Supported imidazolium ionic liquid phases: a new material for solid-phase extraction

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Abstract

This study reports a material that is based on the concept of ionic liquid analogue: a slightly crosslinked polymer-supported imidazolium trifluoroacetate salt (IL-CF_3COO^-) that favorably combines the properties of ionic liquids (ILs) and the advantages of a solid support.

The ionic-liquid-supported material was evaluated for the first time as a solid-phase extraction (SPE) sorbent for selectively and quantitatively extracting pharmaceuticals from aqueous samples.

The novel IL-CF_3COO^- was evaluated under reversed phase (RP), weak anion exchange (WAX), strong anion exchange (SAX) and strong cation exchange (SCX) SPE procedures, and we found that SAX conditions are the most suitable for investigating the behaviour of the IL-CF_3COO^- material. Under SAX conditions, the IL-CF_3COO^- material was capable of selectively and quantitatively extracting a group of acidic compounds from aqueous samples, while washing basic analytes that were also present in the sample.

The SPE method using IL-CF_3COO^- material was used to analyse 1000 ml of different aqueous samples (ultrapure, tap and river) with complete recovery of the acidic compounds studied. Moreover, the method provided clean chromatogram and high recoveries when percolating complex real samples, such as 1000 ml of river water and 250 ml of effluent waste water from a sewage treatment plant spiked at low levels with the analytes studied.

Introduction

Ionic liquids (IL) are inorganic and organic salts with a melting point below 100ºC. The most characteristic features of IL are of negligible volatility and high polarity, comparable to the polarity of lower alcohols [1]. Most organic IL are made up of large cations such as imidazolium, pyridinium, quaternary ammonium and quaternary phosphonium and a suitable anion such as chloride, bromide, trifluoroacetate, trifluoromethane sulfonate, p-toluenosulfonate, etc. By using a proper combination of the cation and anion either hydrophilic ionic liquids or hydrophobic ionic liquids can be obtained. However, even relatively hydrophobic ILs are not totally immiscible with water. The features of high polarity and very low miscibility with water make it possible to use ILs in solvent extraction processes.

In this sense, several examples of IL applications in separation techniques have been reported [2-13]. Thus, ILs are used in many chromatographic applications: as stationary phases in gas chromatography [5-7], as mobile phase additives or stationary phases in liquid chromatography [8,9,14,15], as chemical modifiers in capillary electrophoresis or stationary phases in electrochromatography [16]. Another attractive application is as an extraction solvent, in liquid-liquid extraction for benzene derivatives [2] or for phenol, tyrosol and p-hydroxybenzoic acid [3]or for polyaromatic hydrocarbons in direct-immersion and headspace liquid-phase microextraction [10,11] or in single-drop microextraction [12,13]. The excellent sorptive properties of ionic liquids towards such groups of organic compounds as benzene derivatives [2,12,13], polyaromatic hydrocarbons [10] and alkylphenols [17] prompted some of us to investigate the possibility of polymer-supported imidazolium type ionic liquids [18] and the sorptive properties of such material. We found [18] that the polymer-immobilized imidazolium salts have very good capacity to extract benzene derivatives from aqueous phase. The

polymer-supporting of imidazolium salts opens up new possibilities because it solves the problem of the small but measurable solubility of IL, what is an obvious disadvantage in extraction.

Another field of application in which ILs show potential is solid-phase extraction (SPE), the most widely used preconcentration technique largely because of the variety of different materials that can be used as SPE sorbents [19,20]. To date, polymeric sorbents are regarded as the best SPE materials since they can enhance capacity (i.e. hydrophilic polymers and polymers with high specific surface areas)[21], selectivity (molecularly imprinted polymers – MIPs) [22,23]or both (mixed mode ion-exchange polymers) [24]and, therefore, enlarge the type of sample and the analyte to be extracted. To the best of our knowledge, just two studies [25,26] reported in 2009 the application of immobilized IL onto silica sorbents to isolate tanshinones [25] or enrich polyunsaturated fatty acid methyl esters [26] from complex samples.

