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ORIGINAL PAPER

Polymethacrylate microparticles covalently functionalized with an ionic liquid for solid-phase extraction of fluoroquinolone antibiotics

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Abstract Microparticles were synthesized by suspension copolymerization of the synthetic ionic liquid (IL) 1-allyl-3-methylimidazolium bromide with ethylene glycol dimethacrylate. The particles have a regular spherical shape and an average diameter of 65±24 μm. Their affinity for the fluoroquinolone antibiotics ofloxacin (OFL), lomefloxacin (LOM) and ciprofloxacin (CIP) is much higher than that of the blank polymer (not containing an IL), of polymers using methacrylic acid as functional monomer, of hydrophilic-lipophilic balanced sorbents, and of C_{18} sorbents. The microparticles were applied to the solid-phase extraction and rapid preconcentration of the fluoroquinolones from urine which then were quantified by HPLC. The calibration plot covers the 0.05 to 20 μg mL^{-1} concentration range, and the average recoveries at three spiking levels range from 93.6 to 103.7 %, with RSD of ≤5.7 %. The method was successfully applied to the determination of fluoroquinolones in spiked urine.

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Introduction

Ionic liquids (ILs) are a class of organic molten salts consisting of a pair of soft cationic and anionic species with a melting point close to or below room temperature [1]. They display many fascinating characteristics such as high thermal and chemical stability, negligible vapor pressure, nonvolatility, strong polarity, and good solvating properties [2]. Over the past few years, ILs have aroused increasing interest for their promising role as organic reaction solvents [3], separation-extraction solvents [4], and electrolyte materials [5]. In addition, ILs have been introduced as an important component to form task-specific polymers, which will be capable of interacting with analytes or substrates in specific ways. And the IL-based polymers are favorable candidates as adsorption materials used in sample pretreatment due to their excellent physical and chemical properties [6, 7]. Until now, ILs has been used as a solvent or porogen in the preparation of polymer, which can accelerate the synthesis process and improve the adsorption of the polymers [8]. The low vapor pressure of ILs can assist in reducing the problem of polymer bed shrinkage and can also act as pore template in polymerization reaction [9]. Moreover, ILs has been used as a functional monomer for preparation of polymer which can be used in aqueous media based on π-π interactions or ion-exchange interactions between the analyte and ILs [10].

Fluoroquinolones (FQs) are the most potent antibiotics against gram-positive and gram-negative bacteria through inhibition of their DNA gyrase, a critical enzyme to bacterial chromosome replication [11]. FQs are used in a wide range of pulmonary, gastrointestinal, and urinary as well as respiratory tract and skin infections [12]. The identification and quantification of FQs in various biological matrices are important to ensure that they are not present at levels that may pose health risks to people [13, 14]. Several methods have been developed for analysis of these drugs in various biological matrices mainly including liquid chromatography [11, 12, 15], capillary electrophoresis [16–18], liquid chromatography-mass spectrometry [19–22] and microbiological assay [23]. However, due to the complexity of biological matrices, it is difficult to achieve direct separation of target analytes from complex biological matrices. Therefore, a suitable sample pretreatment is crucial to improving the purification and specificity before instrumental analysis [24]. Liquid-liquid extraction [25], solid-phase extraction (SPE) [26], dispersive liquid-liquid microextraction [27] and matrix solid-phase dispersion [28] are common sample pretreatments used routinely in pharmaceutical laboratories. Among them, SPE with different sorbents such as C_{18}, C_8, Silica, NH_2, PCX, and HLB are the most frequently used. However, most of these sorbents are of high cost, disposability, and poor selectivity [29]. Therefore, the development of cheap, multi-usable and selective sorbent for SPE is desired.

This work using 1-allyl-3-methyl-imidazolium bromide [Amim][Br] as functional monomer to prepare an ionic liquid-functionalized microparticles (IL-FM) by suspension polymerization and applying it as a special sorbent for SPE to extract ofloxacin (OFL), lomefloxacin (LOM) and ciprofloxacin (CIP) from human urine. By using IL-FM as a sorbent, OFL, LOM and CIP were selectively isolated from urine samples and the impurities were eliminated simultaneously.

Experimental

Materials

OFL, LOM, and CIP were obtained from Sigma Co. Ltd. (St Louis, MO, USA, www.sigmaaldrich.com). Trifluoroacetic acid (TFA), polyvinylpyrrolidone (PVP), tetrabutyl ammonium bromide (TBAB), N-methylimidazole and ethyl bromide were obtained from Huaxin Chemical Reagent Co. (Baoding, China). Ethylene glycol dimethacrylate (EDMA) was obtained from Anxin Chemical Co., Ltd. (Fushun, China, www.anxinchem.com.cn). Methacryclic acid (MAA) and 2,2-azodiisobutyronitrile (AIBN) were purchased from Kermel Chemical Co., Ltd. (Tianjin, China, www.chemreagent.com). All the other reagents used in the experiment were of the highest grade commercially available. Double deionized water was filtered through a 0.45 μm fiber membrane before use.

