6 Application of Novel Materials in Sample Treatment and Separation

Cleanup and Chromatographic Improvements

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CONTENTS

6.1 INTRODUCTION

At present, environmental analysis is focused on monitoring the source, fate, effects, and risks associated with contaminants, with a particular shift toward polar ones. Therefore, in recent years, one of the greatest challenges in analytical chemistry has been to develop fast and efficient methods for the trace analysis of target and nontarget organic compounds in complex matrices. In order to achieve this aim, hyphenated chromatography–MS techniques have already been well established for the determination of contaminants in environmental samples. However, one of the different challenges that remains is dealing with multiresidue methods in a reasonably short analysis time, as well as handling complex samples, that might occur in form of signal suppression or enhancement (known as the matrix effect [ME]) during ionization in MS-based detectors (Farré et al., 2012; Richardson, 2014).

Several strategies have been proposed to eliminate the problems resulting from the ME. The most effective strategy lies in sample cleanup, which helps to reduce interferents. However, the risk of analyte loss is still an issue that arises (Caban et al., 2012).

In this respect, significant progress has been achieved in the development of novel materials for sorptive extraction techniques, with selectivity becoming an additional requirement during its development. Of the different sorptive extraction techniques, SPE is the most widely used technique for liquid samples or liquid extracts. However, considerable progress has been made in solid-phase microextraction (SPME) or stir bar sorptive extraction (SBSE). The selectivity of a material in sample preparation can be toward a target analyte or a group of analytes with related properties. Hence, the target analyte or analytes can interact with the selective material, while matrix interferences or nonrelated analytes are less retained or even distinguished. To achieve selectivity, all parameters involved in the material development play an important role. In addition, the conditions used during the sample preparation process should be carefully optimized, enhancing their ability to support an effective cleanup (usually composed of organic solvent) without analyte losses.

Regarding chromatographic separation, liquid chromatography (LC) appears to be the most common approach since it is able to separate quite complicated mixtures of analytes with different properties, including polar analytes. Moreover, progress in LC column technology has been made in recent years in order to achieve multiresidue analysis and, in some cases, deal with the separation of highly polar compounds in a competitive manner (in terms of sensitivity gained) for subsequent MS detection.

Summing up, there have been significant advances over recent years in the development of materials for both sample preparation and chromatographic separation in environmental analysis. These two issues are addressed in the current chapter, with a particular emphasis on material development.

6.2 MATERIALS FOR SORPTIVE EXTRACTION TECHNIQUES

Since the early 1990s, one of the main areas of interest in sample preparation, and specifically in sorptive extraction techniques, has been the development of high-capacity materials. These materials have a greater specific surface area (e.g., hyper-cross-linked sorbents), higher hydrophilicity, or both (Fontanals et al., 2005). The enhanced morphological and chemical properties of these materials are suitable for the effective retention of the increasing number of moderately and highly polar organic contaminants present in the environment. However, they also retain interfering compounds. This situation has led to the emergence of selective materials.

Molecularly imprinted polymers (MIPs), as well as mixed-mode polymeric materials, can be categorized as selective materials. The common feature between MIPs and mixed-mode sorbents is their ability to retain the target analytes after an effective cleanup step that involves organic solvent (that washes out the matrix interferences), representing a great step forward in terms of sample preparation when dealing with complex samples.

MIPs and mixed-mode materials are described in the following two sections. In both cases, the fundamentals and preparation are firstly outlined briefly, and the main part is dedicated to the application of these selective materials in environmental fields and their improvements for cleaning up during the sample preparation step. Most of the application examples in this chapter relate to SPE, since it has become the most widely applied option for preconcentrating target analytes and cleaning the matrix with environmental samples. However, examples with other sorptive extraction techniques, such as SPME and SBSE, are also illustrated.

6.2.1 Molecularly Imprinted Polymers

The selectivity of MIPs arises from the synthetic procedure used, whereby functional monomers (that provide the functional groups that interact with the target compound) and a cross-linker agent (that enhances the morphological properties of the material) are polymerized in the presence of the target compound (template) that controls the sizes and functionality of the cavities during the polymerization. Once polymerization has taken place, the template is removed and binding sites are established with the shape, size, and functionalities that complement the target compound. The resulting MIPs are remarkably robust, relatively cheap, and straightforward to prepare. Therefore, their behavior imitates the interactions established by natural receptors to retain a target molecule selectively (e.g., antibody–antigen) but without the associated limitations on stability. In recent years, the field of MIPs has grown rapidly and become very broad, including a variety of fields, such as sensors, catalysis, and drug delivery, among others (Vasapollo et al., 2011; Schirhagl, 2013). However, ever since Sellergren (1994) first reported their use in SPE, the so-called molecularly imprinted solid-phase extraction (MISPE) is, by far, the most advanced technical application of MIPs. MISPE has been applied for a range of types of analytes from several different matrices (Beltran et al., 2010; Hu et al., 2013; Martín-Esteban, 2013). In this case, the applications of MISPE are reviewed as a part of a method that includes MS as the detection system in environmental analysis, in which multiresidue methods are also of great interest for determining as many analytes as possible in the same analysis. Thus, there is growing interest in MIPs that show cross-reactivity (the retention of target molecule, as well as other structurally related compounds). In view of this scenario, the application of MIPs in environmental analysis is shifting toward an effective cleanup step that reduces the ME. Table 6.1 illustrates some of the representative examples of this. For instance, ciprofloxacin was the template in the synthesis of MIP. However, in its application for the analysis of environmental waters, it was observed that this MIP was class selective for fluoroquinolones, but not for other antibiotics (Chen et al., 2010). With respect to the ME, in this study, different aqueous samples (river, lake, and influent and effluent sewage waters) were analyzed, with either water, methanol (MeOH), or acetonitrile (ACN) being used as a cleanup solvent. According to the results, ACN was the only solvent suitable for removing all the interferences and eliminating the ME while maintaining complete recoveries. The ME was also reduced in a study (Lopez-Nogueroles et al., 2013) in which a MIP for extracting nitro musk was used to analyze ultrapure, river, sea, and effluent sewage water samples. In addition, the ME obtained with this MIP was lower than that obtained with Oasis HLB (a highly retentive sorbent), which was attributed to the effective cleanup step consisting of 1 mL of MeOH/H_2O (80:20 v/v).

Another approach for enhancing class selectivity is multitemplate MIP, consisting of using more than one template during the synthesis. An MIP was developed using 16 PAHs as templates, and it showed superior recoveries than other MIPs for PAHs (Lai et al., 2004; Krupadam et al., 2010) when seawater samples were analyzed. However, the binding capacity of the MIP was still affected by matrices with a high organic and inorganic content (Song et al., 2012). Duan et al. (2013) adopted a similar strategy when they prepared a MIP using five pharmaceuticals as templates. The multitemplate MIP showed high selectivity for the templates, but not for the interferences. In addition, it showed good performance and negligible ME when MISPE was applied as a cleanup step in the extraction of 10 g of sediment sample.

Class-selective MIPs have recently been commercialized by Supelco, Biotage, and Polyintell for different groups of compounds such as estrogens (Affinilute MIP-Estrogens), nonsteroidal anti-inflammatory drugs (Affinilute MIP-NSAIDs or SupelMIP NSAIDs), amphetamines (SupelMIP Amphetamine), among others. However, only some of them have been applied in environmental analysis. For instance, SupelMIP NSAIDs were evaluated in the analysis of sewage water (Zorita et al., 2008b; Gilart et al., 2012), and the cleanup step performed was able to achieve effective cleaning that provided no significant signal recovery differences when analyzing complex samples and lower ME in comparison to Oasis HLB. These results are in agreement with Gros et al. (2008), whose study demonstrated a decrease in the ME provided by SupelMIP β-blocker in comparison to Oasis HLB for the extraction of β-blockers from sewage samples. Affinilute MIP-Estrogen outperformed a C18 cartridge in the determination of a group of estrogens from 100 mL of river and tap water, with the recoveries being acceptable and the ME insignificant (Lucci et al., 2011).

