IONIC LIQUIDS IN SOLID-PHASE EXTRACTION

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Abstract

Supported ionic liquid phases (SILPs), which favourably combine the properties of ionic liquids (ILs) with the advantages of solid supports, were presented in 2009 as an alternative material for solid-phase extraction (SPE). Since then, the number of SILPs used as SPE materials has increased and the results are promising.

This report covers various aspects regarding SILPs: 1) their preparation procedure which is clearly dependent on the support (either silica- or polymer-based) where the ILs are immobilized; 2) their interaction mechanisms which are strongly linked to the SPE protocol as well as the target analytes; 3) their field of application through a number of selected examples. This is the first review that exclusively describes all SILPs that have been developed to date as sorbents in SPE.

Keywords: supported ionic liquids phases; sorbents; solid-phase extraction; interaction mechanisms; preparation

1. Introduction

Sample pretreatment is one of the most important parts of the whole process of analysis. This stage includes analyte preconcentration and removal of interferences from such complex matrices as environmental, biological and foodstuff samples in order to make the analyte more suitable for separation and detection. In spite of the advances made in separation and detection techniques, sample preparation is a vital part of the analytical process and it is essential if reliable results are to be achieved and instrument performance maintained [1]. Modern trends in analytical chemistry are towards the simplification and miniaturization of sample preparation as well as minimization of organic solvent used.

Among the different extraction techniques, solid-phase extraction (SPE) is the most widely used sample preparation technique for liquid samples. SPE belongs to the group of sorptive-based extraction techniques, in which the sample is placed in contact with a suitable material, so the availability of different materials to carry out the extraction is essential. Therefore, research into sample preparation techniques often focuses on developing new materials to achieve higher selectivity and capacity of the technique.

The classic sorbents used in SPE are [2]:

- Silica-based, modified with C_{18}, C_8, phenyl, CH, CN, or NH_2 groups.
- Carbon-based sorbents, including graphitized carbon black (GCB) and porous graphitic carbon (PGC).
- Porous polymeric sorbents, primarily the macroporous polystyrene-divinylbenzene (PS-DVB).

To improve capacity, hypercrosslinked sorbents have been developed which, due to their ultra-high specific surface area of up to 2 000 m^2/g, provide a greater number of interaction points with the analytes to be extracted [3]. The hydrophobic structure of the original porous polymers has also been improved with the introduction of hydrophilic macroporous and hydrophilic hypercrosslinked sorbents. The hydrophilicity of the sorbents can be introduced either through a hydrophilic precursor monomer or by chemically modifying the PS-DVB polymer skeleton [4]. To improve selectivity, molecularly imprinted materials (MIPs) were designed to overcome the limitation of the traditional restricted access materials (RAMs) and immunosorbents (ISs). MIPs have specific cavities matched to a template molecule and a retention mechanism based on molecular recognition, and they have been designed to interact selectively with the target compound(s) while removing all other analytes, including interferents [5]. In the context of the above challenges, research into SPE sorbents in recent decades has focused on improving capacity and selectivity within a single material, leading to the emergence of what are known as dual-phase or mixed-mode sorbents. These sorbents combine a silica or polymeric (the most common for promoting non-ionic interactions) skeleton with ionic groups, with two types of interactions available: reversed-phase (from the skeleton) and ionic-exchange (from the ionic groups). The typical classification in mixed-mode technology is by the type of ion group attached to the skeleton. Thus, these sorbents are classified as cationic or anionic and as strong or weak. The philosophy in mixed-mode sorbent technology is that, once the sorbent type is selected, careful choice of the pH and solvent in each SPE step allows the matrix components and interferents to be eluted separately from the analytes of interest in the washing and elution steps, respectively.

In recent years, ionic liquids (ILs) have been immobilized onto silica or polymeric supports (known as supported IL phases –SILPs) in order to take advantage of the chemical functionality that ILs can impart and, as a result, new groups of stationary phases with different fields of application in different extraction (e.g. SPME and SPE) and separation (e.g. GC, LC and CE) techniques have emerged. Therefore, SILPs can be considered another class of sorptive material [6].

ILs are inorganic and organic salts with melting points below 100ºC. Most ILs are a combination of organic cations − imidazolium, pyridinium, pyrrolidium, ammonium and phosphonium, among others − and anions, which can be inorganic − Cl^-, PF_6^-, BF_4^- and NTf_2^- − or organic − trifluoromethylsulphonate or trifluoroethanoate, among others. They have unique properties such as negligible vapour pressures, high thermal stability, high viscosity, and good conductivity and solubility. One important feature of ILs is that varying the cation or anion can significantly affect their physical and chemical properties. Consequently, combinations of different cations and anions result in a wide range of ILs with different properties, from which the ILs can be selected for specific applications. As a result of their exceptional properties, ILs have attracted interest as green solvents for chemical processes, including organic catalysis, and more recently, analytical chemistry and inorganic synthesis [7,8]. These liquids also exhibit a range of solvent properties, especially for the isolation of compounds from aqueous solutions, and they tend to be highly viscous, which limits their use as conventional solvents. Therefore, in analytical chemistry, they are good candidates for use in conventional solvent-based extraction, and as stationary phases in sorptive extractions [9].

Since the late 1990s, several studies have been published which have demonstrated the potential of ILs in analytical chemistry. Some of these publications are reviews of the state of the art [10-14] while others provide specific applications, mainly focused on stationary phases in separation techniques such as gas chromatography, liquid chromatography and capillary electrochromatography [15,16], and as solvents or modifiers in liquid extraction techniques such as liquid-liquid extraction, liquid-phase microextraction, single-drop microextraction, solid-phase microextraction (SPME) [17-20], among others, or as part of sorptive material in extraction techniques such as SPME [18, 21] or SPE [16], interest in which has been increasing lately. It should be highlighted that the liquid state of ILs is lost when immobilized onto a solid support. Nevertheless, under these conditions, multi-modal type interactions can be still exploited.

With respect to sorptive extraction techniques, SILPs were first applied as an SPME coating in 2005, in a study where ILs were merely adsorbed on the fiber surface [22], which involved a fiber re-coating after each extraction. Subsequently, in order to circumvent this limitation, polymeric ILs (PILs) were developed [23] by the Anderson research group, who recently have extensively reviewed PILs as SPME coatings [21]. Some other recent reviews [18, 20] have also been devoted completely or partially to the use of PILs in SPME.

SILPs as SPE materials emerged later, in 2009. Since then, the number of applications has increased steadily. To date, however, no comprehensive review completely dedicated to SILPs in SPE has been yet published, with only the very recent exception of the work by Vidal *et al*. [16], which reviewed SILPs together with other stationary phases for separation purposes. The present review covers all of the SILPs that have been used as sorptive materials in SPE to date. There is a description of the different synthetic routes for their preparation, a discussion of the interactions generated as well as the suitable SPE protocol for enhancing these interactions. A number of selected examples are then given of applications of SILPs in SPE in order to illustrate their benefits and limitations.