In this paper we present a step forward in SPE sorbent technology: we prepared a new material based on the novel concept of ionic liquid supported phase onto polymer phase, and then pioneered its evaluation as a SPE sorbent to evaluate pharmaceuticals, which are emerging pollutants in the environmental field.

Experimental

Reagents and standards

The reagents used for the supported ionic liquid syntheses were vinylbenzyl chloride (VBC), divinylbenzene (DVB), N-methylimidazole, trifluoroacetic acid and formic acid (HCOOH), all purchased from Sigma-Aldrich (Steinheim, Germany). The VBC (mixture of isomers) was distilled under vacuum before polymerization. DVB (80%) was extracted with 2 M sodium hydroxide (NaOH), washed a few times with water and dried over sodium sulfate. Other reagents were used as received.

The analytes selected to evaluate the sorbents were: salicylic acid, 4-nitrophenol, carbamazepine, nalidixic acid, flumequine, naproxen, fenoprofen, diclofenac sodium, ibuprofen and gemfibrozil, all obtained from Aldrich. The structure and pKa values of all the analytes are shown in Figure 1.

Standard stock solutions at 1000 mg l^{-1} were prepared for each analyte in methanol (MeOH), except nalidixic acid, which was prepared in 0.1 M NaOH aqueous solution, and flumequine, which was prepared in 50/50 (*v/v*) MeOH/H_2O at basic pH with NaOH. Working solutions of the mixture of all the compounds were all prepared in 50/50 (*v/v*) MeOH/H_2O. All the solutions were stored at 4 ºC.

Ultrapure reagent water purified by a Milli-Q gradient system (Millipore, Bedford, MA, USA) was used throughout. Acetonitrile (ACN) and MeOH were purchased from SDS (Peypin, France). Other reagents used in the SPE procedures were: phosphoric acid (H_3PO_4) (Merck, Barcelona, Spain), ammonium hydroxide (NH_4OH) (Merck), HCOOH (Probus, Barcelona, Spain), sodium acetate (CH_3COONa) (VWR, Mollet del Vallès, Spain), acetic acid (CH_3COOH) (SDS) and nitrogen of 99.995% purity (Carburos Metálicos, Barcelona, Spain).

Resin preparation and characterization

The starting polymer was obtained by suspension polymerization of VBC and DVB (2 wt.%) in the presence of 20 wt. % of toluene. The reaction was catalyzed with 0.5 wt.% of benzoyl peroxide and was carried out at 60ºC for 1 h, 70ºC for 1h, and 85ºC for 2 h and it finished after 5 h at 95ºC. After the polymerization, the material obtained was washed with hot water and acetone, dried and then extracted with toluene in a Soxhlet apparatus.

The VBC/DVB was reacted with the excess of N-methylimidazole. Thus, 15.0 g of dry polymer was placed in the round bottom flask and refluxed with the excess of neat N-methylimidazole for 17 h. After this time the polymer was placed in the column and subjected to a conditioning with: water, 1 M HCl, water, 1 M NaOH, water, 0.1 M CF_3COOH and water at a neutral pH.

The chlorine content in polymers was determined by the Volhard method after the samples (ca. 20 mg) had been burned in oxygen and the fumes absorbed in 20 ml of H_2O_2 solution. The nitrogen content was determined by the Kjeldahl method.

Instrumentation

The chromatographic experiments were performed with two LC-10AD$_{VP}$ pumps, a DGU-14A degasser and a CTO-6AS column oven (all from Shimadzu, Tokyo, Japan), an injection valve with a 20 μl loop and a Hewlett-Packard (Avondale, PA, USA) Series 1100 UV spectrophotometric detector. The analytical column was a 250 x 4.6 mm i.d. stainless-steel column packed with Kromasil 100 C_{18}, 5 μm (Teknokroma, Sant Cugat del Vallès, Spain).