The selectivity provided by MIPs has led to the direct coupling of MISPE-MS and MISPE-MS/MS. Recently, SupelMIP NSAIDs directly coupled to MS/MS were applied in the detection and quantification of NSAIDs from 10 mL of influent and 50 mL of effluent sewage without chromatographic separation (Gilart et al., 2013). Even so, the signal suppression achieved (higher than 70%) was attributed to the absence of chromatographic separation in the method. Therefore, inclusion of chromatographic separation or enhancement of the selectivity of the MIP should be further evaluated to deal with the ME in the direct coupling of MISPE-MS/MS.

TABLE 6.1

In-House and Commercial Molecularly Imprinted Materials Applied in Extraction Techniques in Methods with MS Detection in Environmental Analysis

	Technique	Template	Class Selectivity	Sample	Washing Step	Matrix Effect	Ref.
In-house	On-line MISPE-LC-MS/MS	Cyclobarbital	Phenobarbital, amobarbital, and phenytoin	River	Aqueous ammonium acetate	n.d.	Hoshina et al. (2009)
	Off-line MISPE/LC-MS/MS	Carbamazepine	No	Sewage	5 mL water + 2 mL ACN	Low	Beltran et al. (2007)
	Off-line MISPE/LC-MS/MS	Ciprofloxacin	Fluoroquinolones	River and sewage	2 × 3 mL ACN	88%	Chen et al. (2010)
	Off-line MISPE/GC-MS/MS	16 PAHs	16 PAHs	Sea	2 mL MeOH/water (10:90)	Low	Song et al. (2012)
	Off-line MISPE/LC-MS/MS	NSAIDs	NSAIDs	Lake, sewage, and sediments	2 mL DCM/ACN (94:6)	No	Duan et al. (2013)
Commercial	Off-line MISPE/LC-MS/MS	Affinilute MIP-NSAIDs	15 drugs	Sewage	5 mL water + 5 mL ACN/water (40:60)	20–95%	Gilart et al. (2012)
	Off-line MISPE/MS/MS	Affinilute MIP-NSAIDs	NSAIDs	Sewage	5 mL water + 5 mL ACN/water (40:60)	50–100%	Gilart et al. (2013)
	Off-line MISPE/LC-MS/MS	Affinilute MIP-Estrogens	7 estrogens	River and tap	4 mL ACN/water (80:20) + 2 mL water	Low	Lucci et al. (2011)
	Off-line MISPE/LC-MS/MS	MIP4SPE-β-blockers	8 β-blockers	Sewage	2 mL water + 1 mL ACN + 1 mL DCM	Low	Gros et al. (2008)
In-house	MI-SPME-GC-MS	BDE-209	PBDE	Sewage	No	n.d.	Li et al. (2009)
	MI-SPME-GC-MS	DBP	Phthalates	Reservoir water	No	n.d.	He et al. (2010)
	MI-SPME-GC-MS	Ametryn	Triazines	Tap	No	n.d.	Djozan et al. (2009)
	MI-SBSE-LC-MS	(S)-citalopram	Enantioselective	Water	Dipping for 15 min in toluene/DCM (1:3)	n.d.	Gomez-Caballero et al. (2011)

Note: BDE-209, decabromodiphenylether; DBP, dibutylphthalate; DCM, dichloromethane; n.d., no data; NSAIDs, nonsteroidal anti-inflammatory drugs; PAHs, polyaromatic hydrocarbons; PBDE, polybromodiphenylether.

Extraction of organic contaminants from solid samples, mainly sludge and soil, has been performed in recent years, primarily by ultrasonic extraction and pressurized liquid extraction (PLE). Due to the complexity of the matrices extracted, these strategies often also lead to the extraction of unwanted interferences, which are usually removed using an external cleanup step based on SPE. As mentioned previously, the effectiveness of this cleanup step is quite dependent on the sorbent used in SPE. For instance, 10 mL aliquots of PLE extracts from soil samples were further purified using a commercial MIP selective for triazines. The recovery results obtained in this procedure were equivalent to the recoveries obtained in ultrapure water, which might imply, in this case, that the MIP worked for selectively retaining the target analytes despite the presence of interferences. Subsequently, the method based on PLE/MISPE/LC-MS/MS was applied to analyze different types of environmental samples such as sludge-fertilized agricultural soil and sludge samples, and some triazines were found at nanogram per gram concentration levels (García-Galán et al., 2010).

Another strategy used in PLE involves performing internal cleanup with the addition of sorptive material into the cell so that the sample matrix components are adsorbed to the material while the targets are being extracted. This strategy is more straightforward (i.e., it is based on a single extraction step rather than two steps involving PLE followed by SPE). However, to date, its application has been investigated only with classical sorbents, such as alumina, Florisil, and silica-based sorbents, which sometimes helps to clean the extracts from the solid matrix (Runnqvist et al., 2010).

Some very recent studies also used a quick, easy, cheap, effective, rugged, and safe (QuEChERS) technique for the extraction of environmental solid samples (Salvia et al., 2012; Berlioz-Barbier et al., 2014), although this extraction technique was already well established for food samples. In that case, the cleanup step of the QuEChERS extract is performed by dispersive SPE (dSPE), which differs from SPE as the materials are placed in an Eppendorf tube and put into contact with the sample and analytes by means of agitation. To date, the materials used in dSPE include classical sorbents such as primary secondary amine, graphitized carbon black, alumina, and magnesium sulfate and their combinations in different proportions, as they are commercially available, together with the kits for QuEChERS extraction (Wilkowska and Biziuk, 2011). Thus, the field is open to exploit more selective materials, such as MIPs, for cleaning extracts from solid samples.

MIPs have also been applied in a variant of SPE known as magnetic solid-phase extraction, in which typically magnetic nanoparticles (MNPs) are added to sample matrices containing target analytes. After the extraction procedure, the MNPs are easily isolated from the solution by applying an external magnetic field, which simplifies and accelerates the isolation process. In recent years, a significant number of functionalized MNPs have been prepared and recently reviewed by Xie et al. (2014), which also included MIPs. For example, Xia et al. (2013) prepared an MIP coated with MNPs that are selective for a group of structurally similar estrogens, of which the recognition availability was not significantly affected by the presence of matrix interferences. Similarly, Chen et al. (2013) reported a signal enhancement/reduction of around 20–30% for the target analytes (sulfonamides and their acetylated metabolites) when 500 mL of lake or river water was percolated through a magnetic MIP, in comparison to Oasis HLB.

SPME and SBSE are based on establishing a single partitioning equilibrium of analytes between the sample and the solid material (coating). The SPME format is a material coating on an extraction fiber, while the SBSE format is a material that coats a magnetic stir bar. Thus, these formats restrict the morphology and chemistry of the coatings to those that can be deposited onto the fiber and stir bar, respectively. Originally, these techniques were based on polydimethylsiloxane as a coating, but some alternative (more polar) materials have become commercially available and prepared in-house for SPME and, recently, for SBSE. In a trend similar to SPE materials, molecularly imprinted polymer-coated solid-phase microextraction (MI-SPME) fibers and stir bar sorptive extraction molecularly imprinted polymer coatings (MI-SBSE) have been introduced and applied in several different fields (Xu et al., 2013; Gilart et al., 2014a). With respect to environmental field analysis, different MI-SPME coatings have been prepared in-house by using sol–gel (Li et al., 2009) or monolithic (Turiel et al., 2007; Djozan et al., 2009; Tan et al., 2009; He et al., 2010) approaches to extract different analytes. However, only a few of them have been included in a method that used MS for detection, none of which evaluated the ME or even included a cleanup step in the procedure (Table 6.1 provides the details). Only two MI-SPME/LC-diode array detection methods for the determination of bisphenol A (Tan et al., 2009) and triazines (Turiel et al., 2007) included a cleanup step, based on ACN/H_2O (25:75 v/v) and toluene, respectively. MI-SBSE coatings have also been prepared using sol–gel (Zhu et al., 2006) or monolithic technology (Hu et al., 2010; Yang et al., 2010; Chen et al., 2011; Gomez-Caballero et al., 2011; Hu et al., 2011; Sheng et al., 2012), in which the MIP was first chemically bonded to a glass bar where the polymer grew afterward. Similarly to MI-SPME, only one MI-SBSE coating selective for citalopram followed by LC-MS included a cleanup step, consisting of dipping the stir bar for 15 min in a solution of toluene/dichloromethane (3:1 v/v). However, the best signal was attained when no cleaning was performed, which was attributed to the existence of nonspecific interactions with the polymer backbone (Gomez-Caballero et al., 2011). Other authors demonstrated the selectivity of the coating by adding nonstructurally related compounds and evaluating their affinity. In all cases, though, they were highly susceptible to interfering compounds when analyzing complex matrices. In view of these outcomes with MI-SPME and MI-SBSE coatings, further research into selective coating development is highly advisable.