Instrumentation and experimental conditions

Fourier transform infrared (FTIR) data was obtained by a Fourier transform infrared spectrometer IRAffinity-1 (Shimadzu, Kyoto, Japan, www.shimadzu.com) in a range of 400–4000 cm^{-1} using KBr pellets. The morphological evaluation was carried out by JSM-7500F scanning electron microscopy (SEM, FEI Co., Hillsboro, USA, www.fei.com). HPLC analysis was performed using a Shimadzu HPLC system equipped with two LC-20AT Solvent Delivery Units, a SUS20A gradient controller, and a SPD-20A UV–VIS Detector (Shimadzu, Kyoto, Japan, www.shimadzu.com/). An N-2000 workstation (Zheda Zhineng Co. Ltd., Hangzhou, China) was used as the data acquisition system. The analytical column (250×4.6 mm I.D., C_{18}, 5 μm) was obtained from YMC Co. Ltd. (Kyoto, Japan, www.ymc-group.com). The mobile phase was water (containing 0.02 mol L^{-1} TBAB, 0.7‰ TFA)-acetonitrile (90:10, v/v) with a flow rate of 1.0 mL min^{-1}. The injection volume was 10 μL and the detection wavelength of the detector was set at 280 nm.

Preparation of ionic liquid-functionalized polymer

A mixture of N-methylimidazole (8 mmol) and allyl bromide (8 mmol) was reacted in 20 mL of chloroform at 60 °C to obtain [Amim][Br], then EDMA (50 mmol) and AIBN (250 mg) were added and sonicated for 5.0 min to make them fully dissolved. This solution was mixed with 120 mL of PVP aqueous solution (25 g L^{-1}) by stirring under 60 °C. Subsequently, polymerization was performed at 60 °C in a water bath for 24 h. Finally, the solution was filtered and the obtained polymer was washed with water, methanol-acetic acid (9:1, v/v) and methanol respectively to remove the residual monomers and coagulated or soluble impurities. The blank polymer (NIL-FM, in absence of ionic liquid) and the methacrylic acid-functionalized microparticles (methacrylic acid instead of ionic liquid, MAA-FM) was prepared and treated in an identical manner.

Pretreatment of urine samples and standard solution

Urine samples were centrifuged at 1790×*g* for 10.0 min, and then they were stored at −20 °C until analysis was performed with the minimum possible delay. Stock solutions of OFL, LOM and CIP were prepared in methanol. Working standard solutions were prepared by adding appropriate volume of stock solutions into the blank urine and the volume added was always less than 5 % of the final urine volume to preserve the integrity of the samples.

Procedures of solid-phase extraction

Three hundred milligrams of IL-FM were packed into empty SPE cartridge and preconditioned with 3.0 mL of methanol and 2.0 mL of water. After loading 1.0 mL of urine sample, the cartridge was washed with 3.0 mL of water and eluted with 4.0 mL of acetonitrile- acetic acid (87:13, v/v). Finally, the eluent was evaporated to dryness and the residue was re-dissolved with 1.0 mL of mobile phase for further HPLC analysis.

Results and discussion

Choice of materials

N-methylimidazole and allyl bromide were added in the system to synthetize ionic liquid ([Amim][Br]) in one step through bromination reaction. Allyl bromide (8 mmol) was given by passing the stoichiometric amount, which was corresponding to 8 mmol of imidazolium groups in N-methylimidazole. After reaction, the polymer contained the Br^- groups, which can be easily substituted by ion exchange to the desired ionic form (Fig. 1). There are two reasons for using allyl bromide to synthesize ionic liquid: Firstly, the imidazolium cation is thermally stable and its stability increases with the increasing of alkyl substitution, as long as linear alkyl groups are used [30]. Moreover, the bonding density of the imidazolium polymer decreases with the increasing length of imidazole alkyl branches because of the steric hindrance from the alkyl chain [31] which resulted to the low adsorbed ability. To obtain satisfactory thermal stability and degree of polymerization, allyl bromide was chosen as substituent group in this work.

In addition, referring to the previous report on the suspension polymerization [26], several factors affecting the morphology of the obtained microspheres are optimized. The molar ratios of monomer/cross-linker should be proper not only to maintain the mechanical stability and rigidity of the polymer, but also to ensure the formation of binding sites, thus resulting in a higher selectivity and good extraction performance. In this work, the molar ratio of monomer/cross-linker was investigated and 8:50 was selected. PVP is particularly suitable as suspension stabilizers with significant effect on the shape, size, and form of polymers. PVP can keep it stable to form beads of uniform particle size and porous hull [32, 33]. In our experiment, the microspheres were prepared by aqueous suspension polymerization using PVP as dispersing agent in 120 mL of water, which possessed more uniform