Chromatographic conditions

The mobile phase was: ultrapure water adjusted to pH 2.8 with H_3PO_4 and acetonitrile (ACN). The flow-rate was 1 ml min^{-1} and the temperature of the column oven was set at 30 ºC. The gradient profile was 40% initially for 8 min, which was increased to 60% ACN in 12 min, and to 100% ACN in 8 min (held for 2 min). The mobile phase was then returned to the initial conditions (40% ACN) in 2 min.

The wavelength used to detect all the compounds was set at 210 nm throughout the analysis.

Solid-phase extraction procedure

The SPE evaluation was performed in an off-line mode using 500 mg of IL-CF_3COO^- resin packed into 6 ml polypropylene cartridges equipped with two polyethylene frits (Symta, Madrid, Spain). The cartridges were connected to an SPE manifold (Teknokroma), which was connected to a vacuum pump.

The laboratory-synthesized IL-CF_3COO^- resin was compared to the commercially available sorbent Oasis-MAX (500 mg) from Waters (Milford, MA, USA).

The SPE protocols used depended on whether the sorbent was being evaluated as reversed phase (RP), weak anion exchange (WAX), strong anion exchange (SAX), or strong cation exchange (SCX). They are listed in Table 1 and are all adapted from standard SPE procedures [27,28]. After the optimization studies, the sorbent was evaluated under SAX conditions and using the following protocol: sample: ultrapure water at pH 7; equilibration: 1 ml of 25 mM CH_3COONa, pH 5; washing: 20 ml of MeOH; elution: 10 ml of 5% HCOOH in MeOH; regeneration: 5 ml of 5% HCOOH in MeOH.

In real water samples, the optimum protocol was already used, but, the two eluates from the washing and the elution steps were reduced to dryness under a stream of nitrogen and the respective residues were redissolved with 0.5 ml 50/50 (*v/v*) MeOH/H_2O to decrease the analyte concentration levels as close as possible to the low levels found in the environment.

Sample collection and preparation

Real water samples (tap water from Tarragona, Ebro river water and effluent waste water from a treatment plant in Tarragona) were acidified and kept in the fridge at 4ºC. Before analysis they were readjusted to pH 7 with NaOH and filtered through 0.45 μm nylon membranes (Osmonics Inc, Minnetonka, MN, USA) to remove the particulate matter before the SPE step.

Results and discussion

1. Preparation and characterization of the IL-CF_3COO^- material

The polymer-immobilized imidazolium salt was prepared in a one-step simple reaction of VBC-DVB copolymer with N-methylimidazole (Figure 2). The elemental analysis gave 0.32 mmol of residual Cl per g and 5.47 mmol of N per g of dry material in the form of CF_3COO^-, which corresponds to 2.73 mmol of imidazolium groups per g. These results show that the modification leading to the immobilized imidazolium salt proceeds with very high yield and the resultant material contains almost the maximum possible amount of immobilized salt. After the reaction (Figure 2), the polymer contain the Cl^- groups but these groups can be easily substituted by an ion-exchanger to the desired ionic form. These forms, chosen for the purpose of this research, were

trifluoroacetate and formate. The former is used in ionic liquid chemistry, and the latter was tried because HCOOH is being used in the elution solutions of SPE experiments. The high water content (2.55 and 4.26 g of water per g of polymer for trifluoroacetate and formate, respectively) ensures the good kinetics of solute diffusion within the polymeric beads. Moreover, a copolymer with 2 wt. % of crosslinking agent was used to ensure that the resulting material swelled appropriately and to provide sufficient mechanical strength.

2. Selection of the optimum protocol in SPE

We first tested several SPE procedures in order to determine which retention mechanisms the interaction of IL-CF_3COO^- with the analytes is based on. For this, in order to test a wide range of interactions we selected a group pharmaceuticals considered emerging contaminants of environmental interest (see Figure 1), and also 4-NP. The studied compounds include polar analytes with different basic-acidic properties, and particularly acidic compounds.

