Talanta 130 (2014) 388–399

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

Review

Stir bar sorptive extraction: Recent applications, limitations and future trends

F.J. Camino-Sánchez *, R. Rodríguez-Gómez, A. Zafra-Gómez, A. Santos-Fandila, J.L. Vílchez

Research Group of Analytical Chemistry and Life Sciences, Analytical Chemistry Department, Faculty of Sciences, University of Granada, Avda. Fuentenueva s/n, E-18071 Granada, Spain

ARTICLE INFO

Article history:
Received 20 April 2014
Received in revised form
7 July 2014
Accepted 9 July 2014
Available online 19 July 2014

Keywords:
Stir bar sorptive extraction
Solid phase extraction
Sample preparation
Analytical applications
Environmental samples
Food samples
Clinical samples

ABSTRACT

Stir bar sorptive extraction (SBSE) has generated growing interest due to its high effectiveness for the extraction of non-polar and medium-polarity compounds from liquid samples or liquid extracts. In particular, in recent years, a large amount of new analytical applications of SBSE has been proposed for the extraction of natural compounds, pollutants and other organic compounds in foods, biological samples, environmental matrices and pharmaceutical products. The present review summarizes and discusses the theory behind SBSE and the most recent developments concerning its effectiveness. In addition, the main results of recent analytical approaches and their applications, published in the last three years, are described. The advantages, limitations and disadvantages of SBSE are described and an overview of future trends and novel extraction sorbents and supports is given.

Contents

* Corresponding author. Tel.: +34 958 243326; fax: +34 958 243328.
E-mail address: camino@correo.ugr.es (F.J. Camino-Sánchez).

http://dx.doi.org/10.1016/j.talanta.2014.07.022
0039-9140/

1. Introduction

Sample preparation is perhaps one of the most important stages of the analytical process. This step becomes more important as the complexity of the samples increases and when the concentration levels to be detected are minimal. In fact, selecting the detection technique for an analysis is currently considered easier than choosing the sample treatment technique.

Sample preparation involves clean-up and pre-concentration procedures aimed to improve the sensitivity, specificity and selectivity of the analytical methods. Current trends in analytical chemistry focus on miniaturization of these steps and of the amount of toxic reagents in order to reduce wastes [1,2]. Solid phase microextraction (SPME), micro-liquid–liquid extraction (MLLE), dispersive liquid–liquid extraction (DLLE) or stir bar sorptive extraction (SBSE) are the most popular among all the techniques proposed in recent years for reducing wastes. In the last 10 years, these techniques have been widely applied in hundreds of families of compounds, in all analytical fields. During the last few years, research has focused on miniaturization of the entire sample preparation workflow, including the collection of smaller sample sizes that leads to complete automation of almost all these procedures that are tailored to this small sample size.

SPME was developed in the early 90 s by Arthur et al. [3] and was the first modern solventless extraction technique for organic compounds. The technique soon became very popular due to its broad application field, simplicity, and low cost, among other reasons. However, at the beginning, the extraction procedure was completely manual with the consequent loss in reproducibility and sample throughput capacity. This limitation was overcome with the advent of commercial solutions that coupled the extraction fibers to generic autosamplers, allowing a completely automated and unattended analysis in both immersed and head space fiber extraction modes. This new extraction technique was successfully applied by modifying previously well-defined methods [4] and it was also used in novel applications [5]. Different fibers that would allow the extraction of compounds with very different polarities and molecular weights were developed to broaden the applications of SPME. However, because of its limitations, SPME is not the preferred technique for the analysis of organic compounds. Due to the low fiber volume, the mass of analyte extracted was limited by the kinetics of the extraction process, and it was mainly affected by sample volume [6,7]. Certainly, SPME can be applied to very small to extremely large volumes (i.e., an entire lake), but if quantitative recoveries are needed, only small sample volumes could be analyzed, affecting consequently to the sensitivity of the methods. Other limitations include that the precise control of the extraction time, since the extraction is developed out of the equilibrium state; the premature contamination and degradation of the fiber; the displacement effects due to the matrix compounds; and its relatively low specificity that requires the use of several fibers for multiresidue analysis. SBSE has overcome some of these limitations by allowing larger solid phase volumes.

SBSE was introduced in 1999 by Baltussen et al. [8] who proposed a novel application involving polydimethylsiloxane (PDMS) polymer as sorbent for solid phase extraction. PDMS is coated onto a glass-coated magnetic bar. Sampling is done by directly introducing the SBSE device into the aqueous sample. While stirring, the bar adsorbs the organic compounds to be extracted. The bar is removed from the sample, rinsed with deionized water and dried. After sorption, the compounds are chemically desorbed in a liquid or gas chromatography inlet, but capillary electrophoresis (CE) [9] or even inductively coupled plasma (ICP) [10,11] can also be used. SBSE was developed by Gerstel GmbH & Co. KG (Mülheim an der Ruhr, Germany) and is commercialized under the trade name Twister®. Although the first applications of SBSE were published in 2001 [12] and it cannot be considered a novel technique, nowadays a large amount of new applications are being continuously developed. This technique has been successfully applied to all analytical fields, including environmental, clinical and food analysis, and to a large variety of matrices including soils, environmental water and wastewater, solid and liquid foods, gaseous samples, and biological fluids. Due to the high pre-concentration capacity, broad spectrum of applications and simplicity, SBSE is becoming one of the most studied sample extraction techniques for the analysis of organic compounds. However, it has some disadvantages such as the limited spectrum of analyte polarities for the available stationary phases, the presence of strong matrix effects and the need of high control of extraction conditions.

