Crosslinked polymeric ionic liquids as solid-phase microextraction sorbent coatings for high performance liquid chromatography

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Abstract

Neat crosslinked polymeric ionic liquid (PIL) sorbent coatings for solid-phase microextraction (SPME) compatible with high-performance liquid chromatography (HPLC) are reported for the first time. Six structurally different PILs were crosslinked to nitinol supports and applied for the determination of select pharmaceutical drugs, phenolics, and insecticides. Sampling conditions including sample solution pH, extraction time, desorption solvent, desorption time, and desorption solvent volume were optimized using design of experiment (DOE). The developed PIL sorbent coatings were stable when performing extractions under acidic pH and remained intact in various organic desorption solvents (i.e., methanol, acetonitrile, acetone). The PIL-based sorbent coating polymerized from the IL monomer 1-vinyl-3-(10-hydroxydecyl)imidazolium chloride [VC₁₀OHIM][Cl] and IL crosslinker 1,12-di(3-vinylbenzylimidazolium) dodecane dichloride [(VBIM)₂C₁₂]₂[Cl] exhibited superior extraction performance compared to the other studied PILs. The extraction efficiency of pharmaceutical drugs and phenolics increased when the film thickness of the PIL-based sorbent coating was increased while many insecticides were largely unaffected. Satisfactory analytical performance was obtained with limits of detection (LODs) ranging from 0.2 to 2 µg L⁻¹ for the target analytes. The accuracy of the analytical method was examined by studying the relative recovery of analytes in real water samples, including tap water and lake water, with recoveries varying from 50.2% to 115.9% and from 48.8% to 116.6%, respectively.

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Keywords

Polymeric ionic liquids; Solid-phase microextraction; High-performance liquid chromatography;
Pharmaceutical drugs; Phenolics; Pesticides

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1. Introduction

Solid-phase microextraction (SPME) has gained tremendous popularity since its introduction in the early 1990s [1]. SPME is a solvent free, cost-effective, and high throughput method that combines sampling and sample preparation into one step. SPME has been widely applied in different areas including environmental [2], food [3], bioanalytical [4], and clinical analysis [5]. This technique is typically performed in either the headspace or direct immersion mode but can be performed using a combination of these modes [6]. The extraction is based on the adsorption and/or partitioning between a sorbent coating and the analytes within the sample matrix. The desorption of analytes from the sorbent coating is performed by either thermal or solvent desorption. SPME is compatible with different separation techniques including gas chromatography (GC) and high performance liquid chromatography (HPLC).

Even though SPME is a mature technique, the continual development of new sorbent coating materials can greatly expand its applicability to a broader range of analytes and matrices. There are a number of commercially-available SPME coatings possessing a wide range of polarity that are currently available on the market. However, the selectivity of these coatings towards target classes of analytes may be inadequate which can severely limit the overall sensitivity of the method. Polymeric ionic liquids (PILs) were first introduced as SPME sorbent coatings for GC and can provide higher selectivity compared to some of the more traditional sorbent coatings [7]. The selectivity of these materials have been progressively improved through the tailoring of the chemical structure within the cation component and by creating unique combinations of cations and anions [8-16].

An area of intense study in SPME involves the extraction of polar analytes from aqueous sample solutions. Due to their high affinity towards the sample matrix, these analytes are

typically extracted in the direct immersion mode. For analytes that are not sufficiently volatile, the development of HPLC-compatible SPME coatings is crucial. The coupling of PIL-based SPME to HPLC requires that the coatings be highly robust when exposed to organic desorption solvents and not slough from the support material. Crosslinked PIL-based sorbent coatings have been recently developed to address this limitation [11]. By crosslinking the PILs, the durability of the sorbent coating can be significantly enhanced, leading to a robust extraction system [13, 17-19]. Hybrid materials polymerized from an IL monomer and an organic/inorganic crosslinker have been applied as sorbent coatings for the analysis of various analytes in aqueous samples using SPME-HPLC [19-22]. A PIL-based monolith and its graphene oxide derivative were developed as SPME sorbent coatings for the analysis of polar endocrine disrupting chemicals and phenolic compounds with HPLC [23, 24]. These materials were prepared by azobisisobutyronitrile (AIBN)-initiated polymerization which requires high temperatures, lengthy reaction times (12-24 h), and the use of reaction solvents. Recently, a UV-initiated “on-fiber” polymerization method was introduced to prepare crosslinked PIL-based SPME sorbent coatings that can be immobilized to nitinol supports [17]. This approach is solvent-free and the ensuing polymerization can be achieved within 30 min to 2 h through photo-polymerization. Compared to the aforementioned sorbent coating fabrication techniques, this method is simple and efficient. Additionally, the use of sorbent coatings based on neat crosslinked PILs can further enhance the selectivity towards target analytes while imparting necessary structural integrity to the polymeric material when subjected to various organic solvents often used in HPLC.

For the first time, we report the use and development of HPLC compatible neat crosslinked PIL-based SPME sorbent coatings for the analysis of pharmaceutical drugs, phenolics, and insecticides. Six structurally diverse PIL-based sorbent coatings were

immobilized on nitinol supports and applied as sorbent materials for SPME. Optimization of the extraction/desorption conditions including sample solution pH, extraction time, desorption solvent, desorption time, and desorption solvent volume were carried out by using the design of experiment (DOE). The newly developed sorbent coatings were exploited for the extraction of target analytes under optimal SPME conditions. The selectivity of the PIL-based coatings was investigated and compared with the commercial PDMS/DVB fiber. The effect of coating film thickness on the extraction efficiency was also studied. Furthermore, the established analytical method was validated by performing extractions in tap water and lake water.