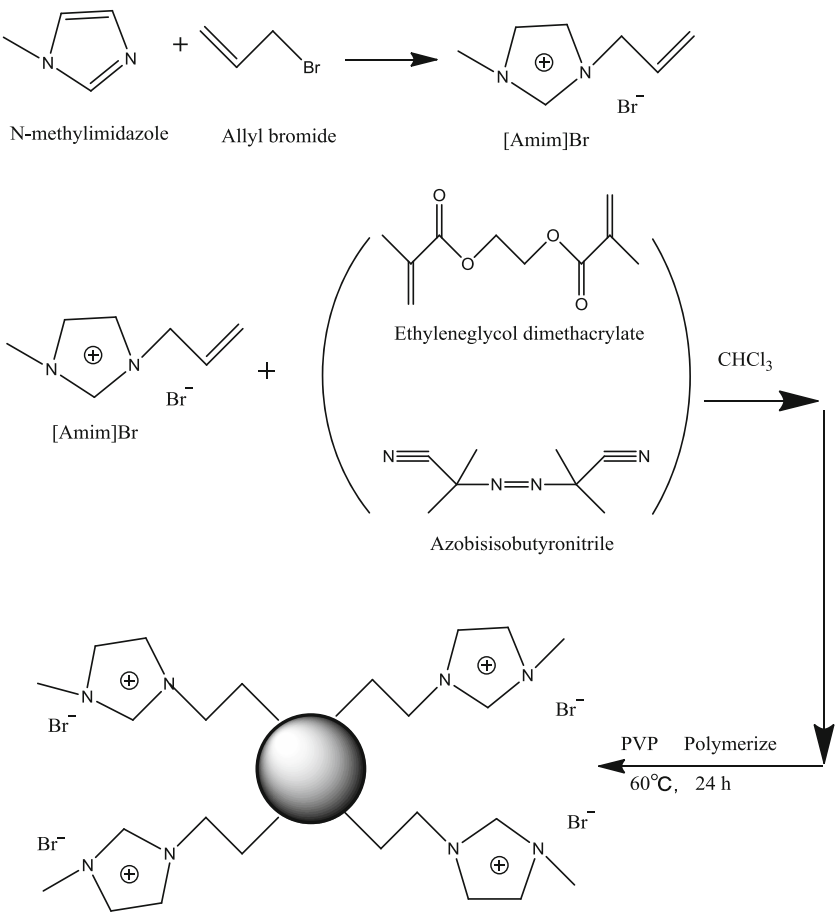

Fig. 1 Schematic illustration of IL and IL-FM formation

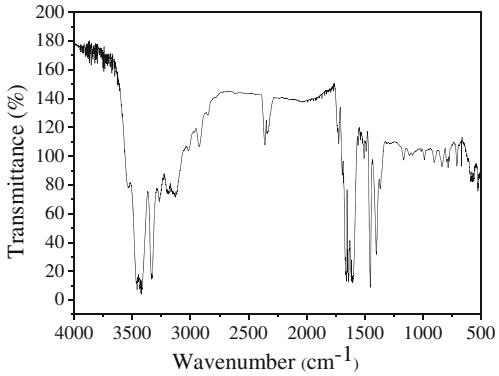

Fig. 2 FI-IR spectra of the IL-FM

particle size and better affinity to analytes than that without PVP. Chloroform (20 mL) was chosen as the porogenic solvent, because it ensured good solubility of the monomer. Moreover, to further improve the recognition ability of the obtained IL-FM in aqueous environment, the IL-FM is prepared using PVP as the dispersant in 120 mL of water.

Performance evaluation of the ionic liquid functionalized polymers

The peak of FT-IR spectroscopy (Fig. 2) at 1459 cm^{-1} was attributable to imidazole groups immobilizing on the polymers and peaks at 1542 and 1565 cm^{-1} corresponded to C-H vibration of the imidazole ring [6]. In addition, the wavelength from 3000 to 3700 cm^{-1} indicated the intensity of the nitrogen fraction (N-H) [34], while 2880–3000 cm^{-1} was the characteristic region for C-H absorption [35]. These results indicated that the ionic liquid ([Amim][Br]) was successfully incorporated into the polymers.

The morphology of IL-FM was evaluated by scanning electron microscopy which indicated that the IL-FM particles were spherical and their surface are rough (Fig. 3) and maybe it is a sign that the ionic liquid was attached tightly to the polymer surface. Additionally, it was important for the adsorption process because it can significantly increase the surface area of the polymer and was suitable for rebinding or releasing the target molecules from its surface. The individual particle size distribution obtained by Particle Size Analyzer was in a range of 41.4–88.9 μm.

Additionally, the solvent-resistant property of IL-FM was also investigated. There was no shrinking and swelling when the polymer was immersed in water, methanol, acetonitrile, methanol–water (7:3, 3:7, and 1:1, v/v), acetone, dichloromethane, ethyl acetate, tetrahydrofuran or even acetic acid and ammonia for 12 h, respectively. Furthermore, the weight of polymer has not changed after drying procedure. The results show the IL-FM is stable in various solvents.