The definition "diode array detection" was used instead of "DAD." Please check if the provided definition is correct.

6.2.2 Mixed-Mode Polymeric Materials

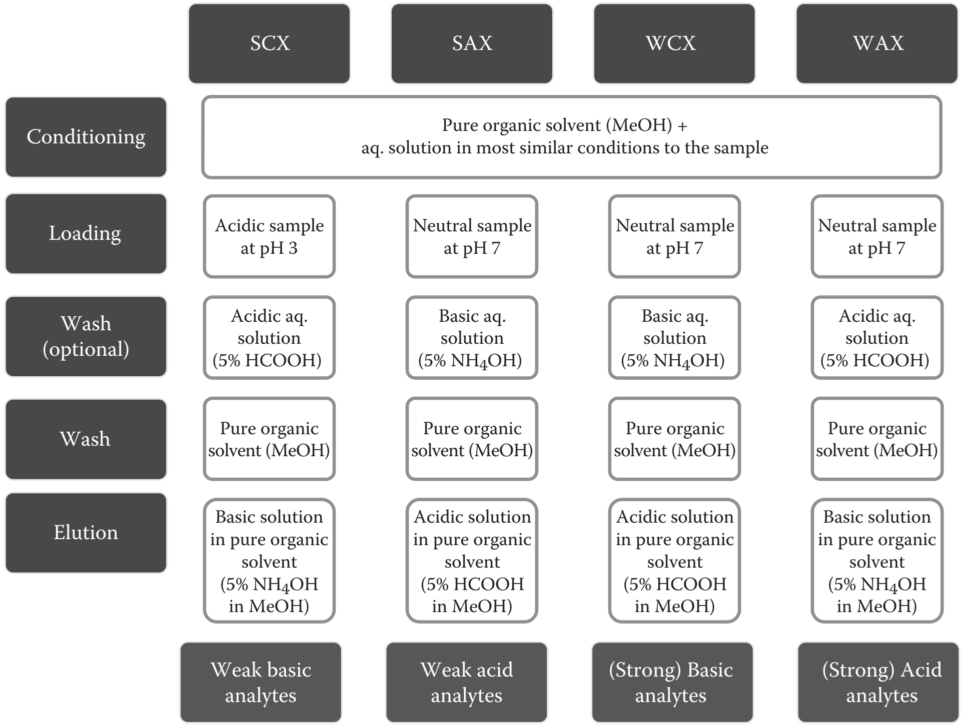
Ion-exchange sorbents are a good alternative for extracting ionic or ionizable compounds, since they are based on ionic interactions. The first ion-exchange sorbents were silica based and chemically modified with an ion-exchange group. Over the last decade, mixed-mode polymeric sorbents have been developed, which combine a polymeric skeleton with ion-exchange groups. Thus, these mixed-mode sorbents display ion-exchange interactions (specific) with the charged analytes and reversed-phase interactions (nonspecific) with the uncharged ones, and they can be classified into four groups (combinations of cationic and anionic, strong and weak) depending upon the ion-exchange group that modifies the polymer skeleton. The main difference between the strong and weak ion-exchange materials relates to the chargeability of the materials. Thus, strong ion-exchange materials always remain charged, whereas in the case of weak ion-exchange materials, they may be charged or not depending on the pH. Therefore, it is important to select the suitable material and follow a suitable SPE protocol to enhance the ionic interactions with the analytes of interest. Figure 6.1 summarizes the recommended protocol for each of the four types of mixed-mode materials. The specific interactions (controlled by the pH in the loading and elution step), as well as the effective cleanup (which always involves adding pure organic solvent), are the key to achieving selectivity and getting rid of interferences with mixed-mode materials.

In contrast to MIPs, to the best of our knowledge, mixed-mode materials have been applied only as SPE sorbents. Therefore, all the details hereafter relate to SPE. In SPE, despite being relatively new, mixed-mode materials have been applied in various fields to extract different types of analytes in a selective manner from complex matrices, such as environmental, foodstuff, and biological samples, among others (Fontanals et al., 2010, 2014a). Due to the widespread use of these materials, several mixed-mode materials are commercially available. Figure 6.2 classifies the commercially available mixed-mode materials, along with their manufacturers, into the four groups. In order to improve the retention features, our research group has pioneered the preparation of mixed-mode hyper-cross-linked polymers (with their own high specific surface area and microporous structure that lead to enhanced reversed-phase interactions). Figure 6.2 also summarizes these in-house mixed-mode materials.

Table 6.2 gives an overview of the applications in which mixed-mode materials are included in a method with MS detection to analyze environmental samples. For instance, Oasis mixed cation-exchange (MCX) sorbent is widely applied to the extraction of drugs of abuse (since most of them are basic analytes and are retained ionically with this strong cation-exchange [SCX] sorbent). However, there are differences in the SPE protocol and its cleanup step and, therefore, in the ME encountered.

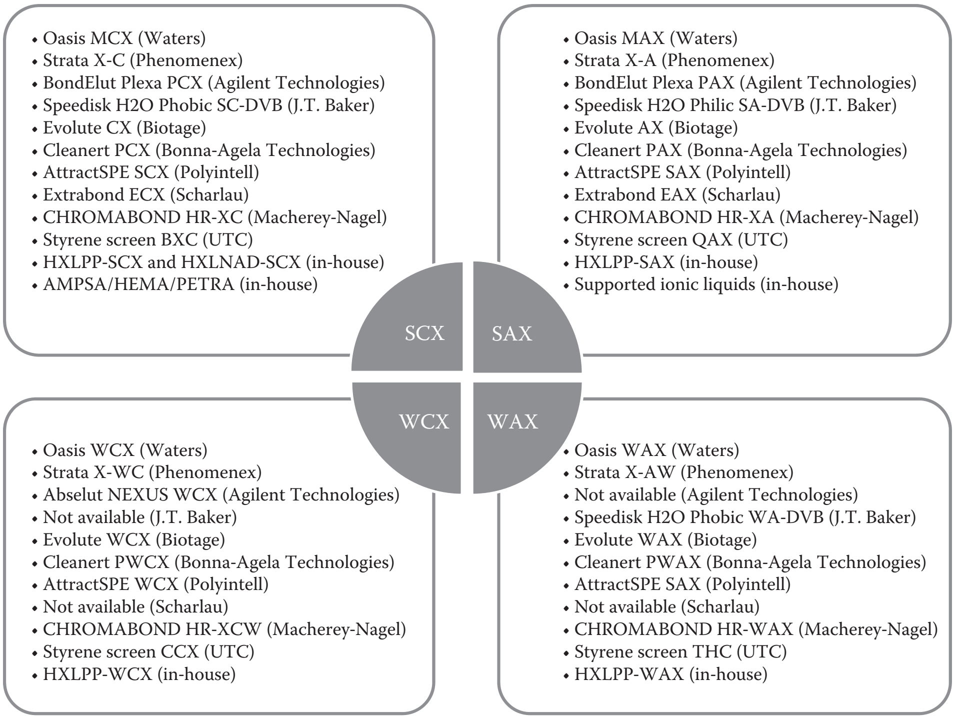
Please verify the definition provided for MCX.

Please verify the definition provided for SCX.