There are few reviews on SBSE in the literature, and they mainly focus on the general theoretical principles of this technique [13] or the recently developed applications [14–16]. In contrast, the present review offers a different point of view. The text is divided into three sections: (1) a review of current procedures and approaches used in SBSE and the correlation between the results obtained and the theoretical data; (2) a review of the most recent trends in SBSE applications published in the last four years; and (3) discussion of the main disadvantages and limitations of SBSE that must be overcome in the future in order to improve this technique. The information presented is intended to be useful for the development of future applications and solutions to overcome the limitations of the technique.

2. Theoretical data and actual data obtained

The theory behind SBSE is the same as that of SPME. Baltussen et al. made an extensive study of the theory and thermodynamic principles of SBSE in 1999 [8]. Previously, they had published other approaches related to this technique that finally led to the development of SBSE [17]. Although, the objective of the present work is not to discuss these principles, some concepts must be explained.

It is well known that the extraction efficiency of SBSE and SPME —in PDMS stationary phases—is correlated to the octanol-water partitioning coefficient ($K_{o/w}$) and to the phase ratio (β). The equations that guide the partition between the liquid and the stationary phases are

$$\frac{m_{SBSE}}{m_0} = \frac{K_{o/w}/\beta}{1+(K_{o/w}/\beta)} \quad (1)$$

$$\beta = \frac{\text{Volume of sample}}{\text{Volume of stationary phase}} \quad (2)$$

where m_{SBSE} is the mass of analyte in the sorbent and m_0 is the mass of the analyte in solution. Both equations are equally valid regardless of the stationary phase or the nature of the sample, but if the stationary phase is not PDMS, the $K_{o/w}$ constants cannot be applied and other appropriated partitioning constants must be used.

The phase ratio is responsible for the better extraction efficiency of SBSE over SPME because the volume of stationary phase used in SBSE is about hundreds to thousands times higher than the one used in SPME. According to this theory, for a sample volume of 10 mL, a quantitative extraction using SPME is only possible for compounds with a $\log K_{o/w}>5$, while for SBSE, a quantitative extraction can be obtained for compounds with $\log K_{o/w}>2.7$ using a common PDMS stir bar.

However, it is possible to obtain quantitative extraction (100%) using the SBSE technique? Certainly, there is a huge number of substances with $\log K_{o/w}$ values higher than 2.7. Quantitative

Table 1
Theoretical recoveries and amount of analyte extracted as a function of the sample volume for two analytes with different $K_{o/w}$, and progression of the $K_{o/w}$ with the sample volume in order to obtain a quantitative recovery.

Sample volumen (mL)	Phase ratio[a]	log $K_{o/w}$[b]	log $K_{o/w}$=2.7		log $K_{o/w}$=4.0	
			Recovery (%)	Extracted amount (μg)[c]	Recovery (%)	Extracted amount (μg)[c]
5	50	2.30	90.9	0.045	99.5	0.049
10	100	2.60	83.3	0.083	99.0	0.099
20	200	2.90	71.4	0.143	98.0	0.196
50	500	3.30	50.0	0.250	95.2	0.476
100	1000	3.60	33.3	0.333	90.9	0.909
200	2000	3.90	20.0	0.400	83.3	1.667
500	5000	4.30	9.1	0.455	66.7	3.333
1000	10000	4.60	4.8	0.476	50.0	5.000

[a] Phase ratio calculated using a PDMS volume of 100 μL.
[b] log $K_{o/w}$ for a theoretical recovery of 80%.
[c] Extracted amount calculated for a concentration of analyte of 10 μg L^{-1}.

extraction was obtained for a volume of 10 mL, which is not a very large volume. In order to obtain lower limits of quantification (LOQs), the sample volume must be increased and recoveries of 100% will only be obtained for compounds with increasing values of $K_{o/w}$. Table 1 shows the theoretical recovery values and the amount of analyte extracted for two substances with a Log $K_{o/w}$= 2.7 and 4.0, respectively, and the estimated log $K_{o/w}$ for what quantitative recovery (>80%) is obtained if sample volume is increased.

These results demonstrate that the increase in sensitivity of a method based on SBSE, and the increase in the number of substances that can be quantitatively extracted are inversely correlated. These data also show that for the substance with log $K_{o/w}$=2.7 there is no significant increase in the mass of analyte extracted for sample volumes over 200 mL (12.5% when the sample volume increases to 500 mL). For the substance with a log $K_{o/w}$=4.0, the loss in extraction efficiency is not as pronounced and an increase of up to 52.9% is obtained when the sample volume increases from 500 to 1000 mL, resulting in a significant improvement. However, a recovery $<$ 80% implies an unacceptable systematic error in the analysis and requires that the calibration standards must be extracted in the same way as the samples. It could be argued that the only parameter that improves the LOQ in SBSE is the $K_{o/w}$ of the analyte, but this does not seem to be true. The reasons why the experimental data deviate from theoretical data are described below.