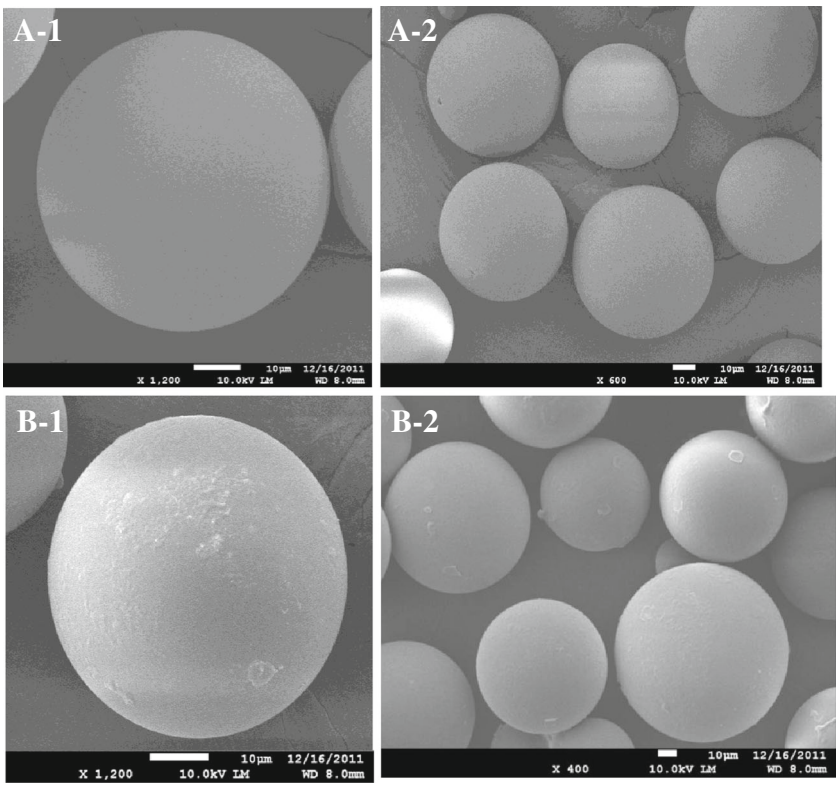

Fig. 3 The SEM images of NIL–FM (A-1, A-2) and IL-FM (B-1, B-2)

Dynamic adsorption experiments for IL-FM and NIL-FM (each loading amount was ranged from 20 to 300 μg) were carried out to evaluate their binding capacity to OFL, LOM and CIP. The results in Fig. 4 show that the adsorption amount of analytes increased gradually with the added amount ranged from 20 to 250 μg, resulting from the ion-exchange interaction between analytes with IL-FM. When the added amount of analytes reached 250 μg, the highest amount of adsorbed analytes was achieved. When the amount of FQs continued to increase, there was no more increase of adsorption amount, indicating that IL-FM reached adsorption/desorption equilibrium. NIL-FM revealed a similar adsorption trend with the IL-FM, however, the maximum adsorbed amount of NIL-FM was obviously lower than that of the IL-FM. All above that demonstrated that IL-FM sorbent possessed a high adsorption capacity to FQs. Furthermore, as the sorbent of SPE, IL-FM can achieve cleaner chromatogram for extracting FQs from complex samples than NIL-FM.

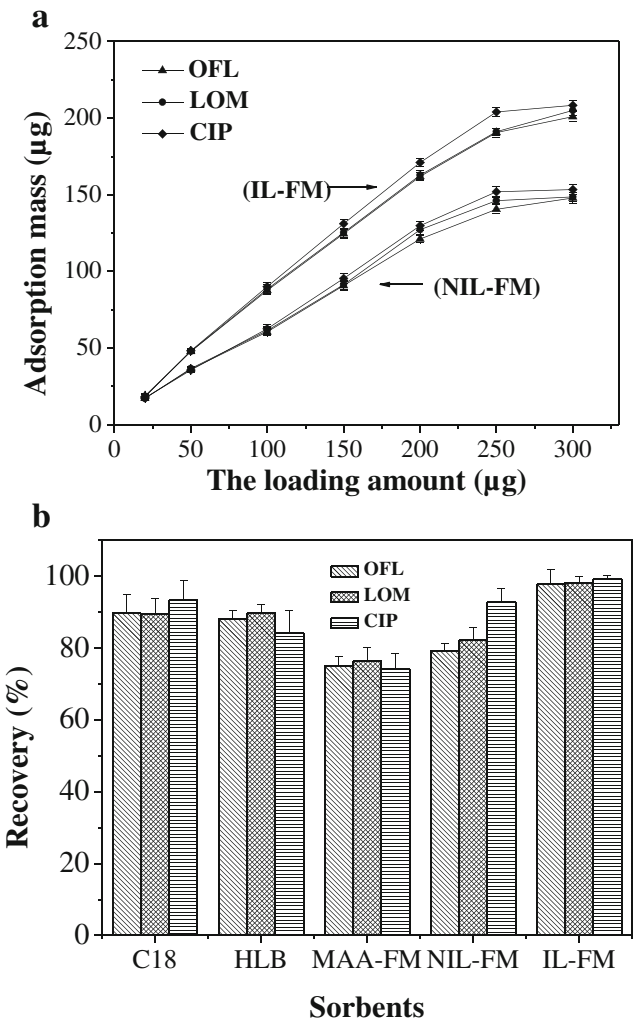

Fig. 4 Adsorption capacity of FQs on IL-FM and NIL-FM (**a**), and comparison of IL-FM with other sorbents (**b**)