2. Experimental

2.1 Reagents and materials

The reagents acrylonitrile (99%), 1-chlorohexadecane (95%), 1, 12-dibromododecane (98%), 4-vinylbenzyl chloride (90%), 10-bromodecanoic acid (95%), 10-chloro-1-decanol (90%), 1-vinylimidazole ($\geq 99\%$), imidazole ($\geq 99\%$), vinyltrimethoxysilane (VTMS) (98%), and 2-hydroxyl-2-methylpropiophenone (DAROCUR 1173) ($>96\%$) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Acetonitrile, acetone, methanol, isopropanol and dimethyl sulfoxide were also purchased from Sigma-Aldrich with purities equal to or higher than 99%. Hydrogen peroxide (30%, w/w), glacial acetic acid, hydrochloric acid, and sodium hydroxide were purchased from Fisher Scientific (Fair Lawn, NJ, USA). Lithium bis[(trifluoromethyl)sulfonyl]imide was purchased from SynQuest Laboratories (Alachua, FL, USA). Phenacetin ($\geq 98\%$), ketoprofen ($\geq 98\%$), 17 α -ethynylestradiol ($\geq 98\%$), fenoprofen calcium ($\geq 97\%$), diclofenac sodium ($\geq 98.5\%$), ibuprofen (98%), 2,4,6-trichlorophenol (98%), hexaflumuron (99.1%), phoxim (98.1%), chlorfenapyr (98.8%), flufenoxuron (98.1%),

hexythiazox (99%), chlorfluazuron (98.9%), deltamethrin (99.7%), fenvalerate (99%), and τ -fluvalinate (99%) were purchased from Sigma-Aldrich. The analyte 2-nitrophenol (99%) was purchased from Acros Organics (Pittsburgh, PA, USA) and 2,4-dinitrophenol was purchased from Eastman Organic Chemicals (Kingsport, TN, USA). Deuterated dimethyl sulfoxide was purchased from Cambridge Isotope Laboratories (Andover, MA, USA). Nitinol wire with a diameter of 128 μm was purchased from Nitinol Devices & Components (Fremont, CA, USA).

The chemical structures and select physicochemical properties of the 18 analytes examined in this study are shown in Table 1. Individual stock solutions of the analytes were prepared at a concentration of 5000 mg L^{-1} . Different organic solvents were used as diluents in the preparation of the individual stock solutions due to the solubility of analytes. Methanol was used as a diluent when preparing the individual stock solutions of phenacetin, 17 α -ethynylestradiol, fenoprofen, and diclofenac sodium while acetone was used for preparing the stock solutions of hexaflumuron, flufenoxuron, and chlorfluazuron. All other analyte stock solutions were prepared in acetonitrile. Stock solutions containing a mixture of all analytes were prepared at concentrations of 250 mg L^{-1} , 200 mg L^{-1} , 10 mg L^{-1} , and 1 mg L^{-1} using acetonitrile as a diluent. The aqueous sample solutions were prepared by spiking an aliquot of the stock solution into the water sample at an adjusted pH (using hydrochloric acid and sodium hydroxide). The amount of organic solvent was consistently kept at 0.2% (v/v) in the sample solution. All aqueous sample solutions, except the real samples, were prepared with deionized water (18.2 $\text{M}\Omega\text{ cm}$) acquired from a Milli-Q water purification system (Bedford, MA, USA).

2.2 Instrumentation

Characterization of all synthesized ILs was performed using a Bruker DRX 500 MHz nuclear magnetic resonance (NMR) spectrometer (Billerica, MA, USA). ¹H NMR spectra were collected in deuterated dimethyl sulfoxide. UV-initiated polymerization was carried out using a RPR-100 UV reactor purchased from Southern New England Ultraviolet Company (Bradford, Connecticut). Sixteen lamps producing the same wavelength were applied for the polymerization reaction. A wavelength of 360 nm was used for the polymerization of the NTf₂⁻ based IL monomers and 254 nm was used for the polymerization of IL monomers containing halide anions. The film thickness of PIL sorbent coatings was examined using a JEOL JSM-6060 LV low vacuum scanning electron microscope (SEM). A representative SEM image of a sorbent coating is shown in Fig. S1.

Chromatographic analysis was performed on a Shimadzu LC-20A HPLC (Tokyo, Japan) equipped with a Rheodyne manual injector, two LC-20AT pumps, a DGU-20A₃ degasser, and a SPD-20 UV/Vis detector. The separation of all analytes was carried out using a Restek Ultra C18 column (250 × 4.6 mm I.D.) with a particle size of 5.0 μm (State College, PA, USA). A gradient separation method was applied starting with 60% of mobile phase A (0.05% acetic acid in water) and 40% of mobile phase B (0.1% acetic acid in acetonitrile). Mobile phase B was gradually increased from 40% to 70% at 2 mL min⁻¹ followed by another ramp from 70% to 85% at 1 mL min⁻¹ and an isocratic hold at 85% for 10 min. The flow rate was maintained at 1 mL min⁻¹. A detection wavelength of 220 nm was used for monitoring 17 α-ethynylestradiol, fenoprofen, ibuprofen, deltamethrin, and fenvalerate while all other analytes were monitored at 254 nm.