2.1. Sample volume and equilibrium time

As previously indicated, the easiest way to improve the recoveries in SBSE is increasing the sample volume. This could be extended until the loss of extraction efficiency according Eq. (1) overcomes the gain of mass analyte obtained by the increase of sample volume. However, increasing the sample volume involves other issues.

SBSE is a particular type of mass transfer process, considered a multiphase system where a substance is transferred from a liquid to a solid phase. As many other physicochemical processes, the SBSE process depends on the corresponding equilibrium constant (K_c), defined as the ratio between the concentration of the substance in the absorbent and in the sample.

If the solid support is PDMS, K_c is closely correlated with $K_{o/w}$ [8,18]. Nonetheless, Eq. (1) is only valid when the equilibrium has been reached, this equation also considers that the absorbent is a liquid, but this is only an approximation. Since the sample transfer process implies two or more insoluble phases, the phases must remain in intimate contact in order to reach a complete equilibrium between them. SBSE uses magnetic stirring for this purpose, but due to the capability of disaggregate in liquid media, much longer equilibrium times are needed in SBSE when PDMS is used as absorbent, in comparison to LLE with octanol. Despite all this, the theory behind Eq. (1) provides a good practical approach to predict recovery data in SBSE.

This is the first example of deviations from the theory. The equations that define the SPME process are valid only when the equilibrium has been reached and because volumes of sample and stationary phase are higher than those used in SPME, much longer equilibrium times are required. As a result, if out-of-equilibrium conditions are selected (e.g., shorter extraction times because the application requires maximum throughput), Eq. (1) would not be applicable. Camino-Sánchez et al. presented data about analyte response as a function of extraction time [19]. Their results showed that compounds with equal $K_{o/w}$ had different curves and equilibrium times. A trend in the experimental data according to $K_{o/w}$ and equilibrium time can be observed; in general, for some medium-polarity compounds, the experimental data show the following tendency: small molecules with high $K_{o/w}$ have short equilibrium times, while substances with low $K_{o/w}$ show longer times (e.g., the equilibrium between water and PDMS for terbuthylazine and atrazine pesticides is not reached before 48 h). Liu et al. reported identical conclusions for the determination of organophosphorus pesticides (POP) in cucumber and potato [20]. They use compromise conditions due to the long extraction times required to reach the equilibrium (5 h). High precision and reproducibility were obtained when extraction time was strictly set at 30 min.

Therefore, extractions under equilibrium conditions are not always possible and compromise conditions must be set. However, if pre-equilibrium conditions are used, small deviations in the selected experimental variables can lead to a significant loss of reproducibility, and in these cases the use of appropriated internal standard to correct these deviations is mandatory.

2.2. Temperature

Unlike SPME, the effect of temperature on SBSE is not usually evaluated and the extractions are usually conducted at room temperature. Only a few authors have analyzed the effect of temperature [21,22]. The reason for this is that SBSE is considered an “in equilibrium” extraction process; nonetheless, as previously stated, this is not always true. Temperature has two opposite effects on SBSE—the equilibrium state is reached faster at higher temperatures, while the amount of extracted analyte must remain constant, and in contrast, according to Henry's Law, the solubility of the analytes in water increases with temperature and therefore the amount of extracted analyte will be lower ($K_{o/w}$ decrease). The possibility of increasing the temperature will depend on the aim of the method—for maximum

sensitivity, the extraction should be performed at room temperature, but for maximum throughput (and minimum extraction time), the temperature should be increased.

Ochiai et al. published one of the first SBSE applications in food analysis [22]. They proposed a method for the determination of different preservatives in diverse aqueous matrices and evaluated the extraction efficiency of SBSE at 25, 45 and 70 °C. For all compounds, increasing the extraction temperature modified the kinetics of the mass transfer process, which resulted in shorter equilibrium times. However, a decrease in analyte recovery was observed at 45 and 70 °C. Responses up to four times higher were obtained for some of the studied analytes at the minimum temperature. Liu et al. also studied the effect of temperature on the extraction process, drawing similar conclusions [20]. They observed that the extraction phase began to degrade at 40 °C, finally setting the temperature at 30 °C.

On the other hand, analyte stability should also be considered when the temperature extraction increases, since many organic compounds are thermally unstable. Balbao et al. reported recoveries of 76.6% and 56.8% for rifampicin in plasma at 38 and 50 °C, respectively, in comparison with the ones obtained at 24 °C [21].