Table 1 Features of the IL-FM-SPE-HPLC method

Analytes	Linear equation[a] (0.05–20 μg mL^{-1})	r^2	LOD[b] (μg mL^{-1})	LOQ[c] (μg mL^{-1})
OFL	$y=2.4\times10^4x+1.8\times10^2$	0.9999	0.0052	0.018
LOM	$y=3.5\times10^4x+5.8\times10^2$	0.9991	0.0073	0.025
CIP	$y=4.6\times10^4x+1.2\times10^2$	0.9996	0.0035	0.012

[a] Spiked urine with the mixed OFL, LOM, and CIP at 0.05–20 μg mL^{-1}

[b] LOD: limits of detection (S/N=3)

[c] LOQ: limits of quantification (S/N=10)

Optimization of ionic liquid-functionalized microparticles-solid phase extraction

To achieve accurate and sensitive chromatographic quantification of trace FQs in urine samples, the optimum conditions of IL-FM-SPE such as washing solvent and the volume, elution solvent and the volume using IL-FM as a sorbent were evaluated. It was important to apply a clean-up step immediately after loading the biological samples, which would ensure reduction of matrix interferences and prevention the impurities from polluting the SPE cartridge and analytical column. Respective data and Figures are given in the Electronic Supplementary Material. It was found to give best results when 3.0 mL of water was chosen as washing solvent and 4.0 mL of acetonitrile-acetic acid (87:13, v/v) was used as the elution solvent.

Comparison of solid-phase extraction sorbents

To evaluate the extraction efficiency of IL-FM sorbent, different sorbents such as C_{18}, HLB, and MAA-FP were also employed in the SPE procedures according to the previous reports [21, 22]. The results (Fig. 4b) show that the recoveries of OFL, LOM, and CIP on these sorbents were lower than that on IL-FM. There is a good explanation to the different results of the two polymers (IL-FM and MAA-FP). The carbonyl group of MAA might interact with OFL, LOM, and CIP by involvement of their hydroxyl along the chain into hydrogen bonds. The adsorption characters show that the adsorbent

Table 2 Recoveries of OFL, LOM and CIP in spiked urine samples (n=3)

Analytes	0.5 μg mL^{-1}		5 μg mL^{-1}		15 μg mL^{-1}	
	Recovery (%)	RSD %	Recovery (%)	RSD %	Recovery (%)	RSD %
OFL	93.6	4.3	102.5	4.0	100.5	1.4
LOM	103.7	2.8	96.9	1.8	102.9	2.1
CIP	97.1	5.7	99.1	2.2	101.8	4.4

Table 3 Figures of merit of reported methods for preconcentration of fluoroquinolones

Material/ sample pretreatment	Detect method	Analytical ranges	LOD	Recovery %	RSD %	Samples	Ref.
–	HPLC-ECL	0.2–4.0 μg mL^{-1}	6–60 ng mL^{-1}	94.5–100.8	1.7–5.0	Milk	11
Polyamidoamine dendrimers/LLE	CE	0.2–50 μg mL^{-1}	25–47 ng mL^{-1}	81.8–105.1	1.95–8.60	Chicken muscles	14
SPE	HPLC-FD	0.5–1000 μg L^{-1}	0.7–2.0 ng L^{-1}	90–116	10	Surface waters	15
SPE	MCE	11.5–51.0 ng mL^{-1}	3.1–3.6 ng mL^{-1}	75–111	3.0–10.2	Water	16
Silica nanoparticles	CE	10–300 μg mL^{-1}	2.0–7.0 μg mL^{-1}	88.9–99.5	8.2	Human serum	17
Oxidized MWCNT /DSPE	CEs	38–450 μg L^{-1}	28–94 ng L^{-1}	62.3–116	7.7	Water samples	18
MIP-SPE	LC-ESI-MS/MS	5–500 ng g^{-1}	0.12–0.85 ng g^{-1}	92–103	4–8	Egg	20
SPE	UPLC–MS/MS	–	0.04–0.52 μg kg^{-1}	84–117	1–17	Powder milk	22
Microbiological assay	HPLC	0.1–1.0 μg mL^{-1}	0.2–3 μg mL^{-1}	73.7–87.1	7.2–12.7	Chicken eggs	23
MIP/SPE	HPLC	0.025–2.0 μg g^{-1}	16–17 ng g^{-1}	94.4–96.9	4.7	Chicken muscle	26
Ionic liquid functionalized polymer/SPE	HPLC	0.05–20 μg mL^{-1}	3.5–7.3 ng mL^{-1}	93.6–103.7	5.7	Urine	Present work