2. Preparation of supported ionic-liquid phases (SILPs) as SPE materials

The SILPs in SPE can be classified as silica- or polymer-based, depending on where they are supported. The first SILP materials used in SPE were silica-based. Subsequently, however, polymers are used as support. Later, both silica- and polymer-based MIPs were also developed involving ILs in their synthesis protocol. In view of this classification, this section is divided into these three subsections.

2.1. Silica-based IL phases

The strategies to anchor ILs to silica surfaces have previously been developed to prepare them as catalytic supports or stationary phases. These materials are prepared by either bonding or grafting ILs to silica, hence, comprising what is known in LC stationary phases as surface-confined ILs.

All of the procedures involve, as a first step, the activation of the silica particles using strongly acidic aqueous solutions (typically nitric acid or hydrochloric acid) to enhance the content of silanol groups on the silica surface and to eliminate metal oxide and nitrogenous impurities. Then, as shown in Figure 1A, one option is to react these activated silica particles in a first step with one silane-coupling agent such as 3-chloropropyltrimethoxysilane (depicted in Fig 1A since it is the most commonly used) or 3-chloropropyltriethoxysilane [24-26], by suspending them together in dry toluene, in order to obtain chloropropyl silica which is reacted with the imidazole or the alkyl-branched chain imidazolium derivatives. Finally, the remaining chlorine group of the ILs can be ion-exchanged with other anions to obtain the desired surface-confined ILs. Alternatively, as shown in Figure 1B, the silane-coupling agent and the imidazole (or any imidazolium derivatives) can be reacted in the first place, and the resulting IL is then reacted to the activated silica particles. It should be noted that Yang *et al.* [27] used a similar approach to that described in Figure 1A, but the silica shell was formed on the surface of the magnetic Fe_3O_4 microspheres.

Another immobilization approach that has also been used in catalytic fields involved the treatment of a solid with a substantial amount of ionic liquid phase (5 – 50 wt). In contrast to the abovementioned approaches, the ILs did not undergo reaction with the support and merely resulted in the formation of multiple layers on the carrier, as depicted in Figure 1C. The resulting material is a solid, although the active species are dissolved in the IL instead of being brought into contact by sorption mechanisms [28]. This approach has been successfully adapted in order to prepare 1-butyl-3-methylimidazolium hexafluorophosphate

([BNIm][PF_6])[29] and bromide-modified silica [30], which were used for the separation and preconcentration of metals from water samples. It should be noted that the level of column reuse when using this last preparative approach is lower than when the approaches involve the covalent bonds between the support and the ILs. For instance, in the extraction of Pb^{+2} [30] and Cd^{+2} [29] using IL-silica that is supported as described in the approach above, it is reported that the material is reused for between 10 [30] and 20 [29] adsorption-elution cycles, without a significant decrease in the recovery of the metals. However, for the extraction of Cr^{+6} using a polymer support covalently attached to the IL, the column is reused up to 300 times, without being modified [31].

With respect to the characteristics of the IL immobilized on these silica supports, N-methylimidazole ([MIm] is the initial and most commonly used reagent to form the IL [24,32-37]. In the most recent studies, however, researchers have compared the synthesis of a series of ILs, including imidazole ([IM]) [25, 38, 39], N-methylimidazole ([MIM]) [25, 38, 39] and 2-ethyl-4-methylimidazole ([EMIm]) [25, 38], 1-butylimidazole [BuIM] [38] and 1-alkyl-3-(propyl-3-sulphonate)imidazole [PSIM] [39]. The bonding density of the imidazolium silica decreased as the alkyl branches of imidazoles increased, which may be explained by steric hindrance from the alkyl chain. However, the separation of the analytes was dominated by the influence of interactions between the analytes and the stationary phase, rather than the influence of the bonding density [38].

In all these last studies, the IL were formed in pairs with $[Cl]^-$ and, in just one case [38], the SILP based on SilprImCl was ion-exchanged afterwards with $NaBF_4$, HPF_6 and $Li(Tf_2N)$ to generate $SilprImBF_4$, $SilprImPF_6$ and $SilprImTf_2N$, respectively. The sorption characteristics of all of these SILPs were compared using two different alkaloids from plants (matrine and oxymatrine) as target analytes. The authors found that SilprImCl had adsorbed higher amounts of the target analytes, which they attributed to the excellent water miscibility of its functional group (Cl^-) [38].

2.2. Polymer-based IL phases

In the case of polymer-based IL sorbents, the variety may result from either the support or the IL attached. It should be noted that all of the polymer precursors were generated using suspension polymerization procedures that provide macroporous or gel-type polymers (depending on the percentage of crosslinker in the polymerization feed). With regard to the preparation and in a similar way to the procedure for obtaining hydrophilic conventional SPE polymeric sorbents [4], polymer-based IL phases can be obtained by introducing an IL into the existing polymer support or by copolymerizing monomer containing suitable functional groups. These two ways of obtaining polymer-based IL phases are discussed in this section.

A) Post-functionalized polymeric supports

With respect to the support, they can be prepared by post-modifying a generated polystyrene-based polymer, such as poly(vinylbenzylchloride-divinylbenzene) (VBC-DVB), with [MIM] [31-33, 36], [IM] further reacted with 3-aminopropyl bromide [40], [BuIM] [41], or a series of imidazole derivatives [42] (Figure 2A). Optionally, the chlorine anions can then be further ion-exchanged for other anions such as CF_3COO^- [32], BF_4^- and $CF_3SO_3^-$ [33] to obtain other ILs combinations.

Other polymers that are not styrene-based have also been also used as a skeleton, such as glycidyl methacrylate (GMA) which was copolymerized with ethylene dimethacrylate (EDMA) and then further modified with [MIM] [36], in a similar way to that depicted in Figure 2A. In that case, however, the authors did not specify which anion the ILs were formed by. Polyvinyl chloride (PVC) was also used as a precursor to immobilize N-methylimidazole via reaction with a chlorovinyl group in order to generate PVC-MImCl [31].

Regardless of the precursor, the final immobilized IL on the polymeric support was achieved by refluxing the polymer support with the solution containing the reagent, for instance [MIM], for a period of at least 8h.

B) Polymeric supports from N-based monomer

An alternative approach is to copolymerize two monomers, one of them being an N-based monomer, and to take advantage of the presence of nitrogen in the monomers in order to generate the IL polymer-based support more straightforwardly. Thus, poly(4-vinylpyridine-divinylbenzene) (PVP-DVB) [43] which was alkyl-modified with butyl chloride to obtain an alkyl pyridinum polymer (as shown in the example given in Fig. 2B) was used. Alternatively, 1-vinyl-3-butylimidazolium chloride [44] copolymerized with EDMA was used to prepare a molecularly imprinted polymer (MIP) for chlorsulfuron (template). More information about the preparation of MIPs is detailed in section 2.3.

In general, it should be mentioned that the preparation of polymer-based SILPs is more straightforward than silica-based SILPs.

