraction procedures

2.3.1. Traditional IL DLLME procedure

Traditional IL DLLME was employed when the FAP-based and BMIM-NTf_2 ILs were utilized as extraction solvents. First, 30 μL of the FAP-based IL or 75 μL of BMIM-NTf_2 was added and dissolved into 0.5 mL of the methanol dispersive solvent. The IL–methanol solution was added to a 15 mL conical centrifuge tube filled with 10 mL deionized water spiked previously with analytes. A turbid solution was formed. After shaking for 30 s, the turbid solution was centrifuged for 5 min at a rate of 3400 rpm. The upper aqueous solution was removed with a pipette and 9 μL of the analyte enriched IL residue was withdrawn into a syringe and injected into HPLC. The syringe was then rinsed with acetonitrile multiple times to remove any residual analytes and IL.

2.3.2. In situ IL DLLME procedures

The procedures of in situ IL DLLME method were described previously [37]. Briefly, 40 μL of BMIM-Cl (as a supercooled liquid) was added to the sample solution followed by gentle shaking to completely disperse and dissolve the IL into the aqueous solution. An aqueous $LiNTf_2$ solution ($LiNTf_2$/BMIM-Cl (n/n): 1/1) was added to the tube resulting in the formation of a turbid solution. After shaking for 30 s, the turbid solution was centrifuged for 5 min at a rate of 3400 rpm. The upper aqueous solution was removed with a pipette and 9 μL of the IL residue enriched with analytes was withdrawn into a syringe and injected into HPLC.

2.4. Water samples

Two water samples, namely tap water and creek water, were examined in this study. Laboratory tap water was taken from a water tap after continual flow for 10 min. Creek water was collected from the Ottawa River in Toledo, OH according to Ground Water Rule (GWR) sample collection and transport reference guidelines provided by the U.S. Environmental Protection Agency. These samples were filtered through Nylon membrane syringe filters with a pore size of 0.45 μm (Fisher Scientific, Fair Lawn, NJ, USA) and stored in the refrigerator.

3. Results and discussion

3.1. Comparison of extraction method and solvent

The extraction efficiencies of 14 emerging contaminants using the traditional IL DLLME method with seven FAP-based ILs were compared. The results were also compared with the in situ IL DLLME using BMIM-NTf_2 (i.e., BMIM-Cl + $LiNTf_2$) as the extraction solvent. To quantitatively assess and compare the extraction performance of all examined ILs, the enrichment factors for the studied CECs were determined and are presented in Table 2. The enrichment factor is defined as the ratio of the analyte concentration in the extraction solvent and the initial analyte concentration in the aqueous sample solution. This can be calculated by comparing the peak areas obtained after injecting the same volume of extraction solvent in which analytes were preconcentrated to that of the sample matrix.

In a previous study, the in situ IL DLLME method exhibited higher extraction efficiency compared to traditional IL DLLME when using the same IL as the extraction solvent [37]. The same trend was observed in this study. As shown in Table 2, the enrichment factors for all the studied analytes (except AMP) using the in situ IL DLLME method were higher than those of the traditional IL DLLME method when employing the BMIM-NTf_2 IL.

The enrichment factors of various pharmaceuticals using seven FAP-based ILs as extraction solvents are listed in Table 2. The data for some analytes are not shown due to the fact that they were partially overlapped with the IL peaks or could not be detected. Interestingly, for AMP, AZM, CAF, SID, SMPZ, SMZI, SMZO, and CMZ, a dramatic increase in the enrichment factors was observed using the HNH_2MPL-FAP IL extraction solvent compared to the other FAP-based ILs. However, for IB, GFZ, and IRG, the enrichment factors obtained using the HNH_2MPL-FAP IL were similar to the other six FAP-based ILs. The possible reason for this enhancement is related to the structures and properties of the analytes and ILs. The logarithm of the partition coefficient (P) and distribution coefficient (D) between the organic phase (1-octanol) and water for all studied analytes are provided in Table 1. The partition coefficient is defined as the ratio of concentrations of the un-ionized compound between

Table 2
Comparison of enrichment factors for emerging contaminants using in situ IL DLLME and traditional IL DLLME.

Analytes	Enrichment factor								
	In situ IL DLLME[a]	Traditional IL DLLME[b]							
	BMIM-Cl + $LiNTf_2$	BMIM-NTf_2	HNH_2MPL-FAP	ECMMPL-FAP	MOEDEA-FAP	MOEMIM-FAP	MOEMMO-FAP	MOEMPL-FAP	MOPMPP-FAP
AMP	1.8	1.8	2.0	0.1	0.1	0.3	0.1	0.1	0.2
AZM	0.91	0.78	0.81	–	–	–	0.14	–	0.13
CAF	1.3	1.2	113.8	4.0	2.5	3.9	4.3	2.3	2.4
SID	16.6	14.5	64.9	3.1	2.4	4.8	5.8	3.0	6.6
SMPZ	27.2	23.8	76.9	4.7	3.4	6.9	9.7	4.1	9.0
SMZI	20.3	–	110.3	5.2	3.9	8.8	7.0	6.5	–
SMZO	112.1	87.7	59.5	11.4	9.4	17.5	17.6	12.1	29.9
CMZ	134.0	86.9	296.5	92.0	71.9	95.1	109.9	90.2	122.2
BP-A	239.8	134.8	31.8	17.5	–	–	–	–	–
NX	359.6	225.8	181.5	143.8	–	–	–	–	–
17EE	193.0	71.3	–	–	–	–	–	–	–
IB	268.5	189.6	194.0	126.9	113.6	167.8	156.9	152.7	234.2
GFZ	292.9	188.9	233.3	202.5	169.9	227.2	232.5	203.2	242.5
IRG	452.1	414.3	361.6	362.2	287.2	404.5	389.1	372.6	439.4
BiPh[c]	114.7	106.2	115.0	110.8	115.0	116.6	113.6	112.7	116.2
FPP[c]	23.6	18.8	318.6	16.2	11.7	19.7	20.7	11.8	13.7
BPCA[c]	451.5	210.0	379.3	339.0	369.0	376.4	329.3	357.6	383.0