We tested four SPE protocols: reversed-phase (RP), weak anion exchange (WAX), strong anion exchange (SAX) and strong cation exchange (SCX). Table 1 summarizes the conditions in each of the procedures tested. At the end of each SPE procedure, an extra 10 ml of 2% HCOOH in 80/20 (*v/v*) MeOH/ACN (called elution 2) was passed through the cartridge to ensure that the compounds, mainly the acidic ones, had completely eluted from the sorbent, since the acidic solution ensures the protonation of the analytes—which at loading sample pH (pH 7) might be in their anionic form—and releases them from the sorbent.

Table 2 summarizes the % recovery values provided in each respective protocol, which point out that the SAX protocol is the more efficient, since all the most acidic

compounds studied (pKa < 5) eluted during the elution step with recovery values ranging between 90 and 100% in all instances. The less acidic compounds (pKa > 5) also eluted (% recoveries from 87 to 69% for all this type of compounds, and 45% for 4-NP) in the washing step. All the analytes, then, completely eluted during the washing and elution steps, and none (or just traces) of the analytes were recovered in elution 2. On the other hand, when the other three protocols were used (*i.e.* RP, WAX and SCX), the analytes did not elute in either the washing or the elution step, and the extra step (elution 2) was required to completely elute all the analytes from the sorbent.

If the SAX conditions are the most suitable for extracting acidic analytes, this means that the IL-CF_3COO^- resin retains the analytes through ionic interactions with its imidazole groups (which involves SAX interactions). Therefore, we shall now focus on the extraction of the most acidic compounds, but we shall maintain all the initial compounds (*i.e.* including the basic and less acidic ones) in order to provide as much information as possible about how IL- CF_3COO^- behaves with compounds of different characteristics.

3. Optimisation of the SAX protocol

Once SAX had been seen to be the optimal procedure for eluting the analytes studied from IL-CF_3COO^-, our next aim was to tune the conditions. For these experiments**,** we increased the sample volume to 250 ml in order to study the effect of each parameter at conditions more pertinent to the off-line SPE extraction.

a) Loading sample conditions

The loading step was fixed at pH 7 in order to ensure the deprotonation of the most acidic compounds (pKa<5) and retain them in the resin (which is charged) through ionic interactions.

The ionic strength of the sample was also tested, to do this, we compared the recovery results of two type of samples both adjusted to pH 7 with H_3PO_4: one based on ultrapure water and another based on isotonic saline buffer. The results were better when the sample was prepared merely with ultrapure water adjusted to pH 7, which may be due to the lower ionic strength of this type of sample.

b) Elution solution

We increased the percentage of the HCOOH (2%, 5% and 10%) in the solution and then we changed the solvent in the solution (20/80 (*v/v*) MeOH/ACN or pure MeOH) in order to completely elute the most acidic compounds with the minimum volume of solvent. We found that 5% HCOOH solution in either 20/80 (*v/v*) MeOH/ACN or pure MeOH provided the best results (data not shown). We finally chose 5% HCOOH in MeOH as the elution solution because it is more straightforward to prepare.

To determine the optimum elution volume, we tested volumes from 1 to 15 ml of 5% HCOOH in MeOH, and the minimum volume to ensure the complete elution of all the acidic compounds was 10 ml of this acidic solution.

c) Washing step

In order to enhance the selectivity of the whole extraction process, another parameter that had to be optimized is the type and volume of solvent in the washing step. We had already used 1 ml of MeOH as washing solvent, but we were interested in increasing the volume to more effectively wash out the interferences, so we tested up to four aliquots of 5 ml of MeOH (total 20 ml of MeOH). With 20 ml of washing solvent, none of the most acidic analytes underwent any loss during the washing step and they were completely recovered in the elution step (data not shown). On the other hand, when 20 ml of MeOH was used as washing solvent, the less acidic compounds partially eluted in

the washing step (as expected, since they are just retained by reversed-phase interactions) and completed their elution in the elution step. However, increasing the volume of washing solvent further led to the elution of some acidic compounds, such as gemfibrozil, but other less acidic compounds still did not elute.