After the synthesis, the materials obtained (both silica- and polymer-based) were characterized in order to evaluate the incorporation yields of IL, as well as the morphology of the resulting materials. In order to test the incorporation of the ILs, authors usually record FT-IR spectres to evaluate the appearance or disappearance of the characteristic bands qualitatively. In addition, elemental analysis allows the quantification of the percentage of different characteristic elements of the IL such as nitrogen and chlorine, as well as the variation of other elements such as carbon and hydrogen, before and after the modification of the support with the IL. Their porous properties were characterized by measuring the surface area, which is generally calculated from N_2 sorption isotherms using the BET method. In most of the cases, the specific surface area of the polymer-based SILPs are larger than silica-based SILPs. These larger specific surface areas are attributed to the porous character of the polymeric support and favourably contribute to the enhancement of the RP interactions.

2.3 MIP sorbents using ILs

ILs have been also reported in the preparation of MIPs. Initially, they have been used as porogen in the polymerization process. In this way, for instance, [BMIM][PF_6] and [BMIM][BF_4] have been used as solvents for the preparation of molecularly imprinted materials that are selective for dichlorvos[45], norfloxacin [46] and testosterone [45], respectively. ILs showed excellent solvation qualities and satisfactory porogen qualities. Furthermore, they are more environmentally friendly than traditional organic solvents. Apart from these general features, as an example, when [BMIM][BF_4] was used as porogen to prepare norfloxacin-imprinted polymers, the materials obtained had enhanced recognition properties and binding capacity for the template compared to materials obtained using a traditional porogen, such as a mixture of decanol/docecanol [46].

In addition, ILs have been reported as functional monomers involved in molecularly imprinted preparation. Imidazolium-based IL supported on silica [47] and on porous polymer [42, 44] was prepared for the selective extraction of tanshinones from *Salvia miltiorrhiza Bunge* (a traditional medicinal herb) [44, 47] and chlorsulfuron in environmental water samples [44].

In the case of the silica-based MIP [47], the authors used the general approach described in Figure 1B. To elaborate in more detail, the synthesis started with the reaction between (3-aminopropyl)trimethoxysilane and 3-chloropropionyl chloride, of which the reaction product was further reacted with imidazole. Finally, this product was immobilized onto a silica particle and the template (9,10-phenanthrenequinone) was added to form the IL groups. Figure 3A shows the preparation scheme of this MIP. Subsequently, the same authors designed a MIP for the same template, but immobilized onto a polymeric support [42]. In this case, they used the general approach depicted in Fig. 2A. In particular, the VBC-DVB template (9,10-phenanthrenequinone) and different ILs were added at the same time. Figure 3B shows the preparation scheme as well as the list of ILs tested. It should be noted that the MIP synthesis was satisfactory using both silica and polymeric supports.

The other two polymer-based MIPs using IL were prepared using the approach depicted in Figure 2B, where the imidazole derivative acts as monomer in the polymerization process. To be specific, 1-vinyl-3-butylimidazolium chloride was used to prepare the MIP selective for chlorsulfuron [44]. Meanwhile, different 1-allylimidazole derivatives (1-allyl-3-ethylimidazolium bromide, 1-allyl-3-butylimidazolium chloride, 1-allyl-3-hexylidazolium chloride and 1-allyl-3-octylimidazolium chloride) were tested for preparing the MIP selective for phenolic acid compounds [48]. They found that increasing the alkyl chain length influenced adsorption, with the most suitable monomer being 1-allyl-3-ethylimidazolium. Thus, the use of SILPs as a functional monomer in MIP preparation has been shown.

3. Evaluation and application of SILPs as SPE sorbents

In SPE, the liquid-phase interactions between the sorbent and the analytes result from the characteristics of the sorbent (in this case, the SILPs) and the analytes. The nature of most of the SILPs, where imidazolium-based functional groups were immobilized on silica or polymer supports, can give rise to the following different interaction mechanisms: 1) strong anion-exchange interactions from the nitrogen moiety in the cation; 2) π-π interactions from the imidazolium or pyridinium groups in the cation as well; 3) hydrophobic interactions may also arise to a higher or lower extent depending on the anion that forms the IL. As an example of hydrophobic interactions, when the [MIM] IL is combined with the water-insoluble anion $[PF_6]^-$, it displays a more hydrophobic character than when exchanged with the water-soluble anion $[Cl]^-$ [49].

Apart from the SILP itself, an important role is also played by the properties of the analyte and the SPE protocol (suitable for activating the interaction sites). Therefore, before selecting the proper protocol, all these points should be carefully identified. With this in mind, in the first ever approach using SILPs as a SPE sorbent [32], our research group tested four different protocols in order to ascertain which resulted in the strongest interaction mechanism of the SILPs with the target analytes (and hence the subsequent retention of the analytes). To be specific, the IL based on $[MIM][CF_3COO]$ was immobilized onto a gel-type polymer based on polyVBC-DVB. The retention properties of this SILP were then tested on a group of pharmaceuticals under four SPE protocols in order to exploit: 1) reversed-phase (RP); 2) weak-anion exchange (WAX); 3) strong-anion exchange (SAX); 4) strong-cation exchange (SCX) interactions. The results obtained showed that the SAX protocol was the most efficient, since all of the most acidic analytes (pK_a < 5) studied were eluted during the elution step with recovery values ranging between 90% and 100% in all instances. Once the optimal protocol had been verified, the IL-based sorbent was applied in order to enrich and clean up these pharmaceuticals from 1 000 mL of river water or 250 mL of effluent wastewater, providing a clean chromatogram and high recoveries of the analytes studied. Figure 4 shows the chromatograms obtained with [MIM][CF_3COO] and Oasis MAX (which is a commercially available sorbent based on a polymeric structure with quaternary amine moieties, so it acts as a SAX sorbent). In these chromatograms, although the samples are complex, the baseline is flatter and allows the most acidic analytes to be quantified properly at low concentration levels, which might be partially attributed to the effective washing step that can be performed with the SAX materials and SILPs in particular. A similar protocol was followed when testing two other SILP materials from the same series, involving the same polymeric support but, in this case, it was ion-exchanged with HBF_4 and CF_3SO_3H to become VBC-DVB[MIM][BF_4] and VBC-DVB[MIM][CF_3SO_3], respectively [33]. When these three SILPs (VBC-DVB[MIM][CF_3COO], VBC-DVB[MIM][BF_4] and VBC-DVB[MIM][CF_3SO_3]) were compared for the extraction of a group of acidic pharmaceuticals from environmental water samples, it was found that VBC-DVB[MIM][CF_3COO] and VBC-DVB[MIM][CF_3SO_3] provided similar and more efficient results than when applying VBC-DVB[MIM][BF_4] as the sorbent. The poorer retention of VBC-DVB[MIM][BF_4] can be attributed to the nature of the [BF_4] anion, which exhibits a higher charge density, which leads to stronger interaction with imidazolium sites and, therefore, fewer interactions with the analytes [33]. Therefore, once again, the type of anion is important for fine-tuning the retention mechanisms. Table 1 summarizes the analytical applications in which SILPs are used as SPE materials.