[a] *Conditions*: BMIM-Cl volume, 40 μL; $LiNTf_2$/BMIM-Cl (*n*/*n*): 1/1; sample volume: 10 mL; sedimented phase volume: ~13 μL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.
[b] *Conditions*: extraction IL volume: 75 μL for BMIM-NTf_2; 30 μL for all the FAP-based IL; dispersive solvent: 0.5 mL methanol; sample volume: 10 mL; sedimented phase volume: ~13 μL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.
[c] Compounds used for selectivity studies. Not included in CECs. (–) Data not obtained due to analyte partial overlap with IL peak or not detected.

the two phases while the distribution coefficient is the ratio of the sum of the concentrations of all forms of the compound, including ionized and un-ionized forms, between the two phases. The equations used to calculate log *P* and log *D* are given by Eqs. (1) and (2):

$$\log P_{\mathrm{oct/wat}} = \log\left(\frac{[\mathrm{solute}]_{\mathrm{octanol}}}{[\mathrm{solute}]_{\mathrm{water}}^{\mathrm{unionized\ form}}}\right) \quad (1)$$

$$\log D_{\mathrm{oct/wat}} = \log\left(\frac{[\mathrm{solute}]_{\mathrm{octanol}}}{[\mathit{solute}]_{\mathrm{water}}^{\mathrm{unionized\ form}} + [\mathrm{solute}]_{\mathrm{water}}^{\mathrm{ionized\ form}}}\right) \quad (2)$$

In a typical extraction process, the higher the values of an analyte's log *P* and log *D*, the greater the amount of analyte that should partition into the organic phase (i.e., the FAP-based IL phase). This was true for compounds IB, GFZ, and IRG using the studied FAP-based ILs as extraction solvents. Higher enrichment factors were obtained for these three compounds due to their relatively high log *P* and log *D* values. For AZM, CAF, SID, SMPZ, SMZI, and SMZO, much lower enrichment factors were obtained using the ECMMPL-FAP, MOEDEA-FAP, MOEMIM-FAP, MOEMMO-FAP, MOEMPL-FAP, and MOPMPP-FAP IL extraction solvents, which is consistent with the lower log *P* and log *D* values of these six analytes. However, an exception was observed for these six compounds when using the HNH_2MPL-FAP IL extraction solvent. An approximate 2–50-fold increase in enrichment factors was observed using HNH_2MPL-FAP compared to the other FAP-based ILs. This enhancement appears to be due to the presence of tertiary amines within the structure of these analytes which are capable of interacting with the primary amine functional group in the HNH_2MPL-FAP IL. This interaction promoted the partitioning of these analytes into the HNH_2MPL-FAP IL phase and much lower enrichment factors resulted for ILs lacking such functional groups. This argument is further supported by additional experimental data presented in Section 3.2.

The extraction performance of the studied CECs using the FAP-based ILs were compared with the BMIM-NTf_2 IL. With exception of the HNH_2MPL-FAP IL, higher extraction efficiencies were obtained for nearly all analytes (except CAF) using BMIM-NTf_2 IL compared to the remaining six FAP-based ILs. This behavior may be attributed to the apparent lower hydrophobicity of the BMIM-NTf_2 IL (to obtain same amount of sedimented IL phase, only 30 μL of the FAP-based IL was needed while a total BMIM-NTf_2 volume of 75 μL was required using the traditional IL DLLME method). Therefore, partitioning of more polar analytes may be preferred by BMIM-NTf_2 IL compared to the FAP-based IL. The hydrogen bond basicities of NTf_2-based IL are generally higher than their FAP-based analogues [41]; therefore, the NTf_2-based ILs would be expected to interact more strongly with acidic compounds. This explains why higher extraction efficiencies were obtained for acidic compounds using the BMIM-NTf_2 IL. For example, a 7.7-fold and 13-fold increase in enrichment factors for BP-A were obtained when using the BMIM-NTf_2 IL as the extraction solvent in traditional IL DLLME and in situ IL DLLME, respectively, compared to the ECMMPL-FAP IL. A comparison between the BMIM-NTf_2 and HNH_2MPL-FAP ILs revealed that higher enrichment factors were obtained for analytes containing tertiary amines when HNH_2MPL-FAP IL was used as extraction solvent. For polar compounds lacking amines such as IRG, GFZ, IB, and BP-A, the extraction efficiencies were higher using the BMIM-NTf_2 IL.

3.2. Effect of amino functionality on extraction selectivities

As described in Section 3.1, higher enrichment factors were obtained for analytes containing tertiary amines utilizing the HNH_2MPL-FAP IL extraction solvent. To further investigate this behavior, two sets of experiments were performed. The first experiment involved the extraction of three selected analytes, FPP, BPCA, and BiPh, utilizing all of the studied FAP-based ILs as well as the BMIM-NTf_2 extraction solvent. FPP contains two tertiary amines within its molecular structure where BPCA and BiPh both lack such functionality. As expected, the enrichment factor for FPP using the HNH_2MPL-FAP IL was significantly higher than other FAP-based ILs, while the enrichment factors for BiPh and BPCA were largely unchanged (see Table 2).