We also tested the effect of combining two types of washing solvents—10 ml of 5% NH_4OH in MeOH followed by 10 ml of MeOH—to check whether the addition of a basic solution helped to completely elute the basic and neutral compounds in the washing step. However, we ruled out this possibility since we could not see any improvement, and some of the less acidic compounds continued eluting in the elution step.

d) Regeneration of the ILs

Another point to consider was the regeneration of the IL after each extraction. We tried to regenerate the cartridge by passing the stoichiometric amount of CF_3COOH, to maintain the IL-CF_3COO^- form, or 5 ml of 5% HCOOH in MeOH (also used in the elution step) to maintain the IL-$HCOO^-$ form, and the results obtained in the following respective SPE experiments were the same. Thus, we predict that the important point is to maintain the IL in the protonated form, but we can use any counter-ion to do so. Moreover, in view of the water content (section 1) of the $HCOO^-$ form in comparison with that of the CF_3COO^- form, we decided to use 5 ml of 5% HCOOH in MeOH as the regeneration solution to maintain the imidazole moiety in its charged form and at the same time to continue working with the more suitable IL-$HCOO^-$ form.

e) Sample volume

After the different conditions that might affect the extraction had been evaluated, the following optimized conditions were selected for all further experiments: sample: ultrapure water at pH 7; equilibration: 1 ml of 25 mM CH_3COONa, pH 7; washing: 20 ml of MeOH; elution: 10 ml of 5% HCOOH in MeOH; regeneration: 5 ml of 5% HCOOH in MeOH.

Once the SPE protocol had been established, we tested different sample loading volumes (i.e. 250, 500 and 1000 ml) and the recovery results were similar for all the tested volumes. Table 3 lists the recoveries (%) obtained after loading 1000 ml of ultrapure water sample (pH 7) spiked at 10 μg l^{-1} with the analyte mixture through IL material. All the most acidic compounds provided % recoveries ~ 100%, with the exception of salicylic acid, which polarity let its recoveries to fall to 68%. Previous studies [29,30] ,where it were used conventional SPE sorbents, also reported problems in the extraction of salicylic acid.

As far as the less acidic compounds studied are concerned, 4-NP showed partial elution with the IL-CF_3COO^- during the elution step, which might be because it interacts through the nitro moiety (see the structure of 4-NP in Figure 1) and the amine moiety in the imidazole ring of IL-CF_3COO^-. On the other hand, carbamazepine is almost lost during the loading step when extracted with IL-CF_3COO^-, because it is retained by the sorbent as a result of the π-π interactions between the aromatic rings in the analyte (see structure in Figure 1) and the ones in the sorbent structure (Figure 2). However, the SAX protocol used enhanced ionic interactions with the analytes rather than RP, which are more suitable for extracting this basic compound.

e) Comparison to conventional sorbent

For purposes of comparison, we also evaluated the SPE performance of Oasis MAX, which is a commercially available polymeric sorbent based on N-vinylpyrrolidone-DVB with a specific surface area of ~ 800 m^2 g^{-1} and it contains quaternary ammonium moieties, so it behaves like a SAX sorbent.

Table 3 also summarizes the recovery values obtained for Oasis MAX under the same conditions as those listed for IL-CF_3COO^-. From these recoveries, we can see that the performance of the IL-CF_3COO^- sorbent is comparable to that of the Oasis MAX sorbent in the extraction of the studied compounds. With this comparison, we demonstrate that polymer-supported IL (with just a 2% crosslinking degree) performance is as good as other established polymeric SPE sorbents that use macroporous resins with crosslinking degrees up to 80%.