Other SILPs that have been tested under SAX SPE protocols are described below. In fact, in the first application of ILs in SPE [50], the conditions used were in line with the SAX SPE conditions. In this case, [C_6MIM][Br] and [C_{12}MIM][Br] were adsorbed on the silica surface to prepare mixed hemi-micelle materials. Only the solution containing the IL was passed through the silica cartridge column, so that the IL is simply adsorbed onto the silica particle and not chemically attached to it (in which case, it could not be regarded as a SILP). As a result of the adsorption isotherm study, the authors concluded that the adsorption of ILs onto the silica surface was not a simple surface phenomenon but a multistep process involving different kinds of interactions. Both novel materials were then evaluated for the extraction of phthalic acid esters, which were eluted from the material using methanol at pH 2. After the optimization of the different parameters in SPE, the recoveries for these targets analytes were higher than 85% when 300 mL of environmental water samples were extracted.

At this point it should be remained that silica-based materials are not amenable to extreme pHs (i.e. out of the pH range 2-8), otherwise the silica decomposed. This is one of the major drawbacks that present silica-based SILPs compared to polymer-based ones, which can work at all pHs without losing their entire properties.

In another study, three different anion-exchange silica-based ILs (Silpr[IM][Cl], Silpr[MIM][Cl] and Silpr[EMIM][Cl]) (see Table 1 for details) were synthesized and applied to solid-phase extract lactic acid from fermentation broth [25]. The acidic nature of the analyte makes it suitable for exploiting the SAX SPE protocols. In this case, the fermentation broth was washed with 4 mL of different solvents, such as water, methanol, acetonitrile, n-hexane and dichloromethane, all of which washed out the interferences, while lactic acid remained retained through SAX interactions between the analyte and the SILP. Finally, aqueous HCl was used for the elution step.

Very recently, Vidal *et al*. [39] compared the selective performance of three IL-functionalized silica sorbents (i.e. Silpr[MIM][Cl], Silpr[IM][Cl] and Silpr[IM][PS]), on the extraction of a group of organic acids, amines and aldehydes (acidic, basic and neutral characteristics, respectively) under different pH levels ranging from 2 to 12. From this study, it was concluded that, although the three SILPs showed different interaction mechanisms (anion-exchange, hydrophobic, hydrogen bonding and π-π interactions), the dominant interaction mechanism is anion-exchange. This feature was found from the lower retention of amines and aldehydes achieved with the SILPs. From the three SILPs tested, Silpr[IM][PS] showed the best retention for amines and aldehydes, which was attributed to the presence of the sulphonic group, as well as having the longest alkyl chain (enhanced reversed-phase properties). Finally, all three SILPs were applied to the extraction of the studied compounds from aerosol samples, as detailed in Table 1.

A VBC-DVB[BIM][Cl] was synthesized and used for the removal of phenol from aqueous solution. The sorption experiments revealed the maximum adsorption is attained at about pH 11, where anion-exchange interaction dominated, whereas under acidic conditions, phenol is molecularly adsorbed to the SILP [41]. Subsequently, the elution of phenolate was performed using alkaline solution based on 0.5M NaOH: 0.5M NaCl. Similar results with respect to loading were found in the preconcentration of three chlorophenols in water using a magnetic microsphere-confined IL [27], where the extraction conditions were best at a pH of 8 or above (as the analytes are in their ionic form). However, among the three different eluents tested (methanol, acetonitrile and methanol at pH 10), the basic solvent was found to be optimal. These results are not in agreement with the SAX protocol, that should involve an acidic solution to disrupt the ionic interactions. In any case, the recoveries of the chlorophenols studied were from 70% to 90% when 200 mL of tap, spring and river water were extracted using the novel SILPs.

Most of the SILPs applied to SPE took advantage of the SAX mechanisms and the possibility of washing out the interferences from the matrix and separating them from the target analytes during the extraction protocol. On some occasions, however, the results were not completely selective due to the nature of the analytes selected and the fact that they cannot display ion-exchange interactions, since they do not contain any ionizable functional group. One such case is the various studies carried out by Row *et al.*, in which some analytes and their metabolites were extracted from very complex samples, mainly medicinal plants (see Table 1 for specific details). In most of the cases, the authors had to design two SPE protocols (one suitable for the ionizable analyte and another for the neutral one). For instance, Silpr[EMIM][Cl] [26] and (alkyl pyridinium polymer-based) PVP-DVB-[Bu][Cl] [43] were applied to solid-phase extract liquiritin and glycyrrhizic acid from licorice (the root of the glycyrrhiza plant). The SPE protocol was optimized in both studies and the findings were similar. Liquiritin which contains phenolic acids (ca. $pk_a \sim 7 - 8$) was completely eluted with such pure organic solvent as methanol and acetonitrile. In contrast, glycyrrhizic acid, which in addition contains carboxylic acids (ca. $pk_a \sim 4 - 5$) that were retained through ionic interactions to the SILPs, had to be eluted using methanol:acetic acid (90:10) in both studies. It should be noted that a washing step involving water [26], and acetonitrile and methanol:water (75:25, v/v) [43] was included in order to increase selectivity. The levels of selectivity achieved with Silpr[EMIM][Cl] and PVP-DVB-[Bu][Cl] were higher than with silica sorbent functionalized with C_{18} [43]. A similar procedure [MIM] was used to synthesize Silpr[MIM][Cl] sorbent in the SPE of tanshinones from *Salvia Miltiorrhiza* (a medicinal herb). A washing step with water and methanol increased the selectivity of the extraction [34].

In other studies [36,38,40], however, the analytes selected had a basic character, which makes it much more complicated to explain the selectivity achieved with the SILPs. For instance, a SILP based on [MIM][Cl] immobilized onto GMA-EGDMA was tested for the extraction of caffeine and theophylline (basic compounds) from green tea, and the results were compared to those with C_{18} sorbent and blank polymer [36]. SILPs exhibit a higher degree of selectivity since they allow the extracts to be washed with pure or aqueous mixtures of organic solvents without losing theophylline, while this compound was completely eluted from C_{18} and blank polymer using a similar washing solvent. Similarly, matrine (which has a ternary nitrogen with $pK_a \sim 9\text{-}10$) and oxymatrine (the same ternary nitrogen is oxidized, so it cannot be protonated) were selectively extracted from *Sophora Flavescens Ait* (a plant used in traditional Chinese medicine) using VBC-DVB[IMN][Br] as a sorbent. In that case, due to the nature of the functional groups in the analytes, the elution protocol was different depending upon the analytes. Therefore, the elution of oxymatrine involved 2 mL of acetonitrile, while the elution of matrine involved 2 mL of methanol:trimethylamine (90:10, v/v). In that case, however, the elution solution had a basic character in order to turn the acidic nitrogen neutral and disrupt the ionic interaction with the sorbent [40]. Subsequently, oxymatrine extraction was further evaluated by the same research group, but in this case using a series of silica-confined ILs (refer to Table 1 for details) [38]. Based on results obtained in a previous study [40], the authors selected water as the washing solvent and methanol as the elution solvent (although acetonitrile also provided good results, as in the previous case). The only conclusion that can be drawn from the selective extraction of all these basic analytes is that the polymeric backbone would undergo some modifications attributed to a suitable polymerization and/or functionalization with the ILs conditions, or some enhancement of the reversed-phase interaction mechanisms when the support is modified with IL. In the end, in both studies, the target compounds were determined using each SILP in SPE followed by LC-UV from *Sophora Flavescens Ait* with suitable figures of merit. The authors also claimed that the presented method was compatible with existing LC methods for analysing matrine and oxymatrine in this type of sample [38,40].