A further investigation into this behavior involved the addition of surfactants into the extraction system. Dodecylamine, a surfactant containing a primary amine moiety, was added to the extraction system containing four selected analytes, namely, SID, SMPZ, FPP, and BPCA. The addition of dodecylamine was performed prior to the addition of the extraction IL. The concentration of

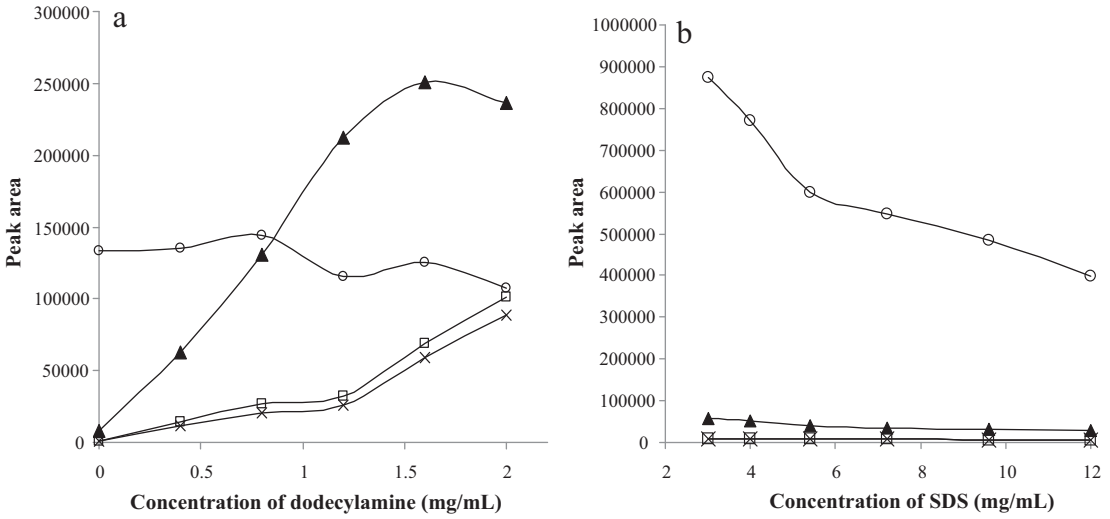


Fig. 2. Effect of added surfactant (a) dodecylamine and (b) SDS on the extraction performance of studied analytes (×) SID, (□) SMPZ, (▲) FPP, (○) BPCA using traditional IL DLLME; extraction solvent, 30 μL BMPL-FAP; dispersive solvent: 0.5 mL MeOH; sample volume: 10 mL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.

dodecylamine was in the range of 0.4–2.0 mg mL^{-1} which was much higher than its critical micelle concentration (0.81 mmol L^{-1}). The analyte–micelle complex was then extracted by the BMPL-FAP IL. As shown in Fig. 2a, with increasing concentration of dodecylamine in the sample solution, a dramatic increase in the extraction efficiency of SID, SMPZ, and FPP was observed. This is due to the fact that the interaction between the primary amine in dodecylamine and the tertiary amines of the three analytes promoted the partitioning of the analyte–micelle complex into the IL phase. However, BPCA, which lacks a tertiary amine, experienced a slight decrease in extraction efficiency with increasing concentration of dodecylamine. To further confirm the findings, sodium dodecyl sulfate (SDS), which has the similar structure to dodecylamine except that it lacks the primary amine group, was applied under the same conditions. The concentration of SDS was varied from 3.0 to 12.0 mg mL^{-1} which is approximately 1.3–5.0-fold higher than its CMC (8.2 mmol L^{-1}). As shown in Fig. 2b, a decrease in the extraction efficiency was observed for all of the studied four analytes with an increasing SDS concentration. Clearly, highly selective extractions can be performed for analytes containing tertiary amines by simply employing an IL extraction solvent containing a primary amine.

3.3. Optimization of extraction conditions

3.3.1. Sample pH effect

The effects of pH on the extraction efficiency are dependent on the specific properties of the studied analytes. Typically, higher extraction efficiency can be obtained when analytes are in their un-ionized forms [32]. In this study, the pH effect was examined by varying the pH from 2.6 to 6.5 using in situ IL DLLME. For NX, IB, SMZO, and GFZ, a decrease in extraction efficiency was observed when the pH value was increased, as shown in Fig. 3a. The pK_a of NX, IB, SMZO, and GFZ are 4.20, 4.91, 5.70, and 4.45, respectively, which are all in the studied pH range. An increase in pH resulted in these analytes to go from their un-ionized form to ionized form producing a dramatic drop in the extraction efficiencies. On the contrary, for IRG, BP-A, CMZ, SMZI, AMP, CAF, and 17EE, which possess pK_a values outside of the range from 2.6 to 6.5, the charged form of the molecule remained unchanged (either ionic or un-ionized). No obvious changes in the extraction efficiencies were observed for these compounds (see Fig. 3b). Therefore, to obtain the highest extraction efficiency, low pH values were preferred for most of the studied analytes. However, at pH 2.6, the volume of the sedimented IL phase decreased which made it difficult to withdraw 9 μL of the IL for injection into HPLC. Thus, pH 3.0 was selected for the subsequent studies.

3.3.2. Effect of IL volume and dispersive solvent

The effect of sample volume, extraction time and centrifugation time on the extraction efficiency with in situ IL DLLME has been thoroughly studied previously [37]. In this study, an extraction time of 0.5 min was selected followed by a centrifugation time of 5.0 min. The sample volume was maintained at 10.0 mL for all extractions. The volume of the IL extraction solvent was optimized to insure approximately 13 μL of the sedimented IL phase. It should be noted that to obtain the same amount of sedimented IL phase, only 30 μL of the FAP-based IL was needed while a total BMIM-NTf_2 volume of 75 μL was required using the traditional IL DLLME method. This is due to the high hydrophobicity and hydrolytic stabilities of the FAP-based ILs which allowed them to be used in the sampling of large volumes of aqueous solutions without loss of the extraction phase.

Using the traditional IL DLLME method, the effect of methanol and acetone (as dispersive solvents) on the extraction efficiency was studied using BMIM-NTf_2 and HNH_2MPL-FAP ILs. The results revealed that the BMIM-NTf_2 IL produced higher extraction efficiencies for nearly all analytes using acetone. However, the opposite trend was observed when using the HNH_2MPL-FAP IL, which favored methanol as the dispersive solvent. Furthermore, the high intensity of the acetone peak completely overlapped the peak of CAF making integration very difficult. Therefore, methanol was selected as the dispersive solvent for all studies involving traditional IL DLLME. The volume of methanol on the extraction efficiency was also studied for the HNH_2MPL-FAP IL. As shown in Fig. 4, when the volume of dispersive solvent was increased from 0.5 mL to 1.5 mL, the extraction efficiencies decreased for all of the studied analytes. Therefore, 0.5 mL methanol was selected as the dispersive solvent volume for subsequent studies.