using MAA as monomer achieved lower recoveries, while the adsorbent reinforced with ionic liquid proceeded with high yield and contained almost the maximum amount of the analytes. The deep reasons resulting in this outcome are generally assumed that there are not only hydrophobic interactions and weak π-π between methyl imidazolium groups and analytes, but also exhibit ion-dipole interaction between the IL-FM ion and the target molecules. Furthermore, the specific surface areas of the obtained microspheres are increased when the polymer was modified with ionic liquid groups and the augmented specific surface can retain large amount of analytes naturally. Compared with HLB which can adsorbs FQs through hydrogen bonds as well as π-π bonds and C_{18} adsorbing targets only through hydrophobic bonds, IL-FM materials which has quantities of ionic binding sites can reach better adsorptive effect about FQs. Additionally, a clean chromatogram was observed by using IL-FM than that of other adsorbents, which demonstrated the high selectivity and purification effect of the IL-FM to the target analytes. The matrix interferences and poor recoveries of other adsorbents were attributed to the low nonspecific interactions between the various components of the sample matrix with the adsorbents. Otherwise, it was worth noting that the IL-FM can be repeatedly used without any noticeable deterioration in performance while other conventional sorbents lost their performance after one or two extractions.

Validation of the method

Under the optimized conditions, calibration curves were established by plotting the chromatographic peak areas versus the concentrations (0.05–20 μg mL^{-1}) of spiked urine samples to perform a regression analysis and the results were shown in Table 1. The limit of detection (LOD) and the limit of quantification (LOQ) are determined at the signal-to-noise ratio of 3 and 10, respectively. Repeatability was evaluated by determining the precision of intra-day which was assessed by replicate analysis of spiked urine samples in five replicates in the

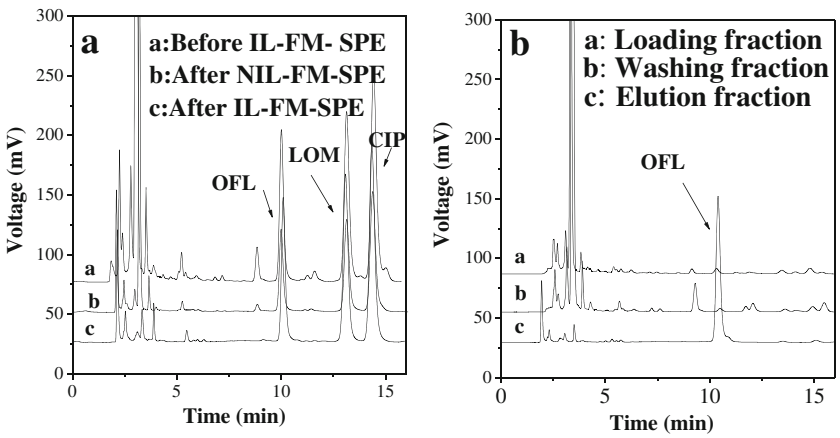

Fig. 5 Chromatograms of spiked urine before and after IL-FM-SPE (**a-a**, **a-c**), NIL-FM-SPE (**a-b**), and urine sample after oral administration (**b**)

same day and the precision of inter-day which was achieved by replicate analysis of spiked samples in consecutive 3 days. The intra-assay and inter-assay deviations of the method were ≤3.2 and ≤4.6 %, respectively. These results indicate that the method has good repeatability. To study the effect of sample matrix, the accuracy of the method was assessed by recovery experiments. Recovery experiments were carried out by three spiked levels of urine samples (Table 2). The average recoveries of the three FQs at three different concentrations (0.5, 5.0 and 15.0 μg mL^{-1}) were in a range of 93.6–103.7 % with RSD≤5.7 % (n=3), which indicated that the method was reliable and was used for the determination of OFL, LOM and CIP in urine samples. The comparison of previous reported methods for preconcentration of fluoroquinolones has been shown in Table 3. Compared with these methods, the method used in this work has several advantages such as high recovery, low LOD, and good analytical range.

Real urine sample analysis

The urine samples were collected before and after 2 h of oral administration of a pharmaceutical product containing 150 mg of OFL. The obtained urine samples were centrifuged at 1790×g for 10.0 min and 1.0 mL of each sample was loading on the SPE cartridges for extraction under the optimized condition and then was analyzed by IL-FM-SPE-HPLC method. The concentration of OFL in the urine after 2 h of oral administration of OFL was 13.9 μg mL^{-1}. The chromatograms of spiked urine (Fig. 5a) and urine sample after oral administration (Fig. 5b) revealed that urine sample was significant cleaner after pretreatment by the presented IL-FM-SPE, and no interference from urine matrices was observed. Besides, the peak of the analytes didn't decrease after the SPE process, which proves that the obtained IL-FM has good extraction performance.