Their other studies did not exploit the SAX properties of the SILPs because the analytes did not contain any ionizable functional group. This is the case when Silpr[MIM][PF_6] was used as a sorbent for the SPE of 12 sulphonylurea herbicides from environmental water and soil samples [51]. In the case of water samples, 250 mL was extracted with 200 mg of sorbent. A soft clean-up step involving water was also included and retained compounds were eluted with dichloromethane/methanol. The authors concluded that in this case hydrophobic interactions became predominant in the IL-SPE process. Using this optimized protocol, the recoveries achieved for the 12 sulphonylurea herbicides in both surface water and soil samples with IL silica-functionalized sorbent were higher than those obtained with C_{18} sorbent. In another study, β-Sitosterol (which has just one cycloaliphatic alcohol as a functional group) was extracted from a medicinal herb (*Salicornia herbacea L.*) using MAA-GMA-EGDMA[BIM][Cl] as the SILP, which the authors had already selected based on existing literature, for its remarkable reversed-phase retention properties due to the imidazolium ring [52]. After this observation, β-Sitosterol could be eluted with high recoveries using 10 mL of water:acetonitrile (90:10, v/v) as the eluent from the plant.

Another application of SILPs is as functional monomers in MIPs. To the best of our knowledge, to date, four MIPs has been synthesized using SILPs [42,44,47,48]. Their preparation is described above in section 2.3 and their application detailed in Table 1, where they are specifically highlighted by the use of the prefix 'MIP' at the start of the SILP acronym. Based on these studies, Tian *et al.* [42] compared the performance of five different imidazolium derivatives (including IM, MIM, IM-COOH, IM-NH_2 and IM-CN) in the extraction of tanshinones from medicinal herb samples. The adsorption isotherm proved that the sorbent with the carboxyl-IM possessed the highest recognition for the target compounds. The optimal protocol for achieving the selective extraction of tanshinones was as follows: loading with 0.4 mL of sample, washing with 4 mL of water:methanol (30:70, v/v) and eluting with pure methanol and acetone. This protocol was also applied to the extraction of six commercial functional drinks revealing the presence of three tanshinones in a levels ranging from 0.14 to 2.46 x 10^{-2} mg/L. Very recently, Row *et al*. [48] compared the performance of different polymer-confined ILs for the extraction of a group of phenolic acid compounds. They prepared 25 different SILPs, either adopting the imprinted (i.e. incorporating the template during the synthesis) or non-imprinted approach. After choosing MIP-AllEIM[Br] as the best material (refer to Table 1 for the others) as well as the optimum SPE conditions (loading: 1 mL of sample; washing: 1 mL of water followed by 1 mL of MeOH; elution: 1 mL of aqueous 0.5 M HCl), the material was used to extract phenolic acids selectively from plant extracts with recoveries higher than 82% for all target compounds and excellent figures of merit.

Some interesting materials based on silica-supported ILs are the π-complexing sorbents. They are prepared by covalently immobilizing ILs onto silica and then coating these silica-supported ILs with silver salts, as described by Li *et al*. [35, 37]. These supported ILs were better at immobilizing and retaining silver salts on silica than traditional π-complexing sorbents formed by the direct anchoring of silver salts onto silica. They were successfully applied to extract and enrich polyunsaturated fatty acid methyl esters from fish oil [35] and from soy-derived biodiesel [37], with high selectivity and capacity. It should be noted that, in spite of the high selectivity reported, the protocol used did not include any washing step.

Although most IL-supported sorbents have been used for the extraction of organic compounds, some have been used for the preconcentration of metals, such as Cd^{+2} [29], Pb^{+2} [30] Cr^{+6} [31] and Pd^{+2} [53]. In these cases, however, the interaction mechanisms involved are cation-exchange type, since the target analytes are positively charged, which may interact with the anions displayed in the SILPs. However, the proposed mechanism is not specified in either of the studies and it remained unclear. Taking the ionic aqueous solution selected to be the eluent HCl aq. 1M [29] or HCl aq. concentrated [30], NH_4NO_3 aq. 0.2 M [31] and thiourea 1M in HCl aq. [53], it seems that the mechanism involves the competition of the metals for the anionic site either in the SILP or in the eluent. In some studies [29,30], the performance of the IL-supported sorbents compared favourably in terms of preconcentration factors and limits of detection achieved with respect to other ionic materials for the extraction of the metals studied. In all cases, the results were best with the IL-based sorbents. As an example, a [C_4MIM][PF_6]-modified silica sorbent was used to preconcentrate Cd^{+2} after the addition of the chelating agent dithizone [29]. Recoveries for 150 mL of lake and tap water were higher than 95% and at least 20 extractions can be made with the same sorbent with no decrease in the recovery of Cd^{+2}.

4. Conclusions and future trends

The development of novel material for SPE is still an evolving field with new material continuously being developed and evaluated for this purpose.

SILP preparation with respect to their application in SPE fields is already well established. Furthermore, SAX in combination with RP interactions is the most rational mechanism that SILPs display during the SPE process. Therefore, the key point for success is to select suitable analytes (i.e. charged analytes) as well as SPE conditions in order to enhance the selectivity and capacity of these materials when applying them to preconcentrate complex samples. Nevertheless, their selectivity and capacity may be further fine-tuned by selecting the IL to be immobilized and the type of immobilizing support.

Once the benefits of SILPs as SPE materials have been demonstrated, their consolidation as conventional SPE material is envisaged in the near future and more so when SILPs are commercialized. Therefore, scientists with an interest in mixed-mode sorbent technology may also find that these materials provide new, exciting opportunities.

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Figure captions.

Figure 1. Synthetic approaches to prepare silica-based SILPs.

Figure 2. Synthetic approaches to prepare polymer-based SILPs.

Figure 3. Example of two approaches where SILPs are involved in the MIP synthesis: A) silica-based (reprinted from [47], copyright 2011, with permission of Springer) and B) polymer-based (reprinted from [42], copyright 2011, with permission of Springer).

Figure 4. Chromatograms obtained after off-line trace enrichment of 250 ml of effluent WWTP sample without (a and c) and with (b and d) the addition of a 5_g l−1 level of the analyte mixture followed by the washing step and elution of the most acidic compounds using [MIM][CF_3COO]: without (a) and with (b), and Oasis MAX: without (c) and with (d), the addition of the analyte mixture (reprinted from [32], copyright 2009, with permission of Elsevier).