2.3. Matrix effect

Matrix effect is one of the major limitations of SBSE. Quantitative recovery strongly depends on sample volume and $K_{o/w}$ coefficients. Samples with high organic matter or suspended solid component, such as environmental samples, biological fluids or foods, are very difficult to extract with SBSE. Adsorption of the analytes onto the organic matter surface competes with the stir bar in the sorption. In addition, partitioning of analytes between water phase and organic matter ($K_{c/w}$) is strongly correlated with $K_{o/w}$, so these compounds with high affinity for PDMS will also exhibit high adsorption to the matrix components. Therefore, lower recoveries are expected for compounds with higher $K_{o/w}$ values. To our knowledge, few authors have developed an exhaustive study of how organic matter influences the recovery of analytes depending on their $K_{o/w}$ or $K_{c/w}$. Further comparison between SBSE and other extraction techniques in terms of recoveries of organic compounds would be useful because otherwise, false negatives could be obtained with SBSE. This matrix effect is not only limited to organic matter or suspended soils, but it also affects any substance present in the sample that can give rise to a three-phase partitioning (solvent, sorbent and competitor) of the analyte.

The simplest way to solve these issues is to dilute the sample until matrix effects are not significant, but higher LOQs and LODs will be obtained. The second way is to perform matrix-matched calibration, which is probably the best approach, where LOQ and LOD are not affected. However, matrix-matched calibration does not overcome other type of matrix effects: uncontrolled differences in the physico-chemical properties between samples and the matrix used for calibration standard matrix-matching. Both matrix effects described imply a decrease in the recovery, but this third type of sample matrix can result in an increase of recoveries over 100%. SBSE recoveries highly depend on the ionic strength of the sample, and therefore, on the salt content. Differences in salt content of samples and calibration standards can lead to unacceptable biases in analyte recovery. Camino-Sánchez et al. [23] developed an SBSE-based method to determine tributyltin species in seawater. For the calibration standards, they prepared water with identical salt content to that of seawater and compared the slope of the calibration graph with the slope from seawater, used as blank for calibration standard. The results demonstrated that there was a significant difference between slopes. Environmental samples have a huge variability between them in their physical and chemical properties, so matrix-matched calibration is not always the best solution for these samples. For wastewater analysis, this effect is even more pronounced.

Actually, the only efficient way to overcome, or at least minimize, matrix effects is using the adequate internal standards. These compounds must be added at the beginning of the extraction process. Although the most expensive option, the use of isotope-labeled compounds is the optimal choice. However, this option is not always feasible when multi-residue methods (MRMs) are used because there are not labeled compounds available for all the substances or because the number compounds included in the method would imply a high number of costly internal standards, making the method unfeasible. In SBSE, internal standards are subjected to the overall analytical process in both the samples and calibration standards. As a result, high deviation in their responses and more random errors in samples and standards are obtained in SBSE-based techniques [15].

But how much surrogate correction can be done? If the recovery of the internal standard (IS) falls to 20%, do the recoveries of all the analytes included in the method also fall in the same percentage? Authors never set the maximum admissible IS correction when they validate a method. The behavior of IS cannot be expected for all the substances when the recoveries are very far from 100%, although all analytes were from the same family. Isotope-labeled internal standards might not show similar behavior to that of the analyte; effects such as matrix bonding are not equal for the analyte and the IS. Robustness should be studied in depth in SBSE applications and setting the maximum admissible IS correction and variability should be compulsory for each matrix in order to avoid false negatives and false positives. These recommendations are particularly important in MRMs.

2.4. Matrix modifiers

In SBSE, like in other extraction techniques, MeOH and NaCl are widely used as matrix modifiers. NaCl is mainly used to cause a salting-out effect, improving the recoveries of polar analytes, and MeOH is added to water samples to increase water solubility of hydrophobic compounds, such as polycyclic aromatic hydrocarbons (PAH) and polychlorobiphenyls (PCBs). The addition of MeOH also prevents the quick adsorption of these compounds over the glass walls of the flask. Both matrix modifiers have a major drawback and in non-polar compounds a decrease in recovery is observed when NaCl is added, which results in increased water density and subsequent lower mass-transfer rate, and in polar compounds an increase in recovery is observed when MeOH is added, which results in decreased water solubility. Therefore, the matrix modifier and its amount must be carefully selected particularly in multi-target methods.

Another matrix modifier commonly used is pH adjustment. The analyte comes from acid to basic form depending on their *pKa*, making the analyte available to be extracted by SBSE based on the presence of neutral or ionic species. In addition to this well-known procedure, pH adjustment can be used in complexation reactions in order to obtain the neutral specie of an ionic compound. Villaverde-de-Sáa et al. used an ion-pair agent in order to extract several very polar compounds including seven perfluorinated carboxylic acids (PFCs) and perfluorooctane sulfonate (PFOS) in aqueous samples [24]. They added tetrabutylammonium (TBA) as ion-pairing agent to the water samples to obtain the neutral species or an ion-pair with a neutral net charge. General procedures of ion-pair extraction or other methods that lead to the formation of neutral species by decreasing the polarity of the compounds can be applied to SBSE.

Hyamine has also been used as modifier by several authors. This is a cationic surfactant that decreases the surface tension and the adsorption of non-polar compounds onto the glass wall. Kolahgar et al. reported an increase of sensitivity in PAH analysis when a concentration of 10 $\mu g\,L^{-1}$ of hyamine was used [25]. Although hyamine was one of the first matrix modifier studied in

SBSE, it is not very used and its effect on newly developed applications is no longer studied.