2.3 Synthesis of ionic liquid monomers and crosslinkers

Structures of the IL monomers and crosslinkers employed in this study are showed in Table 2. The synthesis of IL monomers 1-vinylbenzyl-3-hexadecylimidazolium chloride [VBC₁₆IM][Cl], 1-vinylbenzyl-3-hexadecylimidazolium bis[(trifluoromethyl) sulfonyl]imide [VBC₁₆IM][NTf₂], 1-vinyl-3-(2-hydroxyethyl)imidazolium bromide [VC₂OHIM][Br], 1-vinyl-3-(10-hydroxydecyl)imidazolium chloride [VC₁₀OHIM][Cl], 1-vinyl-3-(10-hydroxydecyl)imidazolium bis[(trifluoromethyl) sulfonyl]imide [VC₁₀OHIM][NTf₂], and crosslinkers 1,12-di(3-vinylbenzylimidazolium) dodecane dichloride [(VBIM)₂C₁₂] 2[Cl], 1,12-di(3-vinylbenzylimidazolium) dodecane dibis[(trifluoromethyl) sulfonyl]imide [(VBIM)₂C₁₂] 2[NTf₂] were carried out according to previously published references [7, 28, 29]. The synthesis of IL monomer 1-vinyl-3-(9-carboxynonyl)imidazolium bromide [VC₉COOHIM][Br] was performed by mixing 13.3 mmol of 1-vinylimidazole and 20.0 mmol of 10-bromodecanoic acid in acetonitrile. The reaction was carried out at 60 °C for 3 days. Afterwards, the solvent was removed under vacuum and the product dissolved in 8 mL of water and washed with ethyl acetate (4 mL × 6) and chloroform (4 mL × 6) to remove unreacted starting materials. The aqueous layer was then collected and dried under vacuum. All final products were characterized by ¹H NMR and the spectral data are shown in Figures S1–S8 S2-S9.

2.4 Fabrication of PIL-based SPME fibers

The preparation of PIL-based fibers was performed according to methods from a previously published study [11]. The crosslinked PIL sorbent coatings were produced by “on-fiber” UV initiated polymerization using derivatized nitinol fibers as supports. Briefly, the nitinol wire was first polished using sand paper and cleaned by acetone and methanol. The metallic wire was then cut into approximately 1.5 cm segments and placed in a hydrogen peroxide solution

(30%, w/w). The system was heated at 72 °C for 2 h to functionalize the nitinol surface with Ni-OH groups. Afterwards, the nitinol segments were rinsed with water and methanol followed by heat treatment at 200 °C for 10 min. The segments were then placed in VTMS and heated at 85 °C for 2 h in order to incorporate vinyl functionality onto the support surface. The fibers were ready for coating after being cleaned with methanol and heat treated at 150 °C for 5 min. A coating mixture consisting of IL monomer, IL crosslinker (50% by weight with respect to the monomer), and DAROCUR 1173 photoinitiator (3% by weight with respect to the coating mixture) was evenly applied to the surface of the nitinol fiber. An additional aliquot of deionized water (25% by weight with respect to the monomer) was added to the coating mixture in order to produce a homogenous coating mixture when preparing Fiber 4. A coating length of 1 cm was maintained for all fibers examined in this study.

2.5 Optimization of SPME parameters

2.5.1 Optimization of SPME parameters for the PIL-based fibers

SPME parameters including sample solution pH, extraction time, desorption solvent, desorption time, and desorption solvent volume were optimized for the PIL-based fibers using Fiber 1 as a model fiber due to its high stability and reproducibility. DOE using the *Statsoft Statistica 8.0* program was utilized during the optimization. The desorption solvent was initially optimized due to its low dependence on other parameters. A mixture design was applied using methanol, acetonitrile, and acetone as potential desorption solvents. The optimization was performed by varying the desorption solvent composition. A desorption solvent volume of 50 µL was applied for all desorptions and all experiments were performed in duplicate. The optimal

desorption solvent was selected based on the surface response obtained from the average peak areas of all analytes.

Prioritization of the other parameters including pH, extraction time, desorption time, and desorption solvent volume were studied using a two level full factorial design. The pH was studied in the range from 2 to 10 and the extraction time was varied from 15 min to 45 min. The desorption solvent volume was studied from 30 μ L to 70 μ L while the desorption time was varied from 5 min to 25 min. Due to the importance of pH and extraction time from the two level full factorial design, these parameters were further optimized as individual variables.

The optimized conditions were applied for all extractions using the PIL-based fibers. Extractions using the PIL-based fibers were performed in 10 mL of sample solution at pH 1.5 using the direct immersion mode. Prior to exposing the fiber to the matrix, the sample solution was agitated for 2 min to achieve pre-equilibration. Following a 60 min extraction under constant agitation (450 rpm), the fiber was retracted from the aqueous sample and immersed in 30 μ L of methanol for 15 min. Afterwards, 20 μ L of the methanolic desorption solvent was withdrawn and subjected to HPLC analysis. Subsequently, the fiber was washed in methanol for 30 min followed by deionized water for 10 min. The washing step was carried out after each extraction-desorption process in order to minimize carryover. Additionally, the deionized water was acidified to pH 3.5 in the washing of Fiber 4 in order to prevent possible ion exchange between the carboxylic acid group in Fiber 4 and ionized analytes.

2.5.2 Optimization of SPME parameters for the PDMS/DVB fiber

The extraction/desorption parameters including desorption solvent, pH, and extraction time were studied individually for the PDMS/DVB fiber. The desorption solvent was optimized

using the same method as the PIL-based fibers. A sorption-time profile was generated with the extraction time ranging from 0 to 120 min. The sample solution pH was varied from 2.5 to 7.5, since the lowest suggested working pH for the PDMS/DVB fiber is 2. The same desorption time and desorption solvent volume used for the PIL-based fibers was applied for the PDMS/DVB fiber.