	SCX	SAX	WCX	WAX
Conditioning	Pure organic solvent (MeOH) + aq. solution in most similar conditions to the sample			
Loading	Acidic sample at pH 3	Neutral sample at pH 7	Neutral sample at pH 7	Neutral sample at pH 7
Wash (optional)	Acidic aq. solution (5% HCOOH)	Basic aq. solution (5% NH_4OH)	Basic aq. solution (5% NH_4OH)	Acidic aq. solution (5% HCOOH)
Wash	Pure organic solvent (MeOH)	Pure organic solvent (MeOH)	Pure organic solvent (MeOH)	Pure organic solvent (MeOH)
Elution	Basic solution in pure organic solvent (5% NH_4OH in MeOH)	Acidic solution in pure organic solvent (5% HCOOH in MeOH)	Acidic solution in pure organic solvent (5% HCOOH in MeOH)	Basic solution in pure organic solvent (5% NH_4OH in MeOH)
	Weak basic analytes	Weak acid analytes	(Strong) Basic analytes	(Strong) Acid analytes

FIGURE 6.1 SPE protocols and type of analytes recommended for each type of mixed-mode ion-exchange polymeric sorbent. In brackets, an example of most usual conditions.



- Oasis MCX (Waters)
- Strata X-C (Phenomenex)
- BondElut Plexa PCX (Agilent Technologies)
- Speedisk H2O Phobic SC-DVB (J.T. Baker)
- Evolute CX (Biotage)
- Cleanert PCX (Bonna-Agela Technologies)
- AttractSPE SCX (Polyintell)
- Extrabond ECX (Scharlau)
- CHROMABOND HR-XC (Macherey-Nagel)
- Styrene screen BXC (UTC)
- HXLPP-SCX and HXLNAD-SCX (in-house)
- AMPSA/HEMA/PETRA (in-house)

- Oasis MAX (Waters)
- Strata X-A (Phenomenex)
- BondElut Plexa PAX (Agilent Technologies)
- Speedisk H2O Philic SA-DVB (J.T. Baker)
- Evolute AX (Biotage)
- Cleanert PAX (Bonna-Agela Technologies)
- AttractSPE SAX (Polyintell)
- Extrabond EAX (Scharlau)
- CHROMABOND HR-XA (Macherey-Nagel)
- Styrene screen QAX (UTC)
- HXLPP-SAX (in-house)
- Supported ionic liquids (in-house)

- Oasis WCX (Waters)
- Strata X-WC (Phenomenex)
- Abselut NEXUS WCX (Agilent Technologies)
- Not available (J.T. Baker)
- Evolute WCX (Biotage)
- Cleanert PWCX (Bonna-Agela Technologies)
- AttractSPE WCX (Polyintell)
- Not available (Scharlau)
- CHROMABOND HR-XCW (Macherey-Nagel)
- Styrene screen CCX (UTC)
- HXLPP-WCX (in-house)

- Oasis WAX (Waters)
- Strata X-AW (Phenomenex)
- Not available (Agilent Technologies)
- Speedisk H2O Phobic WA-DVB (J.T. Baker)
- Evolute WAX (Biotage)
- Cleanert PWAX (Bonna-Agela Technologies)
- AttractSPE SAX (Polyintell)
- Not available (Scharlau)
- CHROMABOND HR-WAX (Macherey-Nagel)
- Styrene screen THC (UTC)
- HXLPP-WAX (in-house)

FIGURE 6.2 Classification of the mixed-mode polymeric sorbents commercially available and in-house prepared.

Please provide the significance of superscript letters found in Table 6.2.

TABLE 6.2
Commercial and In-House Mixed-Mode Polymeric Sorbents Applied in SPE in Methods with MS Detection in Environmental Analysis

	Sorbent	Technique	Analytes	Sample	Washing Step	Matrix Effect	Ref.
SCX	Oasis MCX	Off-line SPE/HILIC-MS/MS	Neurotoxin	Sewage	2 mL MeOH	n.d.	Combes et al. (2013)
	Oasis MCX	Off-line SPE/LC-MS/MS	Herbicides	Soil	10 mL MeOH	n.d.	Nanita et al. (2008)
	Strata-X-C	Off-line SPE/LC-MS/MS	Pharmaceuticals	Sewage	3 mL basic MeOH	No	Van De Steene et al. (2006)
	Oasis MCX	Off-line SPE/HILIC-MS/MS	Illicit drugs	Sewage	Water	High	Gheorghe et al. (2008); van Nuijs et al. (2009)
	Tandem Oasis MCX + HLB	Off-line SPE/LC-MS/MS	Illicit drugs	Sewage	Aqueous + MeOH	Low	Baker and Kasprzyk-Hordern (2011); González-Mariño et al. (2011)
	AMPSA/HEMA/PETRA	Off-line SPE/LC-MS/MS	Drugs	Sewage	5 mL MeOH	Low	Gilart et al. (2014b)
	HXLPP-SCX	Off-line SPE/LC-MS/MS	Drugs	Sewage	5 mL MeOH	Low	Fontanals et al. (2014b)
SAX	Oasis MAX	Off-line SPE/LC-MS/MS	Organophosphorus	Sewage	10 mL water	Low	García-López et al. (2010)
	Tandem Oasis MAX + HLB	Off-line SPE/LC-MS/MS	Benzotriazoles	River and sewage	No	Low	Carpinteiro et al. (2012)
	Tandem Oasis MAX + Plexa SAX	Off-line SPE/LC-MS/MS	Herbicides	Storm water	No	n.d.	Zhang et al. (2014)
WCX	Oasis WCX	Off-line SPE/LC-MS/MS	Fluoroquinolones	Sewage	5 mL[a] or 2 mL[b] MeOH	Low	Lee et al. (2007b)[a] Zorita et al. (2008a)[b]
	Strata-X-CW	Off-line SPE/LC-MS/MS	Therapeutic drugs	River	No	Cleaner extracts	Scheurer et al. (2009)
WAX	Oasis WAX	Off-line SPE/LC-MS	Estrogens	River sediments	3 mL 5% NH_4OH in water/MeOH (85:15) + 3 mL 5% NH_4OH in water/THF (80:20)	n.d.	Matejicek et al. (2007)
	Oasis WAX	Off-line SPE/LC-MS	Fluorescence whiting agents	Water and biota	4 mL MeOH	n.d.	Chen et al. (2006); Taniyasu et al. (2005)

Note: n.d., no data.

Thus, some authors have adopted a cleanup step based on aqueous solution (Gheorghe et al., 2008; Bijlsma et al., 2009; van Nuijs et al., 2009; Pedrouzo et al., 2011), while others have included a methanolic solution in this step (Baker and Kasprzyk-Hordern, 2011; González-Mariño et al., 2011). To a reasonable extent, the ME was lower when the cleanup step was based on MeOH. However, some authors did not include it as the analytes retained by reversed-phase interactions were eluted with MeOH (Pedrouzo et al., 2011). González-Mariño et al. (2011) compared the ME that resulted from Oasis HLB and Oasis MCX with and without the cleanup step with MeOH when a group of drugs of abuse was extracted from effluent sewage. Figure 6.3 represents the % ME (% ME = 100% means that no effect was encountered) for each of the studied analytes. As can be seen in this figure, when the cleanup step was not included with Oasis MCX or Oasis HLB (cases B and C, respectively), the ME was as low as 10% in the case of morphine; meanwhile, when it was included (case A), the MEs were all above 60%. In view of these results, Oasis MCX with methanolic cleanup was the chosen extraction method in this study. In any case, these studies further dealt with the ME by adding isotopically labeled internal or surrogate standard (Van De Steene et al., 2006; Bijlsma et al., 2009; Baker and Kasprzyk-Hordern, 2011; González-Mariño et al., 2011; Pedrouzo et al., 2011; Wilkowska and Biziuk, 2011). However, in more complex samples such as influent sewage, the samples were needed to be diluted up to five times to quantify the analytes properly if the cleanup step was not performed (Lee et al., 2007a; Bijlsma et al., 2009).

If "PETRA" is an abbreviation, please define at first mention.

The definition "divinylbenzene" was used instead of "DVB." Please check if the provided definition is correct.