2.5. Deviations from theoretical data

Organic compounds do not always show the predicted behavior according to the theoretical data. An example of a group of compounds that deviates from the predicted data is the four isomers of hexachlorocyclohexane (BHC). These compounds are non-polar and have log $K_{o/w}$ values ranging from 3.7 to 4.3. Therefore, they should be successfully extracted by SBSE and their behavior could be predicted. However, they have been experimentally proved to show an opposite response to matrix modifiers from that expected. The recovery of those compounds increases when NaCl is added, conversely, the recovery decreases when an organic solvent such as MeOH is added [19,26]. Similar conclusions have also been reported by Margoum et al. and Ochiai et al. [27,28]. Figs. 1 and 2 show the extraction recoveries of the organochlorinated pesticides (OCP) in relation to NaCl and MeOH concentrations, respectively. An opposite behavior is observed between BHC isomers and other OCPs when the content of NaCl or MeOH increases, although they have similar $K_{o/w}$ values.

Another common deviation from theoretical data is shown by compounds with very high log $K_{o/w}$. This issue has been previously reported by many authors and discussed above. This effect is due to the adsorption of very hydrophobic compounds onto the glass walls of the extraction flask, which makes them unavailable to the extraction sorbent. Since this deviation has been well described by other authors, it will not be discussed here.

Methods of analysis that include compounds whose behavior is different the theoretically expected should be carefully optimized and validated. The selection of the appropriate internal standard is essential, especially in multi-compound applications.

3. Latest applications and trends

Since the number of SBSE-based methods published has experienced a linear increase in the last ten years, this paper reviews the literature published in the last four years. Originally, SBSE was intended for environmental analysis, but over time,

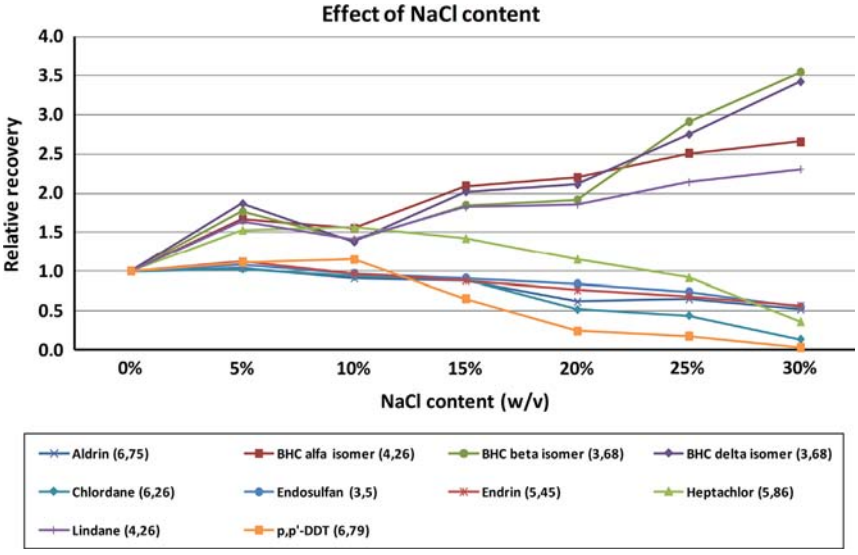

Fig. 1. Effect of matrix modifier NaCl on the recovery of organochlorinated pesticides. Into parentheses is included the log $K_{o/w}$ of each substance.

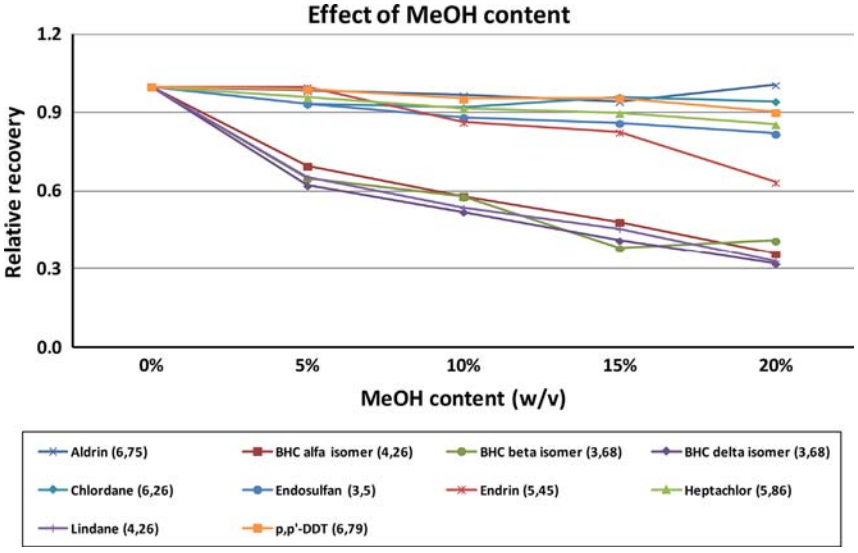

Fig. 2. Effect of matrix modifier MeOH on the recovery of organochlorinated pesticides. Into parentheses is included the log $K_{o/w}$ of each substance.

hundreds of applications for almost every field of analytical chemistry have been developed. In addition, new materials and coatings are being developed in order to overcome the limitations of PDMS and to expand the technical applicability of SBSE. In the present review, the application fields of SBSE are divided into the following groups for further discussion: environmental analysis, food analysis, clinical and pharmaceutical analysis, and development of new coatings.