2.6 Side-by-side comparison of different PIL coatings, bare supports, and PDMS/DVB fiber

The selectivity for target analytes was studied by comparing the extraction efficiency of analytes obtained by the six different PIL sorbent coatings under the optimized extraction/desorption conditions. The effect of PIL sorbent coating film thickness on extraction efficiency was studied by comparing the extraction performance using two fibers polymerized from the $[\text{VC}_{10}\text{OHIM}][\text{Cl}]$ IL monomer and the $[(\text{VBIM})_2\text{C}_{12}] 2[\text{Cl}]$ IL crosslinker with varied film thickness. Two surface derivatized nitinol supports without sorbent coating, namely Fiber **a** and Fiber **b**, were also studied under the same extraction/desorption conditions. Fiber **a** was produced by treating the nitinol fiber with H_2O_2 while Fiber **b** was produced by treating the fiber with H_2O_2 followed by VTMS to functionalize the surface with vinyl moieties. Finally, a PDMS/DVB fiber was also applied for the extraction at the same analyte concentration under the optimized extraction/desorption conditions.

2.7 Method validation and recovery using Fiber 3B

The established analytical method was validated by performing SPME using Fiber **3B** in real water samples, including tap water and lake water. Both tap water and lake water were collected locally in Ames, Iowa (USA). The microscopic particles in lake water were removed

by using a polyethersulfone syringe filter (0.2 μm). The recovery study was carried out by spiking a known amount of analytes into real water samples with an adjusted pH of 1.5. The relative recovery was obtained by comparing the experimental concentration value to the theoretical value.

3. Results and discussion

3.1 Structural design of crosslinked PIL-based sorbent coatings

Six different PIL-based sorbent coatings based on the combination of various IL monomers and crosslinkers were prepared in this study to explore their selectivity towards target analytes. As shown in Table 1, most analytes contain a number of different substituents including aromatic moieties, carbonyls, secondary amines, hydroxyls, and/or halogens. In order to investigate the interaction between the analytes and sorbent coating, the nature of the PIL sorbent coatings was varied by employing different anions and functional groups appended to the IL cations. Table 2 contains the composition of the six sorbent coatings based on the structural make-up of the IL monomers and crosslinkers. The chloride anion was incorporated in Fiber **2**, **3**, and **4** in order to enhance the hydrogen bonding basicity of the sorbent coatings compared to Fiber **1** and **6** which contain the NTf_2^- anion. Furthermore, hydroxyl moieties were incorporated in Fiber **3**, **5**, **6**, and carboxylic acid moieties into Fiber **4** in an effort to enhance the hydrogen bonding acidity, which can improve the hydrogen bonding interactions between the PIL and hydrogen bonding basic analytes. The length of alkyl chain substituents in the cation of the monomer was varied in Fiber **3** and **5** in order to explore the effect of dispersive-type interactions on extraction efficiency. Aromatic moieties were introduced into all of the PIL sorbent coatings to enhance π - π interactions between the sorbent coating and analytes. Additionally, the

crosslinked structures of the studied PILs can enhance the sorbent coating robustness and resilience when performing analyte desorption using organic solvents.

3.2 Optimization of extraction/desorption parameters for PIL-based fibers using Fiber 1

3.2.1 Mixture Design – optimization of desorption solvent

The desorption solvent was optimized using a mixture design consisting of a triangular surface response. Three polar organic solvents including acetonitrile, acetone, and methanol were selected for optimization. The average peak areas of all analytes obtained using the different desorption solvents were plotted to provide insight to their relative desorption strength. A higher average peak area indicates better desorption capability. As shown in Fig. 1A, methanol exhibited slightly better desorption strength compared to acetone while acetonitrile provided the poorest desorption strength. The solvent desorption strength was observed to vary based on the type of analytes. As shown in Fig. S9 S10, methanol was the best desorption solvent for select pharmaceutical drugs and phenolics examined in this study, while acetone exhibited better desorption strength for insecticides. Acetonitrile was found to be the least desirable desorption solvent for all three classes of analytes. Therefore, methanol was chosen as the optimum desorption solvent for subsequent studies.

3.2.2 Two level full factorial design – prioritization of the extraction/desorption parameters

A two level full factorial design was applied for prioritizing the four extraction/desorption parameters including pH, extraction time, desorption time, and desorption solvent volume. A Pareto chart was generated after plotting the average peak areas of all analytes obtained under different experimental conditions. As shown in Fig. 2, all four parameters

exhibited considerable importance based on the standardized effect estimate (p is greater than 0.05). The pH of the sample solution was found to be the most important parameter followed by desorption solvent volume and extraction time. The desorption time was found to be the least important parameter affecting the enrichment of analytes. Additionally, the impact value for the desorption solvent volume is negative indicating that lower desorption solvent volume is more beneficial for the enrichment of analytes. Therefore, a solvent volume of 30 μ L was chosen for subsequent experiments. The impact value for desorption time was positive suggesting that longer desorption times is more beneficial for the enrichment of analytes. A desorption time of 15 min was applied for all subsequent studies to form a compromise between the experiment time and enrichment performance.

3.2.3 Optimization of extraction time and sample solution pH

As two relatively important parameters, the extraction time and sample solution pH were further studied as individual variables. As shown in Fig. 3A, a sorption-time profile using Fiber **1** was generated by varying the extraction time between 0 to 90 min. Most analytes achieved equilibration in approximately 60 min. The peak areas of fenoprofen, ibuprofen, 2,4,6-trichlorophenol, and diclofenac sodium were slightly lower at an extraction time of 90 min compared to 60 min. This may be due to the competition among analytes within the solution. Therefore, an optimal extraction time of 60 min was used when employing the PIL-based fibers for extraction. The precision of the extractions was evaluated at 30 min and 60 min and varied from 1.6% to 18.9%.