3.3.3. Effect of added salt

The effect of added salt on the extraction efficiency of selected CECs using the HNH_2MPL-FAP IL in traditional IL DLLME and BMIM-Cl + $LiNTf_2$ IL with in situ IL DLLME method were studied and compared.

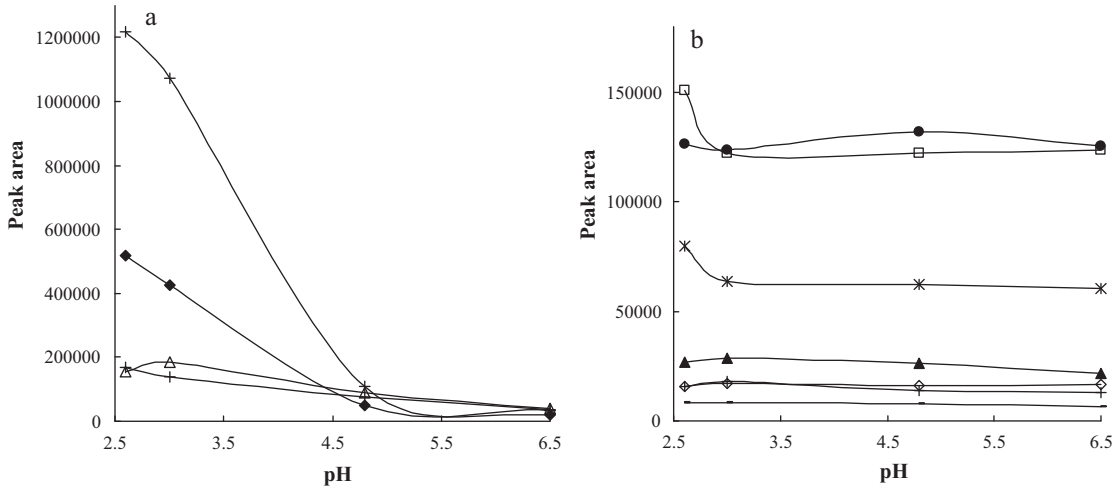


Fig. 3. Effect of pH on the extraction performance of studied analytes (a) (×) NX, (♦) IB, (▲) SMZO, (+) GFZ and (b) (□) IRG, (●) BP-A, (*) CMZ, (▲) SMZI, (♦) AMP, (+) CAF, (−) 17EE using in situ IL DLLME. BMIM-Cl volume: 40 μL; $LiNTf_2$/BMIM-Cl (*n*/*n*): 1/1; sample volume: 10 mL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.

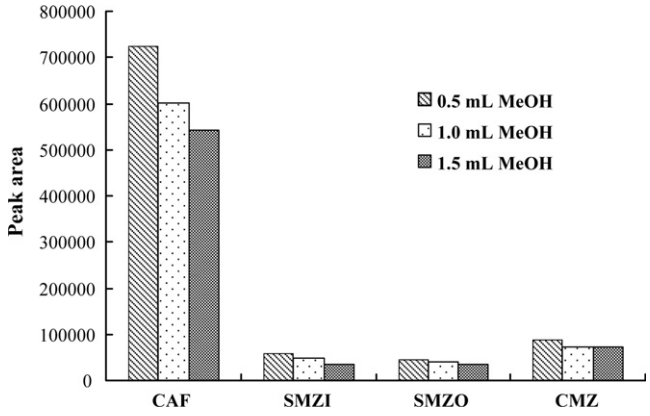


Fig. 4. Effect of dispersive solvent volume on the extraction performance of studied analytes using traditional IL DLLME method; extraction solvent, HNH_2MPL-FAP; dispersive solvent: 0.5 mL MeOH; HNH_2MPL-FAP volume: 30 μL; sample volume: 10 mL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.

Fig. 5a shows the effect of added salt on the extraction efficiency using the HNH_2MPL-FAP IL with traditional IL DLLME method. It can be observed that with an increase of the salt content, the extraction efficiency of most analytes increased, including NX, IB, SMZI, SMZO, AMP, and BP-A. A 2.7-fold improvement in extraction efficiency for AMP was observed when 25% (w/v) of NaCl was added. However, for CAF, IRG, and CMZ, the variation in the extraction efficiency was relatively small (Fig. 5b). A slight decrease in the extraction efficiency was observed for GFZ with an increase in the salt content.

Fig. 6 shows the effect of added salt on the extraction efficiency of selected analytes using the in situ IL DLLME method. With an increase in the salt content, the extraction efficiency of SMZO, AMP, and CAF increased (Fig. 6a). However, for other analytes, the extraction efficiencies decreased with the addition of salt (Fig. 6b). This was presumably due to the fact that the addition of salt affected the ionic strength of the sample solution, possibly influencing the metathesis reaction and the amount of BMIM-NTf_2 IL formed [37].

In order to perform a quantitative study under optimized conditions for most of the analytes, calibration curves were obtained using 25% NaCl (w/v) added to the sample solution and HNH_2MPL-FAP IL as the extraction solvent in the traditional IL DLLME method.