3.1. Environmental analysis

For years, SBSE has been widely applied to the analysis of a large number of compounds known as Persistent Organic Pollutants (POPs), most of them included in the Stockholm Convention. These families of compounds include PAH, organochlorinated pesticides (OCPs), organophosphorus pesticides (OPPs), organonitrogenated pesticides (ONPs), PCBs and polybrominated diphenylethers (PBDE).

Table 2
Recent SBSE-based methods for environmental analysis.

Family of analyzed compounds	Sample type	Analytes	Desorption	Technique	Remarks	Reference
Fungicides/ preservatives	Wastewater	TCC	Liquid	LC–MS/MS	Recovery at 0.5 μg L^{-1}=92 ± 2% Recovery at 5.0 μg L^{-1}=96 ± 5% Precision (%RSD)>2% LOQ=10 ng L^{-1}	[30]
Organic pollutants	Sea water	OCPs, PAHs, PCBs, PBDEs, NP	Thermal	GC–MS	Up to 49 organic pollutants Recovery=86–118% Precision (%RSD)=2–24% LODs=0.011–2.5 ng L^{-1}	[31]
Odors/synthetic compounds/ detergents	Natural water and wastewater	18 Synthetic musk fragrances	Thermal	GC–MS	LOQ in the low ng L^{-1} range	[32]
PAHs	Wastewater	24 PAHs	Thermal	GC–MS/MS	Recovery=19–155% Precision (RSD%)=1–28% LOQ=0.002–0.1 μg L^{-1}	[33]
Organic pollutants	Marine sediments	84 Compounds: OCPs, OPPs, ONPs, ureic pesticides, PAHs, PCBs, PBDEs	Thermal	GC–MS/MS	PLE and SBSE Recovery=63–119% Precision (%RSD)=6–38% LOQs=0.001–0.99 ng g^{-1}	[26]
EDCs	Environmental water samples	20 Compounds: APs, BPA, estrogens and sterols	Thermal	GC–MS	Derivatization after extraction in the desorption tube Recovery=62–147% Precision (%RSD)=2–27% LOD between 0.8–84 ng L^{-1}	[34]
PAHs	Eluates of contaminated soils	15 PAHs	Liquid	HPLC-FLD	Evaluation of the influence of diluted organic matter in the recovery of PAH Recovery=82–104%	[35]
UV-filters	Sea water	6 UV-filters	Liquid	LC-(APCI)–MS/MS	LODs=8–31 ng L^{-1}	[37]
Drugs residues	Wastewater and river water	6 Statin drugs	Liquid	HPLC/Q-TOF-MS	LODs=0.52–2.00 ng L^{-1}	[36]
Pesticides	River water	16 OCPs	Thermal	GC × GC-HRTOF-MS	LODs=10–44 pg L^{-1} Linear range=60–1000 pg L^{-1}	[38]
Odors/synthetic compounds/ detergents	Natural water and wastewater	9 Synthetic musk fragrances	Thermal	GC–MS	LODs=0.02–0.3 ng L^{-1}	[39]
Organic pollutants	Environmental water samples	45 Compounds EU list of priority substances and EPA method 625	Thermal	GC–MS	Screening of 45 organic pollutants Recovery=2.5–89.2% Precision (%RSD)=5.1–23% LODs=1.7–1502.0 ng L^{-1}	[40]
Organic pollutants	River water	77 Compounds: OCPs, OPPs, ONPs, PAHs, PCBs, PBDEs	Thermal	GC–MS/MS	Up to 77 organic pollutants analyzed in the same run at ultra-trace level Recovery=74–116% Precision (%RSD)=3–30% LOQs=0.14–10 ng L^{-1}	[19]
Organotin compounds (anti-fouling)	Sea water	TBTs	Liquid	LC–MS/MS	LOQs=2.5 ng L^{-1} Recovery=92–102% Precision (%RSD)=15.6%	[23]
PAHs	Environmental water samples	6 PAHs	Liquid	HPLC-FLD	DI-SBSE: LODs=0.05–3.41 ng L^{-1} Recovery=88.8–114.3% Head Space-SBSE: LODs=0.03–2.23 ng L^{-1} Continuous flow-SBSE: LODs=0.09–3.75 ng L^{-1} Recovery=87.1–123.6%	[41]
Pesticides	Surface water	15 Pesticides and metabolites	Liquid	LC–MS/MS	LOQs=0.02–1 μg L^{-1} Recovery=93–101% Precision (%RSD)=17% Uncertainty=13–51%	[27]

APs: alkylphenols; BPA: bisphenol A; DI: direct immersion; EDCs: endocrine disrupting chemicals; NP: nonylphenol; OCPs: organochlorinated pesticides; ONPs: organonitrogenated pesticides; OPPs: organophosphorous pesticides; PAHs: polycyclic aromatic hydrocarbons; PBDEs: polybrominated diphenyl ethers; PCBs: polychlorinated biphenyls; PLE: pressurized liquid extraction; TBTs: tributiltin species; TCC: triclocarban.