Four in-house SCX polymers (namely, AMPSA/hydroxyethylmethacrylate [HEMA]/PETRA, sulfonated HEMA/divinylbenzene, and sulfonated hyper-cross-linked precursor particles obtained by precipitation polymerization [HXLPP-SCX] or by nonaqueous dispersion polymerization [HXLNAD-SCX]) were also evaluated in terms of ME and recovery when a group of therapeutic and illicit drugs was determined by SPE/LC-MS/MS from influent and effluent sewage samples. The low ME encountered in these studies was due to the cleanup step performed (with 5 mL of MeOH), which simplifies the complexity of the matrix (Fontanals et al., 2014b; Gilart et al., 2014b).

Please verify the definition provided for MAX.

Oasis mixed-anion exchange (MAX) sorbent was compared to Oasis HLB for the extraction of a group of benzotriazoles and benzothiazoles from aqueous matrices, which were further determined by LC-MS/MS. Both sorbents were used with the same SPE protocol, which did not contain a cleanup step. However, Oasis MAX was selected since it provided clear extracts with lower complexity, which is attributed to the retention of the acidic interferences in the matrix with the amino moieties existing in the structure of the MAX sorbent (Carpinteiro et al., 2012). Zhang et al. (2014) tested Oasis MAX and Bond Elut PAX in the extraction of a broad group of herbicides from environmental waters. Both sorbents enabled the complete extraction of all of the herbicides as neutral, and basic compounds

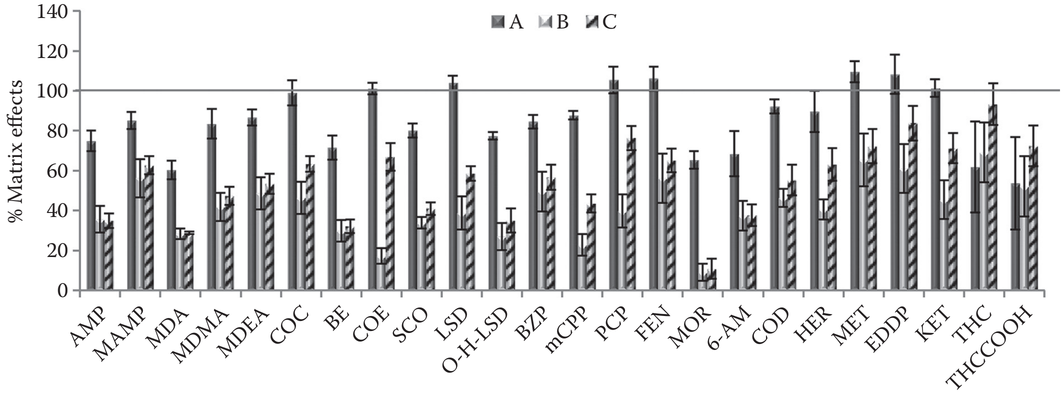


FIGURE 6.3 Percentage of ME in effluent wastewater depending on the SPE protocol: (A) Oasis MCX including cleanup step; (B) Oasis MCX, without cleanup step; and (C) Oasis HLB, without cleanup step. (Reprinted with permission from González-Mariño et al. (2011), 1708–1717. Copyright 2011 American Chemical Society.)

were eluted first with the methanolic fraction (the fraction intended to be the cleanup step), and the acidic compounds were subsequently eluted with acidified MeOH. Therefore, a cleanup step that gets rid of the undesirable compounds was, in fact, not included in this protocol. Nonetheless, the authors found that the ME can be tackled depending on the type and percentage of acid incorporated during the elution step. Thus, of the three eluents tested (1.5% trifluoroacetic acid [TFA], 2% TFA, and 5% HCOOH in MeOH), it was concluded that using TFA as an acidic additive may induce the elution of matrix interferences and the subsequent ion suppression in the LC-MS/MS system. Therefore, 5% HCOOH in MeOH was selected to avoid the elution of matrix interferences as much as possible.

Please verify the definition provided for WCX.

Oasis weak cation-exchange (WCX) sorbent was selected over Oasis HLB and Oasis MCX due to the requirements of high recovery and cleanness of the extract in two studies (Lee et al., 2007b; Zorita et al., 2008a) for the extraction of a group of fluoroquinolones from sewage. Oasis WCX was also tested in the online SPE-LC-MS approach to determine a group of illicit drugs from sewage (Fontanals et al., 2013). This study reported a reduction in the ME when the mixed-mode sorbent involved an effective cleanup step based on MeOH.

With respect to the Strata-X brand, few applications have been reported, especially in environmental analysis. For instance, Strata-X-WC was used in the extraction of a group of antidiabetic drugs from environmental waters by LC-MS/MS (Scheurer et al., 2009). The complete recoveries and the absence of the ME were attributed to the selectivity of the mixed-mode sorbent, as well as the small volume of the sample percolated (10 mL). Strata-X-AW was integrated into a passive sampling device that effectively extracted a wider group of perfluorinated alkyl carboxylates and sulfonates from water than the corresponding nonmixed-mode sorbent (Kaserzon et al., 2012).

Please verify the definition provided for WAX.

Oasis weak anion-exchange (WAX) sorbent was compared to Oasis HLB and Oasis MAX for the determination of estrogens and their conjugates. The results were similar for the three sorbents when the targets were extracted from ultrapure water samples. However, Oasis WAX showed the best results when the targets were extracted from river sediments, which might be attributed to the effectiveness of the cleanup step performed (Matejicek et al., 2007).

Other studies compared the performance of the four types of mixed-mode sorbents (i.e., Oasis MCX, MAX, WCX, and WAX) for the determination of basic/neutral therapeutic and illicit drugs in surface and river waters. Oasis MCX was selected since it provided the best recovery. However, as the cleanup step was based only on aqueous solution, the ME remained, even though several internal and surrogate standards were added (Kasprzyk-Hordern et al., 2007). Oasis MCX, Oasis HLB, and Supel MIP-Amphetamine (commercial MIP selective for amphetamines) were also compared. Regarding the ME, MIP clearly provided better performance than any of the Oasis sorbents, which is the reason why it was selected (González-Mariño et al., 2009). Thus, the choice of one material or another in sample preparation is not straightforward, and conducting a series of preliminary experiments is always recommended before selection.

In view of the suitable results obtained with the mixed-mode materials, they should be applied in the near future to other sorptive extraction techniques, such as SPME or SBSE, to further enhance selectivity in sample preparation.

6.3 MATERIALS FOR STATIONARY PHASES

The developments of materials for stationary phases (SPs) can be divided into two categories: (1) the particle technology approach to achieving fast separation while maintaining resolution and separation efficiency to deal with high-throughput and multiresidue methods and (2) particle chemistry designed for challenging separations of most polar compounds.

6.3.1 Fast and Highly Efficient Separations

In the last few decades, three approaches have been developed and commercialized to improve throughput and efficiency in LC: the use of monolithic columns, the use of ultrahigh-pressure liquid chromatography (UHPLC) using sub-2 μm particle columns, and the use of superficially porous particles and high-temperature liquid chromatography (HTLC). Except HTLC, improvements in throughput and efficiency in all of the cases depend on the column material. In the case of monolithic columns, their main features result in low backpressure and good mass transfer that enable higher flow rates (up to 10 mL min^{-1}) than particle-packed columns, which results in enhanced throughput. However, these high flow rates limit its connection to MS detectors. These limitations have influenced their application, and only a few studies have applied them in environmental analysis, which, to the best of our knowledge, aimed to evaluate the chromatographic parameters that resulted from the monolithic column (Ghanem and Ikegami, 2011; Kurganov, 2013; Urban and Jandera, 2013). The other two approaches concerning particle technology have been more applied in environmental field, and they are described in the following two sections.