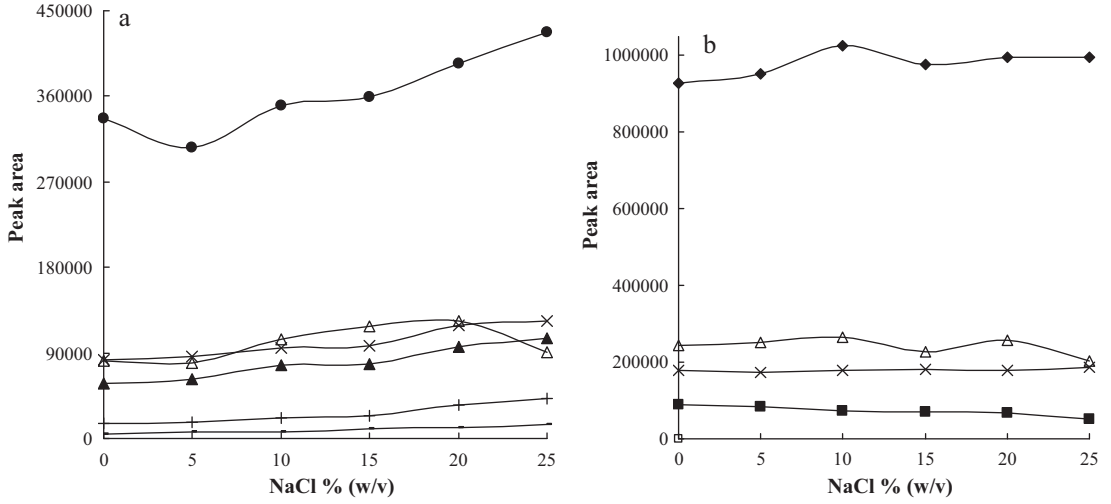


Fig. 5. Effect of added salt on the extraction performance of studied analytes (a) (●) NX, (△) IB, (×) SMZI, (▲) SMZO, (+) AMP, (−) BP-A and (b) (♦) CAF, (△) IRG, (×) CMZ, (■) GFZ using traditional IL DLLME, extraction solvent: 30 μL HNH_2MPL-FAP; dispersive solvent: 0.5 mL MeOH; sample volume: 10 mL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.

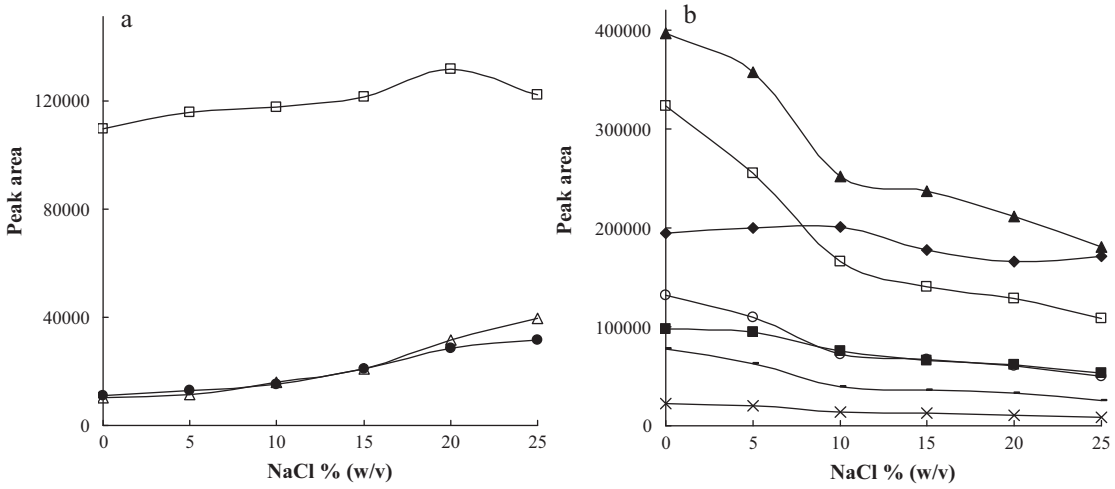


Fig. 6. Effect of added salt on the extraction performance of studied analytes (a) (□) SMZO, (△) AMP, (●) CAF and (b) (▲) NX, (□) IRG, (♦) CMZ, (○) IB, (■) BP-A, (−) GFZ, (×) 17EE using in situ IL DLLME. BMIM-Cl volume: 40 μL; $LiNTf_2$/BMIM-Cl (*n*/*n*): 1/1; sample volume: 10 mL; injection volume: 8 μL; extraction time: 0.5 min; centrifuge time: 5 min.

However, for in situ IL DLLME with BMIM-Cl + $LiNTf_2$ as extraction solvent, no salt was added.

3.4. Analytical performance

The analytical performance in terms of calibration linearity, standard deviation of regression line, linear range, limit of detection (LOD), and reproducibility were studied for both the traditional IL DLLME and in situ IL DLLME methods. The reproducibilities of the in situ IL DLLME and traditional IL DLLME were determined by five repeated extractions resulting in relative standard deviation (RSD) values ranging from 1.9% to 6.1% and 1.5% to 5.8%, respectively. Calibration curves of each analyte were constructed in deionized water (in situ IL DLLME) or 25% NaCl (w/v) solution (traditional IL DLLME) with 10 concentration levels. The figures of merit of the calibration curves using the two extraction methods are listed in Tables 3 and 4. The obtained correlation coefficients (*R*) varied from 0.994 to 0.999 for traditional IL DLLME and 0.997 to 0.999 for in situ IL DLLME method. The small errors of the slope indicate the exceptional linearity for both extraction methods.

The LODs were calculated based on three times the standard deviation of the obtained peak area at the lowest sample concentration divided by the slope of the calibration curve. The obtained LOD for the 17 studied analytes varied from 0.1 to 55.1 μg/L for traditional IL DLLME using HNH_2MPL-FAP IL as extraction solvent, and from 0.1 to 55.8 μg/L for in situ IL DLLME using BMIM-Cl + $LiNTf_2$ as extraction solvent. The LOD of IB using HNH_2MPL-FAP IL as extraction solvent was relatively high due to overlap with the FAP-based IL. Slightly lower LODs were obtained for GFZ and BP-A using the in situ IL DLLME with BMIM-Cl + $LiNTf_2$ as extraction solvent. However, a significant decrease in LODs was observed for analytes containing tertiary amine functional groups when using the HNH_2MPL-FAP IL with traditional IL DLLME. The LODs of CAF and AMP were two orders of magnitude lower when using the HNH_2MPL-FAP IL as extraction solvent compared to in situ IL DLLME.