Conclusions

IL-FM was synthesized by suspension polymerization using synthetic ionic liquid (1-allyl-3-methyl-imidazolium bromide, [Amim][Br]) as functional monomer and applied as a special SPE sorbent to extract OFL, LOM and CIP from human urine sample. By using the IL-FM as a sorbent, the three analytes were selectively isolated from urine samples and the impurities were eliminated simultaneously. Good analytical range was obtained in a range of 0.05–20 μg mL^{-1}, the average recoveries at three spiked levels were ranged from 93.6–103.7 %, with RSD≤5.7 %. The presented IL-FM-SPE-HPLC method exhibited the advantages of simplicity, rapidity, sensitivity and accuracy, and can be potentially applied for the monitoring of FQs residue in urine samples. Meanwhile, The IL-FM-SPE method can be combined with GC-MS, LC-MS, and LC-MS/MS to further improve specificity and make excellent prospects.

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References

1. Zhang R, Li N, Wang C, Bai Y, Ren R, Gao S, Yu W, Zhao T, Zhang H (2011) Ionic liquid foam floatation coupled with solid phase extraction for separation and determination of hormones by high-performance liquid chromatography. Anal Chim Acta 704:98–109
2. Zhou X, Xie P, Wang J, Zhang B, Liu M, Liu H, Feng X (2011) Preparation and characterization of novel crown ether functionalized ionic liquid-based solid-phase microextraction coatings by sol–gel technology. J Chromatogr A 1218:3571–3580
3. Bini R, Chiappe C, Marmugi E, Pieraccini D (2006) The "non-nucleophilic" anion $[Tf_2N]^-$ competes with the nucleophilic Br^-: an unexpected trapping in the dediazoniation reaction in ionic liquids. Chem Commun 8:897–899
4. Yuan Y, Wang Y, Xu R, Huang M, Zeng H (2011) Application of ionic liquids in the microwave-assisted extraction of podophyllotoxin from Chinese herbal medicine. Analyst 136: 2294–2305
5. Moccelini SK, Franzoi AC, Vieira IC, Dupont J, Scheeren CW (2011) A novel support for laccase immobilization: cellulose acetate modified with ionic liquid and application in biosensor for methyldopa detection. Biosens Bioelectron 26:3549–3554
6. Guo L, Deng Q, Fang G, Gao W, Shuo W (2011) Preparation and evaluation of molecularly imprinted ionic liquids polymer as sorbent for on-line solid-phase extraction of chlorsulfuron in environmental water samples. J Chromatogr A 1218:6271–6277
7. González-Álvarez J, Blanco-Gomis D, Arias-Abrodo P, Díaz-Llorente D, Ríos-Lombardía N, Busto E, Gotor-Fernández V, Gutiérrez-Álvarez MD (2012) Polymeric imidazolium ionic liquids as valuable stationary phases in gas chromatography: Chemical synthesis and full characterization. Anal Chim Acta 721:173–181
8. Sun X, He J, Cai G, Lin A, Zheng W, Liu X, Chen L, He X, Zhang Y (2010) Room temperature ionic liquid-mediated molecularly imprinted polymer monolith for the selective recognition of quinolones in pork samples. J Sep Sci 33:3786–3793
9. Xu Z, Fang G, Wang S (2010) Molecularly imprinted solid phase extraction coupled to high-performance liquid chromatography for determination of trace dichlorvos residues in vegetables. Food Chem 119:845–850
10. Fan JP, Tian ZY, Tong S, Zhang XH, Xie YL, Xu R, Qin Y, Li L, Zhu JH, Ouyang XK (2013) A novel molecularly imprinted polymer of the specific ionic liquid monomer for selective separation of synephrine from methanol–water media. Food Chem 141:3578–3585
11. Li Y, Zhang Z, Li J, Li H, Chen Y, Liu Z (2011) Simple, stable and sensitive electrogenerated chemiluminescence detector for high-performance liquid chromatography and its application in direct determination of multiple fluoroquinolone residues in milk. Talanta 84:690–695
12. Yan H, Row KH, Yang G (2008) Water-compatible molecularly imprinted polymers for selective extraction of ciprofloxacin from human urine. Talanta 75:227–232
13. Gajda A, Posyniak A, Zmudzki J, Gbylik M, Bladek T (2012) Determination of (fluoro) quinolones in eggs by liquid chromatography with fluorescence detection and confirmation by liquid