6.3.1.1 Sub-2 μm Particles

The benefits of using smaller particle sizes in the performance of LC were previously reported by Knox and Saleem (1969) some time ago. Later, in 2004, after solving some technical problems, columns packed with totally porous sub-2 μm particles became commercially available. With sub-2 μm particle technology, the throughput results in a ninefold increase, while maintaining a similar kinetic efficiency to the conventional 5 μm particle packing. However, reducing the particle size by a factor of 3 results in an increase in the backpressure by a factor of 27 (600–1000 bar), which makes it unfeasible to work with a conventional LC instrument. To address this problem, UHPLC instruments emerged that can withstand pressures beyond 600 bar. In addition, the UHPLC system must be designed with the ability to work with columns of reduced diameter (up to 2.1 mm internal diameter [i.d.]) in ultrahigh modes, so that the frictional heating and/or the solvent compressibility is limited.

“i.d.” was provided as the definition for “internal diameter.” Please check and amend as necessary.

Another feasibility issue with the UHPLC-MS coupling is the elevated acquisition rate, as very narrow peaks are produced (2–4 s wide on average) in UHPLC compared to those in LC (10 s on average). Regarding quantitative proposals, at least 10–15 acquisition points per peak are recommended to define the chromatographic peak correctly and achieve suitable performance (Rodriguez-Aller et al., 2013). In this context, the determination of 37 multiclass pesticides in wastewater was performed using UHPLC coupled with a fast-acquisition QqQ mass analyzer, which allowed decreasing dwell times or ionization switching time without apparent sensitivity losses. In this study, it was possible to acquire three selected reaction monitoring (SRM) transitions per compound at a dwell time of 10 ms, with a total of 117 SRM transitions acquired, distributed along eight functions in order to reach an acceptable data point rate for UHPLC peaks (5–7 s), in the chromatographic analysis time of 10 min (Barco-Bonilla et al., 2010).

Despite the previously mentioned limitations, nowadays, a wide variety of columns packed with totally porous sub-2 μm particles (more than 100 different columns from about 15 suppliers) are commercially available (Fekete et al., 2014). These have led to numerous applications in different fields wherein UHPLC-MS has been used. Of these, Table 6.3 summarizes some representative examples of the inclusion of sub-2 μm particle-packed columns in environmental fields. It should be noted that, although there are many methods that use UHPLC instruments described in the literature, most of them used conventional columns or chromatographic conditions not pertinent of ultrafast separations. Therefore, only applications that, in fact, used ultrafast separation conditions were focused on. For instance, Kasprzyk-Hordern et al. (2007) selected an Acquity ethylene-bridged hybrid (BEH) C18 column (100 mm × 1 mm, 1.7 μm) that enables high-speed analysis (15 min) and low mobile phase rates (0.07 mL min^{-1}) in the separation of 28 pharmaceutical compounds. Moreover, it enabled direct introduction into the ion source from LC without the need for splitting. The same author selected the same column but longer (150 mm × 1 mm, 1.7 μm) for the separation of 65 compounds (illicit drugs, their metabolites, and internal standards) in less than 23.1 min using a flow rate of 0.04 mL min^{-1} (Baker and Kasprzyk-Hordern, 2011). Gros et al. (2013) used a sub-2 μm column in the determination of a group of 53 residue antibiotics and some of their metabolites in

TABLE 6.3
Examples of Applications of Columns Packed with Sub-2 μm Particles in Environmental Analysis

Column	Instrument	Analytes	Sample	Analysis Time	Ref.
Acquity HSS T3 (50 mm × 2.1 mm, 1.8 μm) Acquity BEH C18 (50 mm × 2.1 mm, 1.7 μm)	UHPLC-QqLIT	81 pharmaceuticals and metabolites	Sewage and river	6 min	Gros et al. (2012)
Acquity BEH C18 (50 mm × 2.1 mm, 1.7 μm)	UHPLC-QqLIT	55 pharmaceuticals and hormones	Sewage	9 min	Huerta-Fontela et al. (2010)
Acquity HSS T3 (50 mm × 2.1 mm, 1.8 μm)	UHPLC-QqLIT	53 antibiotics and their metabolites	Sewage, hospital sewage, and river	2.5 min	Gros et al. (2013)
Agilent Zorbax Eclipse PAHs (50 mm × 2.1 mm, 1.8 μm)	UHPLC-QqQ	16 PAHs	Water	–	Cai et al. (2009)
Acquity BEH C18 (100 mm × 1 mm, 1.7 μm)	UHPLC-QqQ	28 pharmaceuticals and illicit drugs	River	15.5 min	Kasprzyk-Hordern et al. (2007)
Acquity BEH C18 (150 mm × 1 mm, 1.7 μm)	UHPLC-QqQ	65 illicit drugs and metabolites	Sewage	23.1 min	Baker and Kasprzyk-Hordern (2011)
Acquity HSS T3 (100 mm × 2.1 mm, 1.8 μm)	UHPLC-QqQ	37 pesticides	Sewage and surface water	10 min	Marín et al. (2009)
Acquity BEH C18 (100 mm × 1 mm, 1.7 μm)	UHPLC-QqQ	43 polar pesticides	Sewage	9 min	Barco-Bonilla et al. (2010)

“quadrupole linear ion trap” was provided as the definition for “QqLIT.” Please check and amend as necessary.

environmental waters with UHPLC–quadrupole linear ion trap (QqLIT). The authors claimed that higher resolution and sensitivities and reduced analysis time were achieved with this determination when using the UHPLC system. In addition, they further justified its selection by the reduction in the ME produced by isobaric coeluting sample compounds, thanks to the enhanced chromatographic resolving power offered by UHPLC in comparison to conventional LC.

6.3.1.2 Superficially Porous Particles

The most recent approach to improving chromatographic performance is the use of superficially porous particles, also called fused-core particles or core–shell particles. They consist of a solid fused core and a thin porous shell. Today, these columns are commercialized by different suppliers, with particle dimensions differing slightly. In chronological order, released in 2007, HALO (Advanced Material Technology) is a column packed with 2.7 µm superficially porous particles that consist of 1.7 µm of silica core particles coated with 0.5 µm of porous silica. Poroshell (Agilent Technologies) and Ascentis Express (Sigma-Aldrich) have the same dimensions, and very recently, Ascentis Express has also been presented in a 5 µm particle size format. However, in the case of this larger particle, there is no information available about the dimensions of the core and the shell. In 2009, Phenomenex marketed Kinetex columns with core–shell technology in the 2.6 µm particle size and later in the 1.7 or 1.3 µm formats. They consist, respectively, of 1.9, 1.24, and 0.9 µm and a nonporous core layered with 0.35, 0.23, and 0.2 µm porous shells. In a similar fashion, in 2011, other vendors released similar sub-3 µm superficially porous particles, such as Accucore (Thermofisher), Cortects (Waters), Nucleoshell (Macherey-Nagel), and Sunshell (Nacalia).

The solid fused core of silica, which is impenetrable to the analytes, results in a faster mass transfer, shorter diffusion path, and less band broadening. These properties enable the columns to exhibit efficiencies and throughput similar to the sub-2 µm particles. In addition, the more ordered particle distribution also leads to reasonable column pressures (operates at half or third pressure compared to fully porous sub-2 µm particles), without the need for resourcing UHPLC systems (Guillarme et al., 2010). In this context, the column manufacturers advertised that UHPLC performance can be obtained in LC when using these superficially porous particles. However, this assumption was brought into question by Fekete et al. (2014), who considered different cases and drew the conclusion that only superficially porous particles packed in columns of 4.6 mm i.d. can be applied without loss in column efficiency in conventional LC systems, and in the case of columns with 3 and 2.1 mm i.d., the LC systems must be optimized.