3.5. Applications to real water samples

Real water samples including tap water and creek water were examined to validate the applicability and matrix effects for the extraction of CECs using the two IL DLLME methods. Table 5 shows the concentration and recovery of 17 studied analytes spiked into the real water samples. No analytes were detected by blank

Table 3
Figures of merit of the calibration curves and limit of detection by traditional IL DLLME method using HNH_2MPL-FAP as extraction solvent[a].

Analytes	Slope ± error	S_{yx}[b]	Linear range (μg L^{-1})	Linearity (*R*)	LOD (μg L^{-1})
AMP	440.7 ± 4.6	5730	0.3–1115.7	0.999	0.3
AZM	12.5 ± 0.2	2217	50.4–15000	0.999	36.6
CAF	1731.9 ± 28.5	181,934	0.6–5636.4	0.999	0.6
SID	1954.6 ± 25.8	49,224	0.98–1981.2	0.999	0.1
SMPZ	2473.3 ± 21.1	39,438	0.97–1943.9	0.999	0.3
SFZI	3513.6 ± 52.2	15,540	1.4–284.7	0.999	1.5
SFZO	2954.0 ± 35.8	15,086	0.1–379.6	0.999	0.1
CMZ	8923.0 ± 149.1	21,352	0.1–142.4	0.999	0.1
BP-A	46.8 ± 1.4	1363	22.8–1138.9	0.998	13.5
NX	5256.8 ± 48.5	28,896	0.8–592.7	0.999	0.5
17EE	–	–	–	–	–
IB	268.2 ± 4.0	10,740	58.1–2905.4	0.999	55.1
GFZ	326.2 ± 14.5	12,338	9.5–949.1	0.994	7.6
IRG	1888.5 ± 17.2	16,129	1.2–932.7	0.999	1.1
BiPh	8231.3 ± 256.1	182,118	0.47–700.9	0.997	0.2
FPP	5818.7 ± 97.8	186,176	0.48–1925.2	0.999	0.4
BPCA	3545.0 ± 40.5	178,454	0.50–3926.6	0.999	0.4

[a] Conditions: HNH_2MPL-FAP volume: 30 μL; dispersive solvent: 0.5 mL methanol; sample volume: 10 mL; salt content: 25% NaCl; sedimented phase volume: ~13 μL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.
[b] Standard deviation of regression.

Table 4
Figures of merit of the calibration curves and limit of detection by in situ IL DLLME method[a].

Analytes	Slope ± error	S_{yx}[b]	Linear range (μg L^{-1})	Linearity (R)	LOD (μg L^{-1})
AMP	77.8 ± 1.1	877	11.3–848.4	0.999	11.2
AZM	12.5 ± 0.2	3372	51.1–15349.5	0.999	50.2
CAF	18.8 ± 0.3	1857	57.1–5714.4	0.999	55.8
SID	362.1 ± 3.5	10,437	5.0–3013.0	0.999	3.4
AMPZ	661.0 ± 9.3	27,000	4.9–2956.2	0.999	1.4
SFZI	478.2 ± 11.2	3138	4.3–288.7	0.998	4.3
SFZO	2523.0 ± 24.4	7155	1.0–288.7	0.999	0.8
CMZ	2751.1 ± 53.6	10,036	2.9–192.5	0.998	2.9
BP-A	532.3 ± 15.6	23,357	15.4–1539.5	0.997	14.7
NX	3879.8 ± 51.4	32,435	0.4–600.9	0.999	0.5
17EE	199.7 ± 4.3	3757	2.8–854.2	0.998	1.8
IB	263.9 ± 4.4	13,456	2.0–2945.6	0.999	2.0
GFZ	384.9 ± 7.2	10,493	4.8–1443.3	0.999	4.4
IRG	1677.5 ± 28.1	27,127	0.6–945.6	0.999	1.0
BiPh	17336.0 ± 180.4	74,364	0.95–473.7	0.999	0.1
FPP	717.8 ± 18.5	55,272	0.97–2927.8	0.998	1.0
BPCA	5779.5 ± 48.0	92,218	1.01–2027.6	0.999	0.5

[a] Conditions: BMIM-Cl volume: 40 μL; $LiNTf_2$/BMIM-Cl (n/n): 1/1; sample volume: 10 mL; sedimented phase volume: ~13 μL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.
[b] Standard deviation of regression.

Table 5
Recoveries of real water samples spiked with 17 analytes determined by in situ IL DLLME and traditional IL DLLME methods.

Analytes	Concentration (μg L^{-1})	Recovery ± error[a]			
		In situ IL DLLME[b]		Traditional IL DLLME[c]	
		Tap water	Creek water	Tap water	Creek water
AMP	28.6	96 ± 7	95 ± 4	99 ± 7	97 ± 6
AZM	256.0	102 ± 6	104 ± 7	92 ± 10	99 ± 4
CAF	141.4	93 ± 1	107 ± 5	94 ± 2	100 ± 3
SID	50.2	98 ± 7	98 ± 4	104 ± 6	103 ± 8
SMPZ	49.3	104 ± 2	93 ± 2	104 ± 4	98 ± 9
SFZI	7.2	103 ± 2	103 ± 4	101 ± 5	110 ± 6
SFZO	9.6	101 ± 6	91 ± 9	95 ± 5	98 ± 5
CMZ	4.9	105 ± 3	109 ± 4	91 ± 2	96 ± 4
BP-A	38.5	96 ± 1	94 ± 4	104 ± 4	101 ± 3
NX	19.6	99 ± 1	98 ± 2	96 ± 1	100 ± 1
17EE	27.5	100 ± 4	101 ± 1	–	–
IB	98.7	102 ± 6	99 ± 2	102 ± 6	101 ± 3
GFZ	47.6	98 ± 3	102 ± 2	100 ± 3	93 ± 5
IRG	31.5	97 ± 2	104 ± 3	100 ± 3	95 ± 1
BiPh	47.4	98 ± 2	106 ± 2	110 ± 6	108 ± 7
FPP	48.8	106 ± 8	95 ± 3	92 ± 5	92 ± 6
BPCA	50.7	95 ± 7	91 ± 7	108 ± 4	106 ± 3