Annex. Abbreviations

IL cations

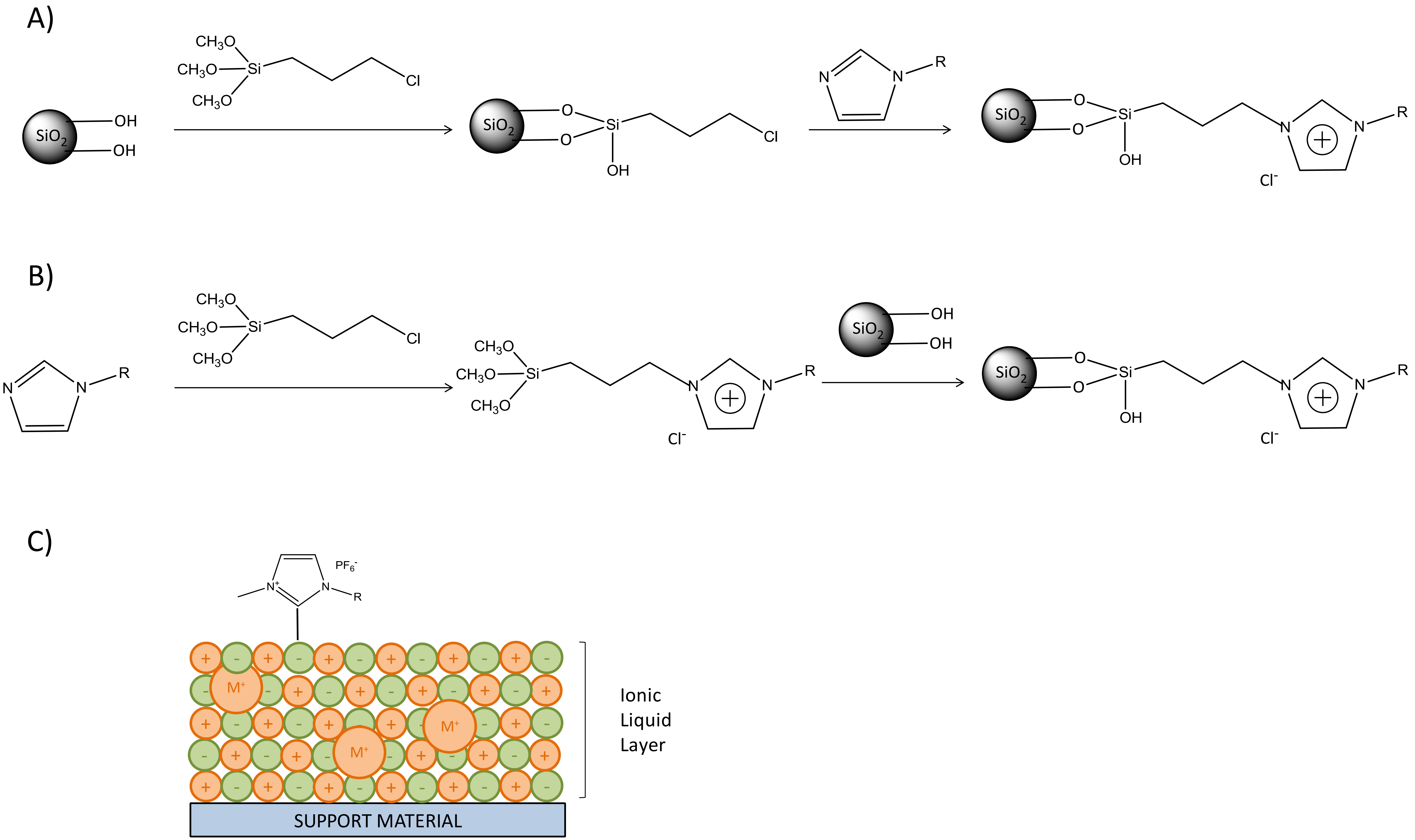
[IM]	Imidazolium
[C_4IM]	N-butylimidazolium
[MIM]	N-methylimidazolium
[EMIM]	1-ethyl-3-methylimidazolium
[C_6MIM]	1-hexyl-3-methylimidazolium
[C_{12}MIM]	1-dodecyl-3-methylimidazolium
[Bu]	butyl
[IMN]	1-(3-amino)-propylimidazolium
[IM-COOH]	Carboxyl-imidazolium
[IM-NH_2][	Amino-imidazolium
[IM-CN]	Cyano-imidazolium

IL anions

[Cl]	chloride
[Br]	bromide
[CF_3SO_3]	trifluoromethanesulfonate or triflate
[CF_3COO]	trifluoroacetate
[PS]	1-alkyl-3-(propyl-3-sulfonate)
[PF_6]	hexafluorophosphate
[BF_4]	tetrafluoroborate
[Tf_2N]	Bis(trifluoromethyl)sulfonylimide