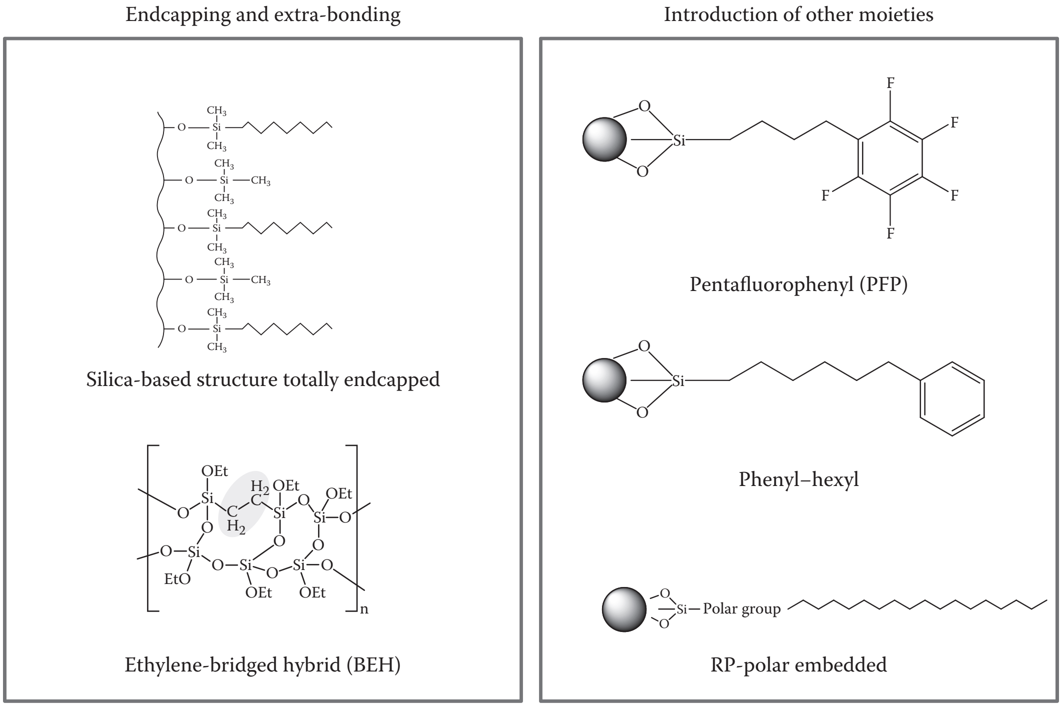
In any case, applications of superficially porous particles are expanding rapidly, and this expansion is expected to be much faster in the near future as a range of chemistry support products have recently become available. Regarding environmental analysis, the number of examples is still limited. For example, Kinetex C18 (100 mm × 2.1 mm, 2.6 µm) was selected for the determination of 15 pharmaceuticals and four of their metabolites in sewage because it provided narrow peaks that improved sensitivity with an analysis time of 9 min (Tarcomnicu et al., 2011). Gilart et al. (2014b) also used an Ascentis Express C18 column (100 mm × 4.6 mm, 2.7 µm) for the separation of a group of 17 illicit and therapeutic drugs that also attained narrow peaks. However, the analysis time was 16 min, which can presumably be attributed to the low flow rate applied in a column with such a large inner diameter.

6.3.2 CHEMISTRY OF STATIONARY PHASES

Although reversed-phase liquid chromatography (RPLC) with alkyl-bonded (C18 and C8) silica is the most common SP in environmental analysis, when dealing with challenging separations, other SPs might be helpful and have been increasingly applied in recent years, such as polar-embedded reversed phase, fluorinated reversed phase, phenyl–hexyl, and also those used in hydrophilic interaction liquid chromatography (HILIC). It is also worth mentioning that alkylsiloxane-bonded silica materials have been improved in recent years in order to enhance endcapping or to improve the bonding of the alkyl groups, among others, resulting in better LC performance. Figure 6.4 groups these improvements in SPs and displays their chemical structure.

Waters commercializes Acquity BEH columns based on BEH technology, which enables its application across a much wider pH range (1–12) and also provides versatile and robust separation due to the intrinsic chemical stability. Later, Acquity HSS T3 became available, which uses a trifunctional C18 alkyl phase bonded at a ligand density together with the T3 endcapping process, which is much more effective than traditional trimethylsilane (TMS) endcapping. This unique combination of bonding and endcapping provides superior polar compound retention and aqueous mobile phase compatibility (Gros et al., 2013). In fact, the Acquity HSS T3 column was selected over the Acquity BEH C18 column for the separation of 53 antibiotics since, in combination with an optimized mobile phase, it provided the best peak shape (Gros et al., 2013). Other companies also have released similar columns with higher ligand bonding density and extreme endcapping. Examples of these are Zorbax Eclipse XDB (Agilent), Hypersil GOLD aQ (Thermo Scientific), Atlantis T3 (Waters), XBridge (Waters), Nucleodur EC (Macherey-Nagel), among others. It should be mentioned that these SPs have progressively been marketed in different particle technologies (e.g., totally porous, sub-2 µm, and superficially porous).

Pentafluorophenyl (PFP) and phenyl–hexyl silica SPs offer alternative selectivity to alkyl-bonded silica through other interactions such as π–π, dipole–dipole, and hydrogen bond interactions. However, the application of such SPs in environmental analyses is still limited. For instance, PFP was selected over C18, C8, or phenyl–hexyl column for the determination of antifouling agent in marine sediment, as the PFP column provided the best combination of retention time and peak shape (Nichols et al., 2014). A superficially porous PFP SP was used to achieve the separation of a group of perfluoralkyl carboxylate, sulfonate, and sulfonamide isomers (Benskin et al., 2012) in landfill leachate samples. In fact, this SP is reported to have displayed enhanced retention and



Endcapping and extra-bonding

Silica-based structure totally endcapped

Ethylene-bridged hybrid (BEH)

Introduction of other moieties

Pentafluorophenyl (PFP)

Phenyl–hexyl

RP-polar embedded

FIGURE 6.4 Examples of enhancements of the alkyl-bonded silica-based materials to improve the RPLC separation of polar compounds.

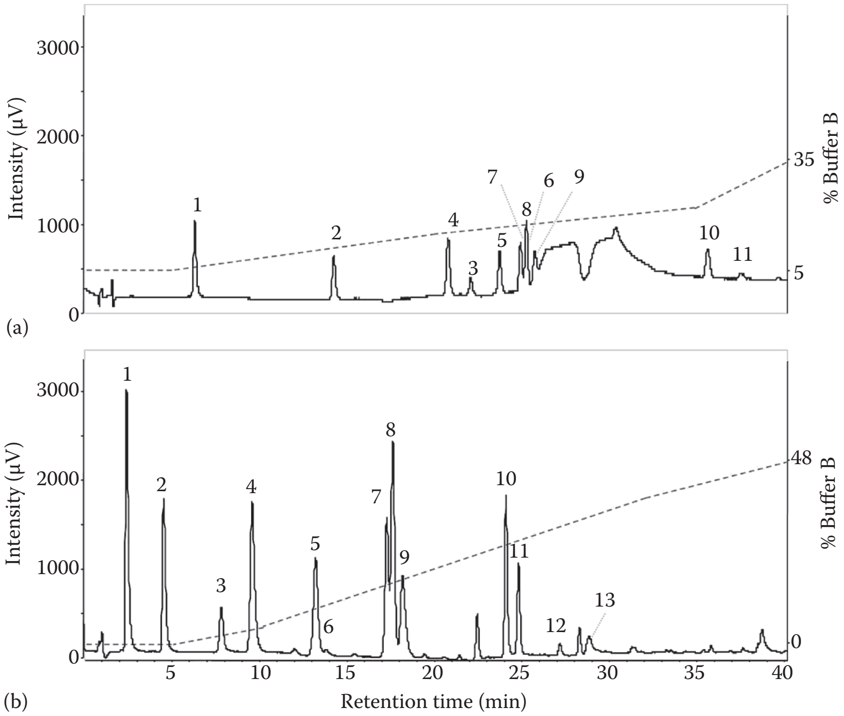


FIGURE 6.5 Chromatograms of standard phenol solution analyzed under optimized conditions with (a) C18 reverse phase column and (b) RP-Amide column. The analytes are gallic acid (1), 3,4-dihydroxybenzoic acid (2), dihydrocaffeic acid (3), 4-hydroxybenzoic acid (4), vanillic acid (5), 2,3-dihydroxybenzoic acid (6), caffeic acid (7), syringic acid (8), 2,4-dihydroxybenzoic acid (9), ferulic acid (10), lawsone (11), juglone (12), and ellagic acid (13). (Reprinted from Restivo et al., *Plos One*, 9, e88762–e88772, 2014. With permission.)

selectivity for the separation of halogenated compounds and also for positional isomers and nonplanar molecules (Núñez et al., 2012).