chromatography-tandem mass spectrometry. Food Chem 135:430–439
14. Tian J, Hu J, Yang F, Guo J, Qin W (2014) Polyamidoamine dendrimers as off-column binding agent and in-column pseudostationary phase for efficient and sensitive capillary electrophoretic analysis of fluoroquinolones in chicken muscles. Food Chem 157:498–503
15. Sturini M, Speltini A, Pretali L, Fasani E, Profumo A (2009) Solid-phase extraction and HPLC determination of fluoroquinolones in surface waters. J Sep Sci 32:3020–3028
16. Sierra-Rodero M, Fernández-Romero JM, Gómez-Hens A (2014) Determination of fluoroquinolone antibiotics by microchip capillary electrophoresis along with time-resolved sensitized luminescence of their terbium(III) complexes. Microchim Acta 181:1897–1904
17. Wang Y, Baeyens WRG, Huang C, Fei G, He L, Ouyang J (2009) Enhanced separation of seven quinolones by capillary electrophoresis with silica nanoparticles as additive. Talanta 77:1667–1674
18. Herrera-Herrera AV, Ravelo-Pérez LM, Hernández-Borges J, Afonso MM, Palenzuela JA, Ángel Rodríguez-Delgado M (2011) Oxidized multi-walled carbon nanotubes for the dispersive solid-phase extraction of quinolone antibiotics from water samples using capillary electrophoresis and large volume sample stacking with polarity switching. J Chromatogr A 1218:5352–5361
19. Xiao Y, Chang H, Jia A, Hu J (2008) Trace analysis of quinolone and fluoroquinolone antibiotics from wastewaters by liquid chromatography- electrospray tandem mass spectrometry. J Chromatogr A 1214:100–108
20. Blasco C, Picó Y (2012) Development of an improved method for trace analysis of quinolones in eggs of laying hens and wildlife species using molecularly imprinted polymers. J Agric Food Chem 60:11005–11014
21. Tang Q, Yang T, Tan X, Luo J (2009) Simultaneous determination of fluoroquinolone antibiotic residues in milk sample by solid-phase extraction−liquid chromatography-tandem mass spectrometry. J Agric Food Chem 57:4535–4539
22. Herrera-Herrera AV, Hernández-Borges J, Rodríguez-Delgado MA, Herrero M, Cifuentes A (2011) Determination of quinolone residues in infant and young children powdered milk combining solid-phase extraction and ultra-performance liquid chromatography-tandem mass spectrometry. J Chromatogr A 1218:7608–7614
23. Cho HJ, El-Aty AMA, Goudah A, Sung GM, Yi H, Seo DC, Kim JS, Shim JH, Jeong JY, Lee SH, Shin HC (2008) Monitoring of fluoroquinolone residual levels in chicken eggs by microbiological assay and confirmation by liquid chromatography. Biomed Chromatogr 22:92–99
24. Malik AK, Blasco C, Picó Y (2010) Liquid chromatography-mass spectrometry in food safety. J Chromatogr A 1217:4018–4040
25. Rezaei F, Hosseini MRM (2012) Improved homogeneous liquid-liquid extraction combined with GC-ECD for the determination of organochlorinated pesticides in water. Chromatographia 75:379–385
26. Qiao J, Yan H, Wang H, Lv Y (2011) Determination of ofloxacin and lomefloxacin in chicken muscle using molecularly imprinted solid-phase extraction coupled with liquid chromatography. J Sep Sci 34:2668–2673
27. Yan H, Liu B, Du J, Yang G, Row KH (2010) Ultrasound-assisted dispersive liquid-liquid microextraction for the determination of six pyrethroids in river water. J Chromatogr A 1217:5152–5157
28. Yu H, Mu H, Hu YM (2012) Determination of fluoroquinolones, sulfonamides, and tetracyclines multiresidues simultaneously in porcine tissue by MSPD and HPLC-DAD. J Pharm Anal 2:76–81
29. Andreu V, Blasco C, Picó Y (2007) Analytical strategies to determine quinolone residues in food and the environment. TrAC Trends Anal Chem 26:534–556
30. Feng J, Sun M, Xu L, Li J, Liu X, Jiang S (2011) Preparation of a polymeric ionic liquid-coated solid-phase microextraction fiber by surface radical chain-transfer polymerization with stainless steel wire as support. J Chromatogr A 1218:7758–7764
31. Bi W, Zhou J, Row KH (2011) Solid phase extraction of lactic acid from fermentation broth by anion-exchangeable silica confined ionic liquids. Talanta 83:974–979
32. Dong Q, Wang XY, Lu YM, Sun HY, Meng QL, Liu SL, Feng W, Han XK (2014) The influence of SiO_2 doping on the microstructure and photochromic behavior of phosphomolybdic acid/polyvinyl pyrrolidone hybrid films. J Mol Struct 1075:154–158
33. Zhang K, Song G, Li Y, Wu X, Li K, Ye B (2014) Voltammetric studies of kaempferol on polyvinyl pyrrolidone cladding quantum dots CdS doped carbon paste electrode and analytical application. Sens Actuators B 191:673–680
34. Tian M, Yan H, Row KH (2010) Solid-phase extraction of caffeine and theophylline from green tea by a new ionic liquid-modified functional polymer sorbent. Anal Lett 43:110–118
35. Tian M, Bi W, Row KH (2011) Separation of monosaccharides by solid-phase extraction with ionic liquid-modified microporous polymers. J Sep Sci 34:3151–3157