[a] Results obtained by 3 replicate extractions.
[b] *Conditions*: BMIM-Cl volume: 40 μL; $LiNTf_2$/BMIM-Cl (n/n): 1/1; sample volume: 10 mL; sedimented phase volume: ~13 μL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.
[c] *Conditions*: HNH_2MPL-FAP volume: 30 μL; dispersive solvent: 0.5 mL methanol; sample volume: 10 mL; salt content: 25% NaCl; sedimented phase volume: ~13 μL; injection volume: 9 μL; extraction time: 0.5 min; centrifuge time: 5 min.

extraction of the water samples. Recoveries ranged from 93 to 106% and 91 to 107% for tap water and creek water, respectively, using in situ IL DLLME method, and 91 to 110% and 92 to 110% using traditional IL DLLME with the HNH_2MPL-FAP IL as extraction solvent. The results indicate that matrix complexity had little effect on the recovery for most analytes using both IL DLLME methods.

4. Conclusions

Seven functionalized FAP-based ILs have been applied for the extraction of 14 emerging contaminants using traditional IL DLLME technique. For compounds containing tertiary amine functional group within their molecular structure, an approximately 2–50-fold enhancement in the enrichment factors were observed using HNH_2MPL-FAP as extraction phase compared to the other FAP-based ILs. The extraction performance of the FAP-based ILs were also compared to those of using BMIM-NTf_2 IL with traditional IL DLLME and in situ IL DLLME method. For polar or acidic compounds without amine groups, highest enrichment factors were obtained with BMIM-NTf_2 IL as the extraction solvent compared to all FAP-based ILs. However, the amount of FAP-based ILs required for the extraction was much less than the NTf_2-based IL, due to their high hydrophobicity and hydrolytic stabilities.

Quantitative studies were performed using both in situ IL DLLME and traditional IL DLLME methods. The LODs for all studied analytes varied from 0.1 to 55.1 μg/L when using traditional IL DLLME with HNH_2MPL-FAP IL as extraction solvent, and ranged from 0.1 to 55.8 μg/L using in situ IL DLLME with BMIM-Cl + $LiNTf_2$ as extraction solvent. A 93-fold decrease in the detection limit was observed for CAF using the HNH_2MPL-FAP as extraction solvent compared to using BMIM-Cl + $LiNTf_2$ IL with in situ IL DLLME. Recoveries of studied analytes spiked in real water samples were studied. The results showed that the extraction performance of the two IL DLLME methods was not significantly affected by the real water sample matrices.

The obtained results indicate that the applied two IL DLLME methods are fast, robust, sensitive, and can be used to selectively screen specific compounds from large volumes of sample matrix. The selectivity and sensitivity of the method can be effectively tuned and modulated by employing functional groups in the structural design of the ILs.

Acknowledgements

J.L.A. acknowledges funding from the Analytical and Surface Chemistry Program in the Division of Chemistry and the Separation and Purification Processes Program in the Chemical, Environmental, Bioengineering, and Transport Systems Division from the National Science Foundation for a CAREER grant (CHE-0748612).

References

[1] EPA work group, White Paper: Aquatic Life Criteria for Contaminants of Emerging Concern, 2008.
[2] G.A. Loraine, M.E. Pettigrove, Environ. Sci. Technol. 40 (2006) 687.
[3] S.D. Richardson, Anal. Chem. 82 (2010) 4742.
[4] A. Nikolaou, S. Meric, D. Fatta, Anal. Bioanal. Chem. 387 (2007) 1225.
[5] M. Whelehan, U. Stockar, I.W. Marison, Water Res. 44 (2010) 2314.
[6] E. Pérez-Carrera, M. Hansen, V.M. León, E. Björklund, K.A. Krogh, B. Halling-Sørensen, E. González-Mazo, Anal. Bioanal. Chem. 398 (2010) 1173.
[7] I. Coille, S. Reder, S. Bucher, G. Gauglitz, Biomol. Eng. 18 (2002) 273.
[8] T.Y. Iguchi, Bioscience 58 (2008) 1061.