5. Application to real samples

To assess the applicability of IL-CF_3COO^- in real water samples, we evaluated tap river and waste water samples. As with the ultrapure water, we initially percolated 1000 ml of each sample spiked at 10 μg l^{-1} and then followed the rest of the SPE procedure as described above. Table 3 shows that the recoveries for real samples are similar to those in ultrapure water, but, in tap water the recoveries slightly decrease, i.e. 60% for gemfibrozil. This decrease in recovery values in tap water samples might be attributed to the chloride content in this type of sample, which might block the amine moiety and prevent interaction with the target analytes. More interesting are the results with river water, the recoveries of which are close to 100%, except for salicylic acid and ibuprofen (63% in both cases). The decrease in the recovery of these two acidic compounds is not surprising; in fact, salicylic acid recoveries are similar to those obtained in ultrapure water and several studies have shown that ibuprofen has more recovery problems than

other compounds with similar acidic and polar characteristics when it is extracted with such neutral polymeric sorbents as Oasis HLB [31-33] and Strata-X [34] or weak anion exchange polymeric sorbent Oasis WAX [27].

For purposes of comparison, we also ran the same experiments using Oasis MAX as the sorbent (see table 3 for the % recovery values). The results obtained for the most acidic compounds when Oasis MAX was used in tap water samples are slightly lower (about 50-60% compared to 60-70% for IL-CF_3COO^-) and in river water samples they are slightly higher (values about 100% for all the compounds studied while the recoveries of salicylic acid and ibuprofen fall to 63% when IL-CF_3COO^- is used) than those obtained with IL-CF_3COO^-.

As expected, the less acidic compounds studied followed the same trends as in ultrapure water.

The next experiments in real water samples consisted of decreasing the analyte concentrations at 0.5 μg l^{-1} so that they ressembled those found in the environment. In order to determine lower concentrations, in this set of experiments the SPE eluate was evaporated to dryness and then reconstituted with 0.5 ml of 50/50 (*v/v*) H_2O/MeOH solution. With the evaporation step, an additional concentration factor of 20 was achieved. Recovery values were similar to those of the extraction of the Ebro river water sample spiked at higher concentration (i.e. 10 μg l^{-1}). Figure 3 shows the chromatograms obtained after preconcentrating 1000 ml of Ebro river water on IL-CF_3COO^- (a) and Oasis MAX (b) with the addition of the analyte mixture at 0.5 μg l^{-1}, and performing first the washing step and then the elution. It is worth mentioning that non-spiked sample chromatograms (not shown) were run with each respective sample, and neither any compounds studied nor any important interference were detected. We can also see that the chromatogram profile for IL-CF_3COO^- (Figure 3a) shows a smaller

initial hump than Oasis MAX (Figure 3b), which might help to quantify the analytes that appear at the initial retention times, such as salicylic acid.

To further show the capacity of ILs material to selectively extract acidic compounds, we used the IL-CF_3COO^- to percolate much more complex aqueous samples, such as effluent water from the waste water treatment plant (WWTP) in Tarragona. Table 4 summarizes the recovery results after 250 ml of effluent WWTP sample at pH 7 were extracted spiked at 5 μg l^{-1} with the analyte mixture. At this point, we would like to clarify that the sample volume was decreased to 250 ml because the WWTP sample is much more complex than the rest of water samples analysed. The SPE material IL-CF_3COO^- and Oasis MAX were used for purposes of comparison. The results for IL-CF_3COO^- are satisfactory and comparable to those for Oasis MAX, though slightly lower in the case of ibuprofen and gemfibrozil (~75 % for IL-CF_3COO^- compared to ~100 % for Oasis MAX) and salicylic acid (~55 % for IL-CF_3COO^- compared to ~100 % for Oasis MAX). In fact, these compounds have also shown some recovery problems in the other matrices analyzed in this study; and when samples are more complex, the weaker retention of these compounds might be further weakened by the presence of interferences that mask the interaction points of the sorbent, thus preventing proper interaction with the target compounds.