According to Fig. 2, a negative impact value for pH was shown in the Pareto chart indicating better enrichment can be achieved at relatively lower pH values. Therefore, a pH

range of 1.5-5.5 was chosen for the optimization experiments. As shown in Fig. 4A, the enrichment of most analytes was enhanced when the pH of the sample solution was decreased from 5.5 to 1.5. Additionally, the extraction efficiency of phenacetin and 17 α -ethynylestradiol were similar when the pH was varied from 1.5 to 4.5, while the extraction efficiency decreased when the pH was increased to 5.5. Therefore, a sample solution pH of 1.5 was applied for the subsequent studies since the best overall extraction efficiency was obtained for most analytes at this pH. A Doehlert design was also performed for simultaneous optimization of sample solution pH and extraction time. As shown in Fig. S10 S11, the obtained results were consistent with the aforementioned optimization results.

3.3 Optimization of extraction/desorption parameters for the PDMS/DVB fiber

Analogous to the PIL-based sorbent coatings, the desorption solvent, extraction time, and sample solution pH were optimized for the commercial PDMS/DVB coating. Compared to the PIL-based sorbent coating, varying desorption abilities of the studied organic solvents for the analytes were observed when the mixture design was performed for the PDMS/DVB fiber. As shown in Fig. 1B, acetonitrile exhibited the best desorption of the analytes. Interestingly, a mixture of acetonitrile and methanol (50:50, v/v) was the optimal desorption solvent for select pharmaceutical drugs (see Fig. S11 S12). However, acetonitrile was found to be the best desorption solvent for phenolics and insecticides. Additionally, methanol exhibited the poorest desorption strength for phenolics and insecticides. In light of these results, acetonitrile was applied as the desorption solvent of choice for the PDMS/DVB fiber.

A sorption-time profile, as shown in Fig. 3B, was generated using the PDMS/DVB fiber at extraction times varying from 0 min to 120 min. Since most analytes achieved equilibrium at

90 min, an extraction time of 90 min was selected for further studies. The precision was evaluated at extraction times of 30 min and 60 min. As shown in Table S1B, the relative standard deviation obtained for all analytes ranged from 0.8% to 14.7%.

The sample solution pH, as shown in Fig. 4B, was studied from 2.5 to 7.5 using the PDMS/DVB fiber. The peak areas of most analytes decreased when the pH increased from 2.5 to 7.5, especially for 2,4-dinitrophenol, ketoprofen, fenoprofen, diclofenac sodium, and ibuprofen. On the other hand, the peak areas of other analytes, such as 17 α -ethynylestradiol, 2-nitrophenol, 2,4,6-trichlorophenol, hexaflumuron, chlorfenapyr, and hexythiazox, were not largely affected when the pH was varied.

3.4 Side-by-side comparison of commercial and PIL-based sorbent coatings

The selectivity of the six different PIL sorbent coatings towards the studied target analytes can be evaluated by comparing their extraction efficiencies, as shown in Fig. 5A and 5B. Fiber **3**, possessing a decanol substituent on the imidazolium cation and the chloride counter-ion, exhibited the best extraction performance for most analytes compared to other PIL-based fibers. Fiber **3**, **4**, **5**, and **6** all contain hydroxyl or carboxylic acid moieties within the monomer cations and exhibited higher selectivity for 17 α -ethynylestradiol compared to Fiber **1** and **2**, which possess a hexadecyl alkyl chain. This may be due to an enhanced hydrogen bonding interaction between these sorbent coatings and the two hydroxyl groups within the analyte structure. It was also found that Fiber **2** exhibited the lowest extraction efficiency of insecticides compared to the other PIL-based fibers. The film thicknesses of all PIL fibers (shown in Table 2 based on SEM images) were comparable, with the exception of Fiber **3B**.

The effect of film thickness for the PIL-based sorbent coating on the extraction efficiency of all analytes was examined by studying two fibers, namely, Fiber **3A** and **3B**, comprised of the

same PIL composition but with varying film thicknesses. As shown in Fig. 5A and 5B, the extraction efficiency of pharmaceutical drugs and phenolics increased when using the thicker sorbent coating while the selectivity for the analytes remained the same. Nevertheless, the extraction efficiency of most insecticides remained largely unchanged between the two fibers, with the exception of phoxim and chlorfenapyr. The extraction efficiency of phoxim and chlorfenapyr improved when the film thickness of the sorbent coating was increased. The select pharmaceutical drugs, phenolics, and the two aforementioned insecticides are relatively more polar ($\log P$ varying from 1.65 to 4.88) and possess a less bulky structure compared to the rest of the insecticides ($\log P$ varying from 4.81 to 6.55), which may play a role in the observed extraction behavior.

Two surface derivatized supports lacking any PIL sorbent coating, namely, Fiber **a** and Fiber **b**, were also studied in the extraction of target analytes. As shown in Figure 5A and 5B, the peak areas of pharmaceutical drugs and phenolics were less than 3% compared to those obtained for Fiber **3B**, except in the case of 2-nitrophenol extracted by Fiber **b** (8.5%). Even though the bare supports exhibited noticeable extraction of insecticides, they were still considerably lower than most of the PIL-based sorbent coatings. The extraction efficiency of analytes obtained by the PDMS/DVB fiber was comparable to Fiber **3B**. The PDMS/DVB fiber exhibited higher extraction efficiency for 2-nitrophenol, 2, 4, 6-trichlorophenol, fenoprofen, ibuprofen, phoxim, chlorfenapyr, and hexythiazox compared to the PIL fiber. However, the extraction efficiency of 17 α -ethynylestradiol, hexaflumuron, flufenoxuron, chlorfluazuron, deltamethrin, fenvalerate, and τ -fluvalinate were significantly poorer than Fiber **3B**. It is also worth noting that extractions using the PDMS/DVB fiber were performed at an extraction time of 90 min which was longer than the PIL fiber.