[9] T. Einsle, H. Paschke, K. Bruns, S. Schrader, P. Popp, M. Moeder, J. Chromatogr. A 1124 (2006) 196.
[10] M.A. Soliman, J.A. Pedersen, I.H. Suffet, J. Chromatogr. A 1029 (2004) 223.
[11] S. Rodriguez-Mozaz, M.J. Lopez de Alda, D. Barceló, J. Chromatogr. A 1152 (2007) 97.
[12] C. Postigo, M.J. Lopez de Alda, D. Barceló, Anal. Chem. 80 (2008) 3123.
[13] J. Pawliszyn, Solid Phase Microextraction: Theory and Practice, Wiley, New York, 1997.
[14] M.E. Torres Padrón, Z. Sosa Ferrera, J.J. Santana Rodríguez, Biomed. Chromatogr. 23 (2009) 1175.
[15] E.A. Suchara, D. Budziak, E. Martendal, L.L.F. Costa, E. Carasek, Anal. Chim. Acta 613 (2008) 169.
[16] J.B. Quintanan, R. Rodil, S. Muniategui-Lorenzo, P. López-Mahía, D. Prada-Rodríguez, J. Chromatogr. A 1174 (2007) 27.
[17] X. Wen, C. Tu, H.K. Lee, Anal. Chem. 76 (2004) 228.
[18] Z. Zhang, C. Zhang, X. Su, M. Ma, B. Chen, S. Yao, Anal. Chim. Acta 621 (2008) 185.
[19] J. Zhang, H.K. Lee, J. Chromatogr. A 1216 (2009) 7527.
[20] M. Rezaee, Y. Assadi, M.R. Milani Hosseini, E. Aghaee, F. Ahmadi, S. Berijani, J. Chromatogr. A 1116 (2006) 1.
[21] H. Chen, H. Chen, J. Ying, J. Huang, L. Liao, Anal. Chim. Acta 632 (2009) 80.
[22] C. Xiong, J. Ruan, Y. Cai, Y. Tang, J. Pharm. Biomed. Anal. 49 (2009) 572.
[23] Z. Li, J. Chang, H. Shan, J. Pan, Rev. Anal. Chem. 26 (2007) 109.
[24] H. Zhao, S. Xia, P. Ma, J. Chem. Technol. Biotechnol. 80 (2005) 1089.
[25] J.F. Liu, N. Li, G.B. Jiang, J.M. Liu, J. Jönsson, M.J. Wen, J. Chromatogr. A 1066 (2005) 27.
[26] F. Zhao, Y. Meng, J.L. Anderson, J. Chromatogr. A 1208 (2008) 1.
[27] Q. Zhao, J.C. Wajert, J.L. Anderson, Anal. Chem. 82 (2010) 707.
[28] J.F. Peng, J.F. Liu, X.L. Hu, G.B. Jiang, J. Chromatogr. A 1139 (2007) 165.
[29] C. Basheer, A.A. Alnedhary, B.S.M. Rao, R. Balasubramanian, H.K. Lee, J. Chromatogr. A 1210 (2008) 19.
[30] J.-F. Liu, G.-B. Jiang, Y.-G. Chi, Y.-Q. Cai, Q.-X. Zhou, J.-T. Hu, Anal. Chem. 75 (2003) 5870.
[31] C. Yao, W.R. Pitner, J.L. Anderson, Anal. Chem. 81 (2009) 5054.
[32] Y. Liu, E. Zhao, W. Zhu, H. Gao, Z. Zhou, J. Chromatogr. A 1216 (2009) 885.
[33] M.T. Pena, M.C. Casais, M.C. Mejuto, R. Cela, J. Chromatogr. A 1216 (2009) 6356.
[34] Q. Zhou, H. Bai, G. Xie, J. Xiao, J. Chromatogr. A 1177 (2008) 43.
[35] M. Baghdadi, F. Shemirani, Anal. Chim. Acta 613 (2008) 56.
[36] Q. Zhou, X. Zhang, J. Xiao, J. Chromatogr. A 1216 (2009) 4361.
[37] C. Yao, J.L. Anderson, Anal. Bioanal. Chem. 395 (2009) 1491.
[38] N. Ignat'ev, P. Sartori, J. Fluorine Chem. 103 (2000) 57.
[39] S. Zein El Abedin, N. Borissenko, F. Endres, Electrochem. Commun. 6 (2004) 422.
[40] M.J. Muldoon, S.N.V.K. Aki, J.L. Anderson, J.K. Dixon, J.F.J. Brennecke, Phys. Chem. B 111 (2007) 9001.
[41] Q. Zhao, J. Eichhorn, W.R. Pitner, J.L. Anderson, Anal. Bioanal. Chem. 395 (2009) 225.
[42] Y. Wang, J. Sun, H. Liu, Z. He, Electrophoresis 28 (2007) 2391.
[43] O. Lorphensri, J. Intravijit, D.A. Sabatini, T.C.G. Kibbey, K. Osathaphan, C. Saiwan, Water Res. 40 (2006) 1481.
[44] M. Remko, C.-W. von der Lieth, Bioorg. Med. Chem. 12 (2004) 5395.
[45] H. Idborg, L. Zamani, P.-O. Edlund, I. Schuppe-Koistinen, S.P. Jacobsson, J. Chromatogr. B 828 (2005) 9.
[46] C. Ehlert, H. Strunz, K. Visser, M. Wiese, J.K. Seydel, J. Pharm. Sci. 87 (1998) 101.
[47] M.S. Díaz-Cruz, M.J.L. de Alda, D. Barceló, J. Chromatogr. A 1130 (2006) 72.
[48] C. Dagenais, A. Avdeef, O. Tsinman, A. Dudley, R. Beliveau, Eur. J. Pharm. Sci. 38 (2009) 121.
[49] T. Scheytt, P. Mersmann, R. Lindstädt, T. Heberer, Water Air Soil Pollut. 165 (2005) 3.
[50] Y.S. Keum, H.R. Lee, H.W. Park, J.-H. Kim, Biodegradation 21 (2010) 989.
[51] H. Sambe, K. Hoshina, K. Hosoya, J. Haginaka, J. Chromatogr. A 1134 (2006) 16.
[52] A. Kokate, X. Li, P.J. Williams, P. Singh, B.R. Jasti, Pharm. Res. 26 (2009) 1130.
[53] A.K. Sarmah, G.L. Northcott, F.D.L. Leusch, L.A. Tremblay, Sci. Total Environ. 355 (2006) 135.
[54] N.M. Vieno, H. Härkki, T. Tuhkanen, L. Kronberg, Environ. Sci. Technol. 41 (2007) 5077.
[55] A.R.D. Verliefde, E.R. Cornelissen, S.G.J. Heijmana, J.Q.J.C. Verberk, G.L. Amy, B. Van der Bruggen, J.C. van Dijk, J. Membr. Sci. 322 (2008) 52.
[56] T. Loftsson, Í.B. Össurardóttir, T. Thorsteinsson, M. Duan, M. Másson, J. Incl. Phenom. Macro. 52 (2005) 109.
[57] J.S. Arey, R.K. Nelson, L. Xu, C.M. Reddy, Anal. Chem. 77 (2005) 7172.