Polar-embedded RPs are another class of SPs that offer an alternative in terms of enhancing retention and selectivity for polar compounds. One example is amide-functionalized (RP-Amide) silica SP (which contains a polar amide group on the bonded alkyl chain). The polar amide moieties can interact with the residual silanol groups in the phase through electrostatic and/or hydrogen bonding interactions and also add retention increments for polar compounds (Benhaim and Grushka, 2010). RP-Amide SP has been used in some instances to determine compounds from environmental samples. The separation of a group of phenolic acids and derivatives was conducted with a classical C18 column and an Ascentis Express RP-Amide column. The two columns differ completely in terms of retention, as can be seen in Figure 6.5. The RP-Amide column separated several peaks that almost coeluted with the C18 column (Restivo et al., 2014). Similar comparison (C18 over RP-Amide) was performed in the separation of a group of polyether ionophores. In that case, the retention factors for both columns were similar, but there were significant differences in selectivity, resulting in very different elution profiles for the two columns. Eventually, RP-Amide was selected, which, under optimized conditions, provided a chromatographic separation in less than 5 min with good resolution (Herrero et al., 2012).

6.3.2.1 Hydrophilic Interaction Liquid Chromatography

HILIC mode was first employed by Alpert (1990), but it has since gained popularity, as it is well suited for the separation of polar and/or ionizable compounds. HILIC is a method in which a polar SP is used in combination with hydrophobic mobile phase (which contains a high percentage of organic solvent). This has the effect of increasing retention as the polarity of the compounds increases, providing alternative selectivity to reversed-phase LC (McCalley, 2010). The retention mechanisms in HILIC are quite complex, involving the partition mechanism together with adsorption, ion-exchange, and even hydrophobic interactions. The reader is advised to read detailed information elsewhere (Chauve et al., 2010; McCalley, 2010; Jandera, 2011; Buszewski and Noga, 2012; Greco and Letzel, 2013). In summary, these interactions are, in fact, related to the hydrophilicity of the SP, which establishes its capacity to hold water, and also the presence of charged groups.

Although the novelty in HILIC does not arise from the SP itself, the widespread use of HILIC in recent years has also motivated the emergence of several SPs for HILIC applications.

Thus, any SPs and any polar SPs (widely used in normal phase LC) that can retain water may be used in HILIC mode. They are classified on the basis of the charged state of the functional groups into neutral, charged, and zwitterionic phases. Figure 6.6 illustrates some selected HILIC phases with their relative properties.

Regarding the HILIC-MS coupling, the highly organic mobile phase used in HILIC provides enhanced sensitivity in MS, due to its efficient desolvation and low backpressures resulting from their low viscosity. In this respect, both features (ability to separate polar compounds and increasing sensitivity) provide HILIC with a suitable scenario to expand the field of application. As regard environmental fields, van Nuijs et al. (2011) reviewed the applications of HILIC for the analysis of polar contaminants in environmental samples.

Some of these applications used a bare silica column that contains silanol and siloxane bridges, which can display hydrogen bonding interactions, as well as ion-exchange interactions when working at pH levels above 4–5, as the silanol groups are deprotonated. These features mean that bare silica columns are most commonly used for the separation of neutral and basic compounds. For example, Peru et al. (2006) developed a HILIC-MS/MS method for the detection and quantification of a group of (basic) veterinary drugs from liquid manure and rainfall runoff. HILIC-MS/MS surpassed the already established RPLC methods, since the compounds were well separated from the matrix interferences, resulting in lower ME. In addition, the high amount of organic solvent in

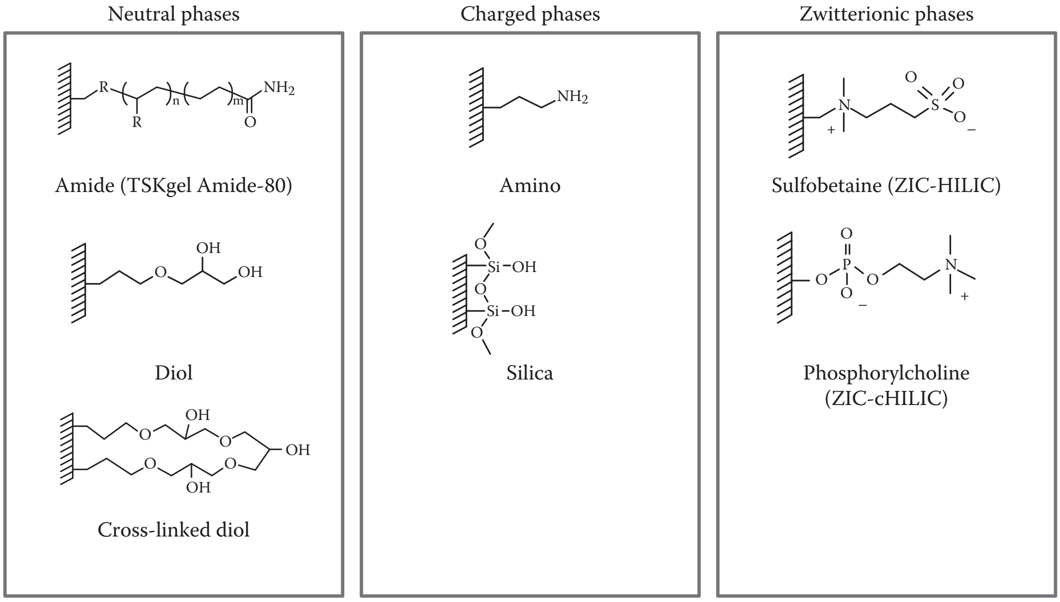


FIGURE 6.6 Classification of the polar stationary phases used in HILIC separations.

the mobile phase leads to a high electrospray ionization efficiency, resulting in increased sensitivity. A significant increase in sensitivity for a group of (basic) illicit drugs was also found when the HILIC-MS/MS method was compared to RPLC-MS/MS (Gheorghe et al., 2008).

Zwitterionic columns (see Figure 6.6) generally contain both a strongly acidic and basic functionality bonded to the silica surface, providing a net surface charge equal to zero. However, the different spatial disposition of the charge groups or the length of the chain is responsible for the chargeability of the phase. Therefore, it may display ion-exchange interactions. In addition, the ionic functionalities strongly absorb water and polar (hydrogen bonding and dipole–dipole) interactions are of primary importance. In this respect, the chromatographic properties of zwitterionic phases significantly differ from those of other HILIC phases (Jandera, 2011). Salas et al. (2014) compared a bare silica column (Atlantis HILIC, Waters) with a zwitterionic column (Syncronis, Thermo Scientific) for the determination of a group of sweeteners from environmental water. Under optimal conditions, the zwitterionic column was the only column able to separate all of the studied analytes, whereas with the bare silica column, some of the charged analytes were poorly retained. A similar zwitterionic column (ZIC-HILIC, Merck) was selected over C18 and RP-Amide phases for the separation of a group of iodinated X-ray contrast media. The authors selected this column, as it overcame certain limitations of the other columns, such as the early elution of the compounds (leading to the ME) and the high aqueous content of the mobile phase used (Echeverría et al., 2013).

The introduction of these novel SPs is becoming increasingly attractive in the environmental field, and they are expected to become well established in the future.

The sentence "The introduction of these novel SPs…" has been edited for clarity. Please check that the intended meaning was retained.

6.4 CONCLUSIONS

The development of materials that improve selectivity in the sample preparation process is a growing research topic in environmental analysis. This is widely demonstrated by the range of successful applications where these materials are used.

Materials focusing on improvements in particle technologies and in phase chemistry are also a cutting-edge issue in environmental analysis.

Despite all of the research in this field over years, further developments can be expected in materials that continue to improve the cleaning of the samples and the chromatographic separation.

ACKNOWLEDGMENT

The author thanks the Ministry of Science and Innovation (CTQ2011-24179) for financial support.

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