3.5 Analytical performance, method validation, and recovery from real water samples

The analytical performance was determined for Fiber **3B** by constructing calibration curves and determining limits of detection (LODs) for all analytes as well as the precision of the method. As shown in Table 3, the linear range varied from 1 to 500 $\mu\text{g L}^{-1}$ for most analytes except for ibuprofen and fenvalerate, which were studied from 5 to 500 $\mu\text{g L}^{-1}$. Good linearity with correlation coefficients (R) varying from 0.998 to 0.999 was obtained using five concentration levels. The LOD was determined by reducing the analyte concentration until a 3 : 1 signal : noise ratio was achieved. The LODs of all target analytes using Fiber **3B** varied from 0.2 to 2 $\mu\text{g L}^{-1}$. The precision of the method was determined at different analyte concentrations, including, the respective LODs, 1 $\mu\text{g L}^{-1}$, and 100 $\mu\text{g L}^{-1}$; wherein the relative standard deviations (%RSD) varied from 0.3% to 19.2%.

A recovery study was performed using Fiber **3B** in two water samples, namely, tap water and lake water. No detectable signal was observed for any of the analytes studied within both water samples. The recovery study was carried out by performing extractions from the water samples spiked at two different analyte concentration levels. As shown in Table 4, recoveries ranged from 50.2% to 103.2% at a spiked concentration of 1.5 $\mu\text{g L}^{-1}$ in tap water, while recoveries ranged from 77.8% to 115.9% at 150 $\mu\text{g L}^{-1}$. Acceptable recoveries were also obtained in the lake water matrix; recoveries ranged from 51.2% to 116.6% at a spiked concentration of 1.5 $\mu\text{g L}^{-1}$ and from 48.8% to 111.8% at 150 $\mu\text{g L}^{-1}$.

4. Conclusions

Neat crosslinked PIL-based SPME sorbent coatings were coupled for the first time to HPLC for the analysis of pharmaceutical drugs, phenolics, and insecticides. Fiber **3**, comprised of a decanol side chain appended to an imidazolium cation and a chloride anion, exhibited the best extraction efficiency for most analytes compared to other coatings. The effect of film thickness on the extraction efficiency was explored, wherein the peak areas of select pharmaceutical drugs and phenolics were increased while the peak areas of most insecticides remained similar when the film thickness increased. LODs at the sub part-per-billion levels were obtained using UV detection. Furthermore, good recoveries were achieved in real water samples, including tap water and lake water. **The coatings exhibited long lifetimes; Fiber 1 was used for a total of 155 extraction/desorption cycles.** The development of HPLC-compatible PIL sorbent coatings broadens the applicability of these materials towards a larger pool of analytes, particularly non-volatile, polar, and ionizable compounds. The ability to vary the selectivity of the extraction by tailoring the PIL chemical structure as well as enhancing the durability of the materials by crosslinking to super elastic nitinol supports further demonstrates the advantages of these sorbent coatings. On-going studies are aimed at understanding the structure-function relationship of these materials with regard to extraction selectivity as well as examining them in complex environmental and biological matrices.

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Figure Captions

Figure 1: Triangular surface responses obtained from the mixture design for optimizing the desorption solvent type using (A) Fiber 1 and (B) PDMS/DVB fiber. Concentration of analytes: 400 $\mu\text{g L}^{-1}$; Extraction time: 30 min; Desorption time: 15 min; Desorption solvent volume: 50 μL .

Figure 2: Pareto chart obtained using Fiber 1 for prioritizing the four extraction/desorption parameters pH, extraction time, desorption time, and desorption solvent volume.

Figure 3: Sorption-time profiles obtained using (A) Fiber 1 and (B) PDMS/DVB fiber. Concentration of analytes: 400 $\mu\text{g L}^{-1}$; Desorption time: 15 min. (A). pH: 1.5; Desorption solvent: 30 μL of methanol. (B). pH: 2.0; Desorption solvent 30 μL of acetonitrile. ($\square$) Phenacetin; ($\diamond$) 2,4-Dinitrophenol; (Δ) 2-Nitrophenol; ($\times$) Ketoprofen; ($\ast$) 17 α -Ethinylestradiol; (-) Fenoprofen calcium; (-) 2,4,6-Trichlorophenol; ($\circ$) Diclofenac sodium; (+) Ibuprofen; ($\blacksquare$) Hexaflumuron; ($\diamond$) Phoxim; (Δ) Chlorfenapyr; ($\ast$) Flufenoxuron; ($\ast$) Hexythiazox; ($\blacksquare$) Chlorfluazuron; ($\odot$) Deltamethrin; ($\bullet$) Fenvalerate; ($\#$) τ -Fluvalinate.

Figure 4: Optimization of sample solution pH using (A) Fiber 1 and (B) PDMS/DVB fiber. Concentration of analytes: 400 $\mu\text{g L}^{-1}$; Desorption time: 15 min. (A). Extraction time: 60 min; Desorption solvent: 30 μL of methanol. (B). Extraction time: 90 min; Desorption solvent volume: 30 μL of acetonitrile. ($\square$) Phenacetin; ($\blacksquare$) 2,4-Dinitrophenol; ($\blacksquare$) 2-Nitrophenol; ($\blacksquare$) Ketoprofen; ($\blacksquare$) 17 α -Ethinylestradiol; ($\blacksquare$) Fenoprofen calcium; ($\blacksquare$) 2,4,6-Trichlorophenol; ($\blacksquare$) Diclofenac sodium; ($\blacksquare$) Ibuprofen; ($\blacksquare$) Hexaflumuron; ($\blacksquare$) Phoxim; ($\blacksquare$) Chlorfenapyr; ($\blacksquare$) Flufenoxuron; ($\blacksquare$) Hexythiazox; ($\blacksquare$) Chlorfluazuron; ($\blacksquare$) Deltamethrin; ($\blacksquare$) Fenvalerate; ($\blacksquare$) τ -Fluvalinate.