Figure 4 shows the chromatograms obtained after preconcentrating 250 ml of effluent WWTP sample on IL-CF_3COO^- (a, b) and Oasis MAX (c, d) with the addition of the analyte mixture at 5 μg l^{-1} (b,d). The most acidic compounds of the group studied were first washed and then eluted (see chromatograms). Figure 4 also shows the non-spike sample chromatograms (a, c) for each SPE material evaluated (i.e. IL-CF_3COO^- (a) and Oasis MAX (c)), which display some unknown peaks and two peaks at the same retention time as diclofenac and gemfibrozil; therefore, we took them into account in the

quantification of these compounds. The chromatograms in Figure 4 show that, although the samples are complex, the baseline is flatter and allows the most acidic analytes to be properly quantified at low concentration levels, which might be partially attributed to the effective washing step that can be performed in this type of material. Again, a comparison of the chromatograms reveals a smaller initial hump in the IL-CF_3COO^- (Figure 4 a,b) than in the Oasis MAX (Figure 4 c,d), due to the contribution of the non-specific RP interactions of Oasis MAX material. It should also be pointed out that the chromatograms are clean thanks to the material used in the SPE, and that both the cleanliness and the sensitivity achieved with this type of complex samples could be further enhanced by using a more powerful detection technique, such as mass spectrometry.

Conclusions

This paper describes a pioneering study of the synthesis, evaluation and application of polymer-supported ILs as SPE material, which effectively extracts a group of acidic compounds from complex aqueous samples.

The imidazolium trifluoroacetate was linked to a 2% crosslinked resin in order to combine the advantages of ionic liquid properties and those of a solid material.

We tested the different functional groups of the ionic liquid resin and their capacity to interact with the analytes selected by using various SPE protocols. We found that the SPE performed best when using the SAX interaction that the imidazole group provides with the acidic compounds studied.

We have shown that the IL-CF_3COO^- is a good alternative for extracting acidic analytes at low concentration levels from complex samples (tap, river and effluent WWTP), since it presented clear chromatograms and high recoveries; using ILs as a

SPE material is sometimes even a better option than such well-established anionic exchange SPE sorbents as Oasis MAX sorbent.

We have, then, described a novel application of these promising media, which are still in the process of being explored. This study is just the first step towards new applications of these materials in the sorptive extraction field.

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Table 1. SPE conditions for RP, WAX, SAX and SCX evaluation.

	SPE CONDITIONS			
	Reversed-phase (RP)	**Weak anion exchange (WAX)**	**Strong anion exchange (SAX)[a]**	**Strong cation exchange (SCX)**
1. Condition	5 ml MeOH + drying at 10 mmHg for 10 min. + 5 ml water			
2. Load	5 ml ultrapure water, pH 7	5 ml ultrapure water, pH 7	5 ml ultrapure water, pH 7	5 ml 2% HCOOH in ultrapure water
3. Equilibrate	1 ml water	1 ml 25mM sodium acetate buffer, pH 5	1 ml 25mM sodium acetate buffer, pH 7	-
4. Washing	-	1 ml MeOH	1 ml MeOH	1 ml MeOH 1 ml of 2% HCOOH in 20/80 (*v/v*) MeOH/ACN
5. Elution 1	4 x 5 ml MeOH	5 ml of 2% NH_4OH in 20/80 (*v/v*) MeOH/ACN	5 ml of 2% HCOOH in 20/80 (*v/v*) MeOH/ACN	5 ml of 5% NH_4OH in MeOH
6. Elution 2	10 ml of 2% HCOOH in 20/80 (*v/v*) MeOH/ACN			

[a] The conditions detailed for the SAX procedure are the initial conditions. They vary as they are optimized along the manuscript.

Table 2. % Recovery values of the analytes with the IL sorbent using the different SPE protocols after extracting 5 ml of ultrapure water solution at pH 7 with the analyte mixture. For the experimental conditions, see text.