Table 3
Recent SBSE-based methods for food analysis.

Family of analyzed compounds	Sample type	Analytes	Desorption	Technique	Remarks	Reference
Strobilurin pesticides	Fruits	Metominostrobin, azoxystrobin, dimoxystrobin, kresoxim-methyl, picoxystrobin, pyraclostrobin, trifloxystrobin	Liquid	HPLC-DAD	Recovery=80–105% Repeatability (RSD%) $<11\%$ LODs=0.3 and 2 ng g^{-1}	[45]
Volatile compounds (aroma)	Grapes	Glycosidic aroma compounds	Thermal	GC–MS	Glycosyl-glucose terpenes, C_{13}-norisoprenoids, phenols, total % favorable aromas and total % unfavorable aromas content profile to identify grape varieties	[46]
Furan	Coffee and jarred baby food	Furan	Thermal	GC–MS	Recovery=97–119% Precision (%RSD)=2.4–7.9% LOQs=2 ng g^{-1}	[47]
Haloanisoles	Cork stoppers	2,4,6-TCA	Thermal	GC–MS	MAE-SBSE LODs=0.5 ng L^{-1} Precision (%RSD)=9.1–16.5%	[48]
Pesticides	Fruit-based soft drinks	7 OCPs, 6 OPPs	Thermal	GC–MS	Variance component model approaching was set for calibration Recovery=38.5–123.4% LOQs=21 and 43 ng L^{-1}	[49]
EDCs (bisphenols)	Canned beverages and filling liquids of canned vegetables	BPA, BPF, BPZ, BP	Thermal	GC–MS	Two derivatization procedures Recovery=86–122% Repeatability (%RSD) $<9.7\%$ LODs=4.7–12.5 ng L^{-1}	[50]
Pyrethroid pesticides	Tea	Fenson, allethrin, ovex, tetramethrin, fenpropathrin, permethrin, t-cypermethrin, c-cypermethrin, deltamethrin, fenvalerato, bifenthrin, cyfluthrin	Thermal	GC–MS	Recovery=93–105% Precision (%RSD)=2.4–7.9%	[51]
Volatile compounds	Vinegars	Short-chain esters, acids, acetates and alcohols, phenols, lactones and benzenic and furanic compounds	Thermal	GC–MS	Up to 113 VOCs PCA applied to characterize vinegar origin	[52]
Volatile compounds (aroma)	Rice wine	E,E-farnesol and other volatile compounds: volatile alcohols, 1-butanol-3-methyl acetate, stearol, and phytane	Thermal	GC–MS	Comparison between DHS and SBSE 41 compounds analyzed Recovery=96–109% Precision (%RSD) $<9.9\%$ LOQs=0.02–0.05 ng mL^{-1}	[43]

BP: bisphenol; BPA: bisphenol A; BPF: bisphenol F; BPZ: bisphenol Z; DHS: dynamic headspace sampling; EDCs: endocrine disrupting chemicals; MAE: microwave extraction; OCPs: organochlorinated pesticides; OPPs: organophosphorous pesticides; PCA: principal components analysis; TCA: trichloroanisole; VOCs: volatile organic compounds.

Water and soil were the most commonly studied matrices using SBSE, but air, sewage sludge and other complex matrices are left out of the scope of SBSE. It has been demonstrated that SBSE can be applied for the analysis of almost all of these pollutants. Accurate results, good recoveries and very low LOQs have been reported for these applications [12,29]. Recently, the application of SBSE has extended to a new group of pollutants generically known as emerging contaminants. Since the awareness of the risk of these pollutants is recent, the development of new analytical methods is mandatory. The most recently developed methods are summarized in Table 2.

3.2. Food analysis

In this field, SBSE has been mainly used for the analysis of pollutants and toxics. Very few SBSE-based methods have been validated for the analysis of nutrients or major constituents, with some exceptions, such as the method published by Horák et al. for the determination of free medium-chain fatty acids in beer [42].

Recently, Ha et al. (2014) have reported an SBSE-based method for the determination of E,E-farnesol and other related volatile compounds in rice wine [43]. They compared the efficiency of SBSE and the dynamic headspace sampling (DHS) obtaining sensitive and accurate results, and they conclude that SBSE is a good option for volatile compounds analysis. Jin et al. [44] developed a method for the simultaneous determination of six commonly used preservatives with low $K_{o/w}$ in beverages. Since PDMS cannot extract these compounds efficiently, dual coated bars were tested. The performance of the proposed coatings was evaluated against PDMS, resulting in a dramatic improvement of the extraction efficiency. The SBSE-based methods more recently published for food analysis are summarized in Table 3.