Figure 5: Extraction efficiency comparison of 18 analytes using the various sorbent coatings examined in this study. Concentration of analytes: 200 $\mu\text{g L}^{-1}$; Extraction time: 60 min (*PIL fibers*), 90 min (*PDMS/DVB*); Desorption solvent: methanol (*PIL fibers*), acetonitrile (*PDMS/DVB*); pH: 1.5 (*PIL fibers*), 2 (*PDMS/DVB*); Desorption time: 15 min; Desorption solvent volume: 30 μL . (A). ($\square$) Phenacetin; ($\blacksquare$) 2,4-Dinitrophenol; ($\blacksquare$) 2-Nitrophenol; ($\blacksquare$) Ketoprofen; ($\blacksquare$) 17 α -Ethinylestradiol; ($\blacksquare$) Fenoprofen calcium; ($\blacksquare$) 2,4,6-Trichlorophenol; ($\blacksquare$) Diclofenac sodium; ($\blacksquare$) Ibuprofen. (B). ($\blacksquare$) Hexaflumuron; ($\blacksquare$) Phoxim; ($\blacksquare$) Chlorfenapyr; ($\blacksquare$) Flufenoxuron; ($\blacksquare$) Hexythiazox; ($\blacksquare$) Chlorfluazuron; ($\blacksquare$) Deltamethrin; ($\blacksquare$) Fenvalerate; ($\blacksquare$) τ -Fluvalinate.

Fig. 1

A.

B.

Fig. 2

Fig. 3

A.

B.

A.

Figure 1 is a bar chart showing the peak area versus sample solution pH for various concentrations of 2,2,4,4-tetrachloro-5,5-dimethyl-3-pentanone. The x-axis represents the sample solution pH, ranging from 1.0 to 6.0. The y-axis represents the peak area, ranging from 0 to 400,000. The chart shows that the peak area is highest at pH 2.0 and decreases as pH increases. The peak area is also higher for higher concentrations of the compound.

Figure 10 is a bar chart showing the peak area versus sample solution pH for various concentrations of 2,4-dichlorophenoxyacetic acid. The x-axis represents the sample solution pH, with major ticks at 2.5, 3.5, 5.5, and 7.5. The y-axis represents the peak area, ranging from 0 to 1,000,000. For each pH, there are eight bars representing concentrations of 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, and 0.8 mg/L. The peak area generally increases with pH and concentration. The 0.8 mg/L concentration (hatched bars) consistently shows the highest peak areas across all pH values.

Fig. 5

A.

B.

Table 1. Chemical structures and properties of the analytes examined in this study

Name	Structure	Classification	Log <i>P</i> ^b	Log <i>D</i> ^b (pH = 2)	p <i>K</i> _a
Phenacetin		Pain-relieving/ fever-reducing drug	1.65	1.55	5.2 [25]
Ketoprofen		NSAID ^a	2.91	2.91	4.23 ^b
17 α -Ethinylestradiol		Oral contraceptive component	4.11	4.11	10.24 ^b
Fenopropfen calcium		NSAID ^a	-	-	-
Diclofenac sodium		NSAID ^a	4.06 [26]	-	4.01 [26]
Ibuprofen		NSAID ^a	3.50	3.50	4.41 ^b
2,4,6-Trichlorophenol		Phenolics; Organic pollutant	3.77	3.77	6.59 ^b
2-Nitrophenol		Phenolics; Organic pollutant	1.67	1.67	7.14 ^b

2,4-Dinitrophenol		Phenolics; Organic pollutant	1.71	1.72	4.04 ^b
Hexaflumuron		Benzoylurea insecticide	5.67	5.67	8.54 ^b
Phoxim		Organophosph- ate insecticide	4.39	4.39	-
Chlorfenapyr		Insecticide	4.88	4.88	-
Flufenoxuron		Benzoylurea insecticide	4.81	4.81	10.1 [27]
Hexythiazox		Insecticide	5.03	5.03	12.77 ^b
Chlorfluazuron		Benzoylurea insecticide	5.43	5.43	8.10 [27]

Deltamethrin		Pyrethroid insecticide	6.42	6.42	-
Fenvalerate		Pyrethroid insecticide	6.55	6.55	-
τ -Fluvalinate		Pyrethroid insecticide	5.93	5.93	-

^a NSAID: Nonsteroidal anti-inflammatory drug

^b Obtained from Scifinder and calculated using Advanced Chemistry Development (ACD/Labs) Software V11.02

Table 2. Structural composition and approximate film thickness of all PIL-based sorbent coatings examined in this study

Fiber	IL monomer and IL crosslinker composition ^a	Approximate film thickness (μm) ^b
Fiber 1		29
Fiber 2		20
Fiber 3		23 (Fiber 3A) 89 (Fiber 3B)
Fiber 4		16
Fiber 5		28
Fiber 6		21

^a The IL crosslinker applied within each sorbent coating was 50% by weight with respect to the IL monomer.

^b Approximate film thicknesses of the PIL-based sorbent coatings were obtained by SEM imaging.