Support

Sil	silica
Silpr	propyl silica
VBC	vinylbenzylchloride
PVP	4-vinylpyridine
DVB	divinylbenzene
GMA	glycidylmethacrylate
MAA	methacrylic acid
EGDMA	ethylenglycol dimethacrylate
PVC	polyvinylchloride
ViBuIM	1-vinyl-3-butylimidazolium
AllEIM	1-allyl-3-ethylimidazolium
AllBuIM	1-allyl-3-butylimidazolium
AllHeIM	1-allyl-3-hexylimidazolium
AllOcIM	1-allyl-3-octylimidazolium
MIP	molecularly imprinted polymer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OH
CH3O
CH3O
CH3O
Si
Cl
SiO2
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O
Si
OH
Cl
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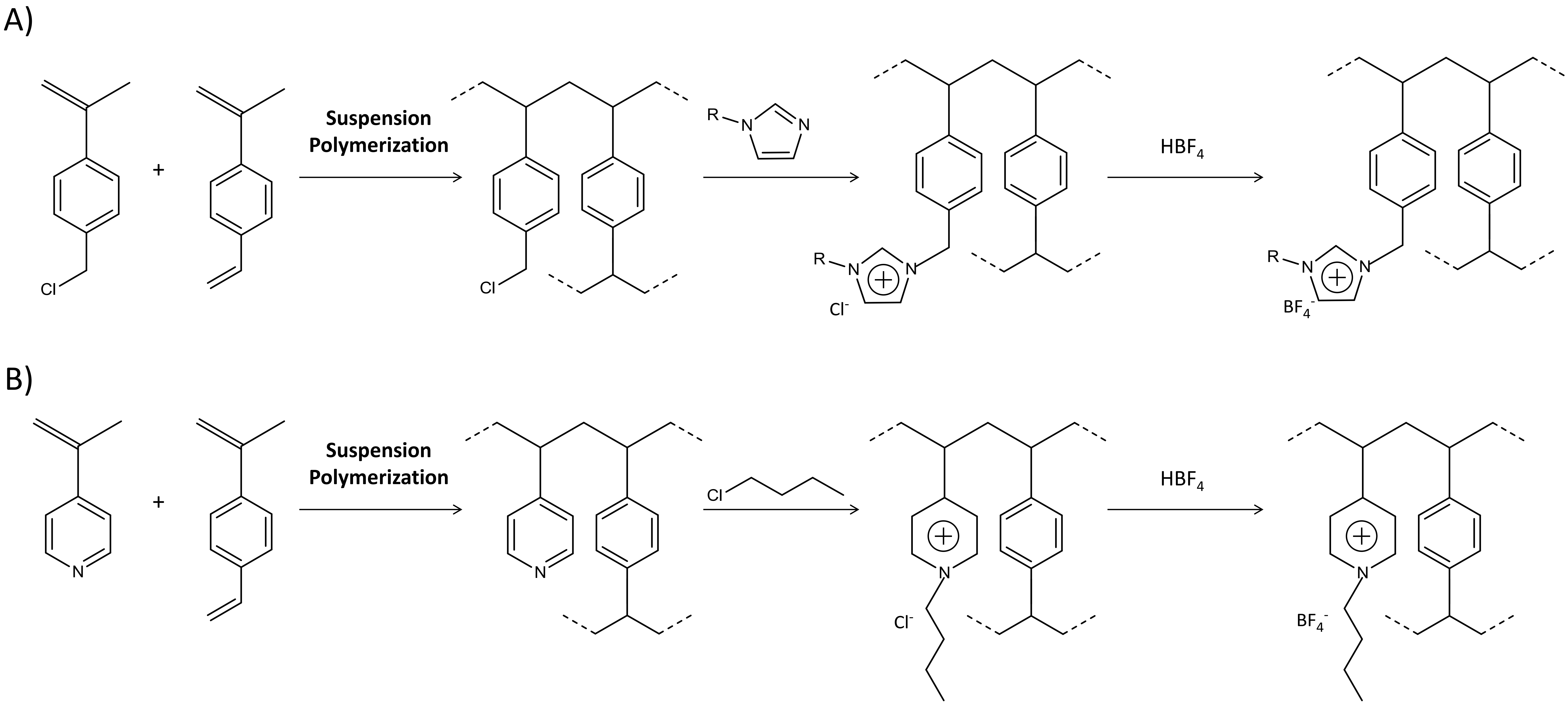
R
SiO2
O
O
Si
OH
N
N
R
Cl-
B)
N
N
R
CH3O
CH3O
CH3O
Si
Cl
CH3O
CH3O
CH3O
Si
N
N
R
Cl-
SiO2
OH
OH
SiO2
O
O
Si
OH
N
N
R
Cl-
C)
N+
N
R
PF6-
M+
M+
M+
+
-
SUPPORT MATERIAL
Ionic
Liquid
Layer

Figure 1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+
Suspension Polymerization
Cl
R
N
N
R
N
N
Cl-
HBF4
R
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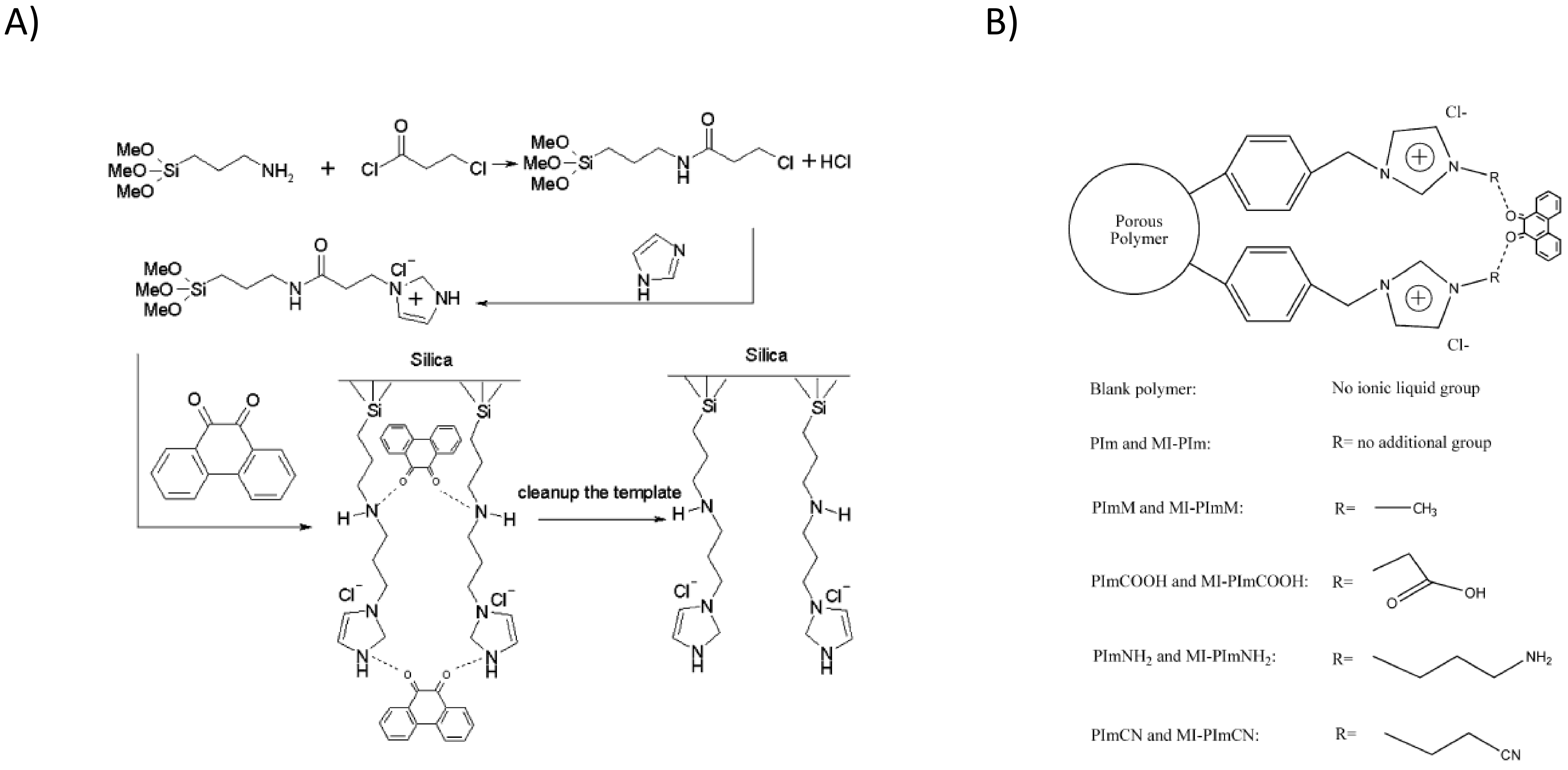
HBF4
N
BF4-

Figure 2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MeO–Si
MeO
NH₂
+
Cl
O
Cl
MeO–Si
N
H
Cl + HCl
Cl⁻
+ NH
Silica
Si
cleanup the template
H–N
N–H
B)
Cl-
Porous Polymer
N
R
O
Blank polymer: No ionic liquid group
PIm and MI-PIm: R= no additional group
PImM and MI-PImM: R= CH₃
PImCOOH and MI-PImCOOH: R= OH O
PImNH₂ and MI-PImNH₂: R= NH₂
PImCN and MI-PImCN: R= CN