		% Recovery											
		RP			WAX			SAX			SCX		
Solutes	pKa	wash	elution1	elution2	wash	elution1	elution2	wash	elution1	elution2	wash	elution1	elution2
Carbamazepine	13	5	61	0	89	2	11	69	4	5	15	73	0
4-NP	7.1	12	63	0	33	0	50	45	39	12	9	26	54
Nalidixic acid	6.5	14	43	11	85	6	18	81	27	0	25	54	8
Flumequine	6	10	46	12	88	2	19	87	20	0	15	47	9
Gemfibrozil	4.7	3	90	10	82	2	11	0	96	0	25	36	21
Ibuprofen	4.6	2	38	63	49	1	48	0	98	3	19	45	7
Fenoprofen	4.5	3	13	92	31	2	52	0	93	8	13	37	17
Naproxen	4.2	0	11	85	25	3	44	0	101	13	8	23	28
Diclofenac	3.9	4	11	96	12	2	43	0	102	5	16	19	24
Salicylic acid	3	10	4	5	3	3	12	0	89	0	0	0	18

% relative standard deviation (RSD) (n = 3) were lower than 4% when %recovery > 15 %.

Table 3. % Recovery values of the analytes with the different sorbents studied (IL and Oasis MAX) after extracting 1000 ml of ultrapure, tap and Ebro river water sample at pH 7 with the analyte mixture spiked at 10 μg l^{-1}. For the experimental conditions, see text.

		% Recovery											
		Ultrapure water				**Tap water**				**Ebro river water**			
		IL		**Oasis - MAX**		**IL**		**Oasis - MAX**		**IL**		**Oasis - MAX**	
Solutes	pKa	wash	elution	wash	elution	wash	elution	wash	elution	wash	elution	wash	elution
Carbamazepine	13	16	0	89	0	15	0	101	0	13	0	89	1
4-NP	7.1	30	81	0	97	40	0	0	67	43	57	0	102
Nalidixic acid	6.5	71	25	44	54	7	4	83	23	4	0	97	6
Flumequine	6	75	20	48	47	9	0	62	32	7	0	99	8
Gemfibrozil	4.7	0	100	0	96	0	60	0	83	0	80	0	110
Ibuprofen	4.6	0	98	0	93	0	76	23	56	0	63	0	106
Fenoprofen	4.5	0	102	0	103	0	92	0	105	0	92	0	102
Naproxen	4.2	0	99	0	94	0	74	0	59	0	87	0	97
Diclofenac	3.9	0	98	0	92	0	76	0	57	0	100	0	101
Salicylic acid	3	0	68	0	99	0	76	0	20	2	63	0	100

% relative standard deviation (RSD) (n = 3) were lower than 5% when %recovery > 25 %.

Table 4. % Recovery values of the studied analytes with IL sorbent and Oasis MAX in SPE after percolating 250 ml of effluent WWTP water sample at pH 7 spiked at 5 μg l^{-1} with the analyte mixture. For the experimental conditions, see text.

		% Recovery			
		IL		OASIS - MAX	
Solutes	pKa	wash	elution	wash	elution
Carbamazepine	13	43	0	104	0
4-NP	7.1	0	81	0	57
Nalidixic acid	6.5	61	0	79	0
Flumequine	6	2	0	84	0
Gemfibrozil	4.7	0	72	0	97
Ibuprofen	4.6	0	77	0	99
Fenoprofen	4.5	0	93	0	102
Naproxen	4.2	0	101	0	100
Diclofenac	3.9	0	101	0	99
Salicylic acid	3	0	55	0	94

% relative standard deviation (RSD) (n = 3) were lower than 7%.

Figure captions

Figure 1. Structures and pKa values (calculated using Advanced Chemistry Development (ACD/Labs) Software V8.1) of the studied analytes.

Figure 2. Scheme of the IL-CF_3COO^- synthesis.

Figure 3. Chromatograms obtained after off-line trace enrichment of 1000 ml of Ebro river water sample with the addition of a 0.5 μg l^{-1} level of the analyte mixture followed by the washing step and elution of the most acidic compounds using IL- CF_3COO^- (a) and Oasis MAX (b).

Figure 4. Chromatograms obtained after off-line trace enrichment of 250 ml of effluent WWTP sample without (a,c) and with (b,d) the addition of a 5 μg l^{-1} level of the analyte mixture followed by the washing step and elution of the most acidic compounds using IL- CF_3COO^-: without (a) and with (b), and Oasis MAX: without (c) and with (d), the addition of the analyte mixture.