Table 3. Figures of merit for Fiber **3B** in the analysis of target analytes

Analyte	Linear range ($\mu\text{g L}^{-1}$)	Slope $\pm$ error	LOD ($\mu\text{g L}^{-1}$)	R	%RSD (n = 3)		
					LOD ^a	1 $\mu\text{g L}^{-1}$ ^b	100 $\mu\text{g L}^{-1}$ ^c
Phenacetin	1-500	129 $\pm$ 0.9	0.5	0.999	11.9	3.1	1.3
2,4-Dinitrophenol	1-500	431 $\pm$ 5.2	0.2	0.999	17.7	15.7	2.5
2-Nitrophenol	1-500	67 $\pm$ 0.8	0.5	0.999	8.6	17.8	0.8
Ketoprofen	1-500	977 $\pm$ 10.7	0.2	0.999	13.4	6.6	3.7
17 α -Ethinylestradiol	1-500	1429 $\pm$ 5.0	0.5	0.999	8.3	13.2	1.7
Fenoprofen	1-500	1178 $\pm$ 5.3	0.5	0.999	14.0	14.5	3.0
2,4,6-Trichlorophenol	1-500	1224 $\pm$ 9.8	0.5	0.999	19.0	9.2	0.3
Diclofenac sodium	1-500	630 $\pm$ 7.6	0.2	0.999	19.2	17.4	4.5
Ibuprofen	5-500	571 $\pm$ 17.7	2.0	0.999	13.3	N/A ^d	3.5
Hexaflumuron	1-500	1822 $\pm$ 17.8	0.2	0.999	8.6	8.3	10.5
Phoxim	1-500	761 $\pm$ 16.1	0.5	0.999	14.2	13.1	3.3
Chlorfenapyr	1-500	1160 $\pm$ 36.5	0.2	0.999	4.6	6.6	7.5
Flufenoxuron	1-500	2028 $\pm$ 57.2	0.2	0.999	14.2	13.6	15.7
Hexythiazox	1-500	447 $\pm$ 8.9	0.5	0.999	4.5	16.6	8.1
Chlorfluazuron	1-500	2531 $\pm$ 86.7	0.2	0.998	5.6	13.6	17.3
Deltamethrin	1-500	2279 $\pm$ 89.9	0.5	0.998	7.1	7.4	16.9
Fenvalerate	5-500	2461 $\pm$ 112	1.0	0.998	11.3	11.3	15.7
τ -Fluvalinate	1-500	1411 $\pm$ 55.2	0.5	0.998	10.3	18.6	18.3

^a Precision at LOD; ^b Precision at 1 $\mu\text{g L}^{-1}$; ^c Precision at 100 $\mu\text{g L}^{-1}$; ^d Not detected

Table 4. Applications to real water samples using Fiber **3B**

Analyte	%Recovery $\pm$ SD			
	Tap water		Lake water	
	1.5 $\mu\text{g L}^{-1}$ ^a	150 $\mu\text{g L}^{-1}$ ^a	1.5 $\mu\text{g L}^{-1}$ ^a	150 $\mu\text{g L}^{-1}$ ^a
Phenacetin	80.2 $\pm$ 3.8	85.8 $\pm$ 5.9	79.8 $\pm$ 10.6	102.1 $\pm$ 12.8
2,4-Dinitrophenol	80.5 $\pm$ 3.3	84.2 $\pm$ 7.3	74.0 $\pm$ 9.0	101.1 $\pm$ 12.6
2-Nitrophenol	73.8 $\pm$ 2.5	96.0 $\pm$ 7.3	97.4 $\pm$ 14.5	113.6 $\pm$ 5.1
Ketoprofen	90.9 $\pm$ 1.3	81.6 $\pm$ 7.2	77.5 $\pm$ 3.2	94.8 $\pm$ 10.1
17 α -Ethinylestradiol	56.3 $\pm$ 1.0	91.5 $\pm$ 9.8	53.9 $\pm$ 4.7	104.0 $\pm$ 10.1
Fenoprofen	86.0 $\pm$ 1.8	82.1 $\pm$ 7.4	81.9 $\pm$ 3.4	93.0 $\pm$ 10.2
2,4,6-Trichlorophenol	61.7 $\pm$ 2.4	96.3 $\pm$ 8.5	51.7 $\pm$ 3.3	111.8 $\pm$ 12.3
Diclofenac sodium	70.8 $\pm$ 1.5	87.2 $\pm$ 9.4	58.1 $\pm$ 1.3	95.3 $\pm$ 11.4
Ibuprofen	94.2 $\pm$ 10.7	77.8 $\pm$ 11.4	106.9 $\pm$ 12.3	89.1 $\pm$ 10.1
Hexaflumuron	50.2 $\pm$ 2.1	100.8 $\pm$ 16.5	51.2 $\pm$ 4.0	64.2 $\pm$ 3.9
Phoxim	75.0 $\pm$ 1.2	115.9 $\pm$ 14.4	76.9 $\pm$ 4.2	54.0 $\pm$ 9.7
Chlorfenapyr	78.1 $\pm$ 1.4	105.8 $\pm$ 15.6	73.7 $\pm$ 5.3	67.6 $\pm$ 3.8
Flufenoxuron	80.1 $\pm$ 1.4	91.1 $\pm$ 18.3	84.6 $\pm$ 13.9	52.9 $\pm$ 3.5
Hexythiazox	69.2 $\pm$ 7.4	104.5 $\pm$ 11.2	78.7 $\pm$ 1.8	68.7 $\pm$ 1.5
Chlorfluazuron	86.1 $\pm$ 2.0	86.9 $\pm$ 17.9	92.3 $\pm$ 14.1	48.8 $\pm$ 2.9
Deltamethrin	80.4 $\pm$ 6.1	86.1 $\pm$ 16.6	91.0 $\pm$ 12.6	49.7 $\pm$ 3.4
Fenvalerate	103.2 $\pm$ 13.0	87.4 $\pm$ 17.5	116.6 $\pm$ 15.5	52.4 $\pm$ 4.0
τ -Fluvalinate	86.6 $\pm$ 4.0	86.4 $\pm$ 18.0	95.0 $\pm$ 19.0	49.1 $\pm$ 4.1

^a Spiked concentrations