Figure 3

Figure4

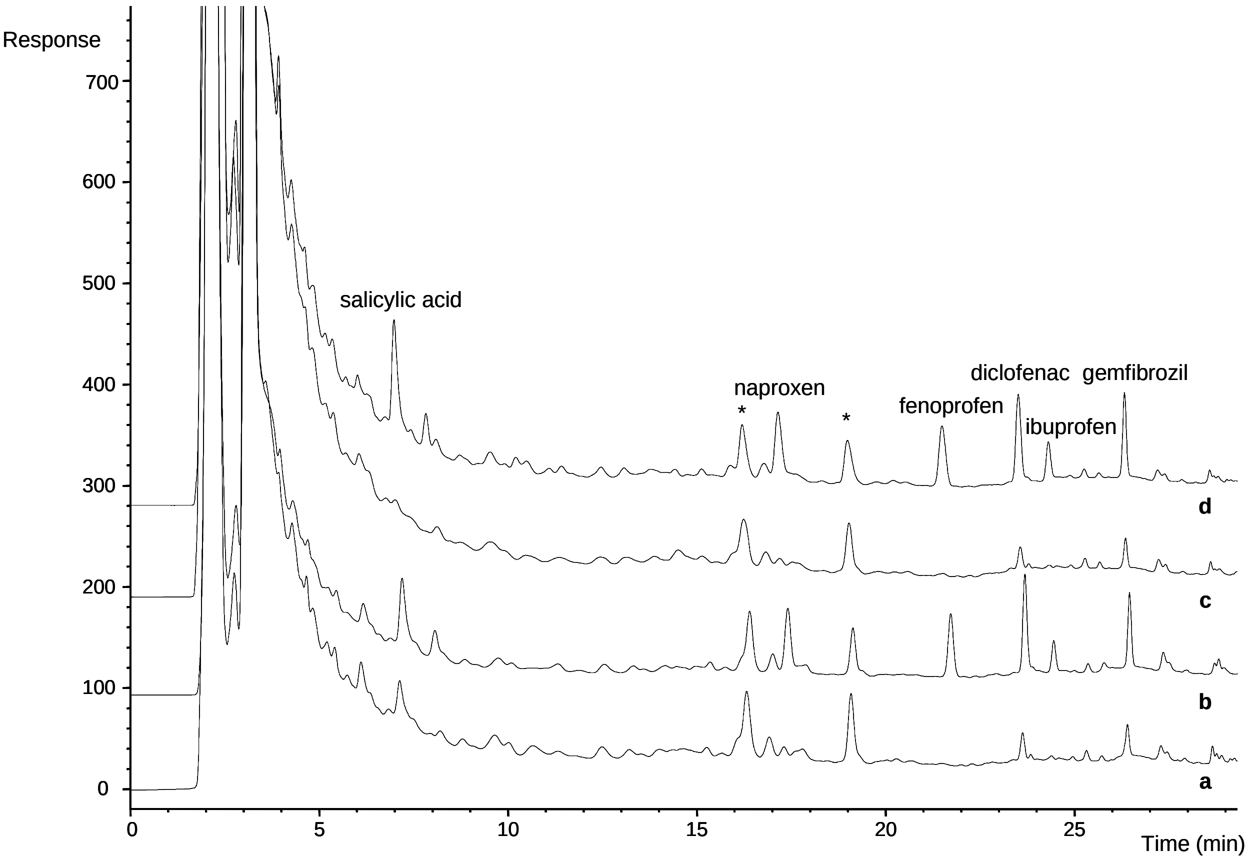

Figure 4

Table1

Table 1. Applications of SILP to SPE**.**

Application classification		SILP	Compounds	Sample	Ref.
ENVIRONMENTAL SAMPLES	ORGANIC COMPOUNDS	Silpr[MIM][PF_6]	12 sulphonylurea herbicides	Water and soil	[24]
		VBC-DVB[MIM][CF_3COO]	Acidic pharmaceuticals	River water and wastewater	[32]
		VBC-DVB[MIM][CF_3SO_3] VBC-DVB[MIM][BF_4]			[33]
		VBC-DVB[MIM][Cl]	Phenol	Waters	[41]
		Fe_3O_4Silpr[MIM][Cl]	Chlorophenols	Waters	[27]
		MIP-ViBuIM[Cl]	Chlorsulfuron	Surface water	[44]
		Silpr[IM][Cl] Silpr[MIM][Cl] Silpr[EMIM][Cl]	Organic acids, amines and aldehydes	Atmospheric	[39]
		Sil impregnated with [C_6MIM][Br] or [C_{12}MIM][Br]	Phthalates	Tap, canal. River and effluent water	[50]
	METALS	Sil[C_4MIM][PF_6]	Cd^{+2}	Tap and lake water	[29]
		PVC[MIM][Cl]	Cr^{+4}	Tap and snow water	[31]
		Sil[C_4MIM][Br]	Pb^{+2}	River water	[30]

MEDICINAL HERBS and PALNTS	Silpr[MIM][Cl]	Tanshinones	Salvia Miltiorrhiza Bunge	[34]
	MIP-Silpr[IM][Cl]			[47]
	MIP-VBC-DVB[IM][Cl] MIP-VBC-DVB[MIM][Cl] MIP-VBC-DVB[IM-COOH][Cl] MIP-VBC-DVB[IM-NH_2][Cl] MIP-VBC-DVB[IM-CN][Cl]			[42]
	GMA-EGDMA[MIM][Cl]	Caffeine Theophylline	Green tea	[36]
	VBC-DVB[MIN][Br]	Matrine Oxymetrine	*Sophora flavescens Ait*	[40]
	Silpr[IM][Cl] Silpr[MIM][Cl] Silpr[EIM][Cl] Silpr[C_4IM][Cl] Silpr[IM][BF_4] Silpr[IM][PF_6] Silpr[IM][Tf_2N]			[38]
	MAA-GMA-EGDMA[BIM][Cl]	β-Sitosterol	*Salicornia herbacea L.*	[52]
	MIP-AllEIM[Br] MIP-AllBuIM[Cl] MIP-AllHeIM[Cl] MIP-AllOcIM[Br]	Phenolic acids		[48]
	Silpr[EMIM][Cl]	Liquiritin Glycyrrhizin	Licorice	[26]

OTHERS	PVP-DVB[Bu][Cl]			[43]
	Silpr[IM][Cl] Silpr[MIM][Cl] Silpr[EMIM][Cl]	Lactic acid	Fermentation broth	[25]
	Sil-AgBF$_4$/SiO$_2$[IM][PF$_6$] Sil-AgNO$_3$/SiO$_2$[IM][PF$_6$] Sil-AgBF$_4$/SiO$_2$[IM][BF$_4$] Sil-AgNO$_3$/SiO$_2$[IM][BF$_4$]	Polyunsaturated fatty acid methyl esters	Fish oil	[35]
			Soy-derived biodiesel	[37]