3.3. Pharmaceutical and clinical applications

Table 4 summarizes the SBSE-based methods most recently developed in the pharmaceutical and clinical fields and in related fields. The number of applications is lower than in the fields of environmental and food analysis. The pharmaceutical and medical field is perhaps the area where SBSE has been less applied because of the following reasons: (i) in pharmaceutical production and quality assurance (QA) analysis, the concentration of the target analytes is usually in a range in which pre-concentration is not necessary; a dilution of the initial sample is usually performed, therefore, SBSE is not useful and simpler extraction procedures are used. (ii) Biological matrices are generally very complex samples and SBSE may be not the best choice for the elimination of matrix interferences because this is not a highly selective or specific extraction technique. SPE has been used instead during the last decades for treatment of biological samples with better results than SBSE or SPME. (iii) In medical and pharmaceutical research, the sample volume is often limited to few milliliters or few microliters due to the nature of the sample (plasma, serum, tissues, etc.) and the difficulty in sample collection. Although SBSE requires very low sample volumes, a minimal volume is required to cover adequately the stationary phase and to obtain reliable extractions. (iv) The two most important reasons are related to the polarity of the analytes. First, these substances are polar compounds and they have a poor extraction efficiency when PDMS is used as stationary phase. Secondly, the compounds are commonly analyzed by liquid chromatography using liquid desorption. The procedure cannot be easily automated and it is less sensitive than thermal desorption.

Table 4
Recent SBSE-based methods for medical and pharmaceutical analysis.

Family of analyzed compounds	Sample type	Analytes	Desorption	Technique	Remarks	Reference
Drugs	Plasma	Rifampicin	Liquid	HPLC-UV	Recovery = 75–80% Precision (%RSD) = < 10% LOQ = 0.125 μg mL^{-1}	[21]
SRI	Brain tissue, plasma and urine	Fluoxetine, citalopram, venlafaxine, norfluoxetine, desmethylcitalopram didesmethylcitalopran and o-desmethylvenlafaxine.	Liquid	HPLC-FLD	Recovery = 89–113% Precision (%RSD) = 13% LOQ (plasma) = 0.2–2 μg L^{-1} LOQ (brain) = 2–20 ng g^{-1} LOQ (urine) = 1–10 μg L^{-1}	[53]
CCS	Smoke	17 VOCs	Thermal	GC–MS	Repeatability (%RSD) = 10.1–12.9%	[54]
Drugs	Urine	DIC	Liquid	HPLC-UV	Effect of ageing of the stir bars was investigated and acceptance criteria were established Recovery = 75% Precision (%RSD) = 20% LOD = 12.03 ng m L^{-1} LOQ = 36.37 ng mL^{-1}	[55]
Drugs	Pharmaceutical liquid formulations	DIC	Liquid	HPLC-UV	Recovery = 70% Repeatability (%RSD) = 1.7% Reproducibility (%RSD) = 2.1% LOD = 16.06 ng m L^{-1} LOQ = 48.68 ng mL^{-1} Effect of ageing of the stir bars was investigated and acceptance criteria were established.	[56]
Phenols	Solid drugs	2,4,6-TBA, 2,4,6-TBP, 2,4,6-TCA and 2,4,6-TCP	Thermal	GC–MS/MS	Recovery = TCA (79.4–97.1%); TCP (67.4–89.4%); TBA (68.3–75.7%); TBP (55.5–67.4%) Precision (%RSD) = TCA (6.17–15.83%); TCP (6.03–14.9%); TBA (2.08–11.04%); TBP (6.47–15.62%). LOQ = TCA (4 pg); TCP (285.7 pg); TBA (9.0 pg); TBP (371.3 pg)	[57]
Antioxidants	HMWP implantable medical devices	2-Tert-butyl-6-(prop-1-en-2-yl)phenol, 2,6-Di-tert-butylphenol, BHT-quinone, BHT, BHT-aldehyde, Metilox®	Thermal	GC–MS/MS	Recovery = 90–95% Precision (%RSD) = 9.8–17.8% LOD = 8.3–15.2 pg m L^{-1}	[58]

BHT: butylated hydroxytoluene; CCS: components of cigarette smoke; DIC: diclofenac; HMWPE: high molecular weight polyethylene; SRI: serotonin reuptake inhibitors; TBA: tribromoanisole; TBP: tribromophenol; TCA: trichloroanisole; TCP: trichlorophenol; VOCs: volatile organic compounds

Table 5
Recent SBSE-based methods that use new coating materials.

Family of analyzed compounds	Sample type	Analytes	Desorption	Technique	Stir bar coating material	Reference
Triazine herbicides	Rice, apple, lettuce and soil	Cyanazine, simazine, simetryne, atrazine, ametryn, propazine, terbuthylazine, prometryn, terbutryn	Liquid	HPLC-UV	MIP	[66]
Inorganic anions	Purified water	Br^-, NO_3, PO_4^{3-} and SO_4^{2-}	Liquid	IC	Monolithic material poly(2-(methacryloyloxy) ethyltrimethylammonium chloride-co-divinylbenzene)	[67]
Drugs	Urine	AMP, mAMP, 3,4-methylenedioxy-AMP, 3,4-methylenedioxy-mAMP and ketamine	Liquid	HPLC-UV	Titania-OH-TSO	[68]
β2-agonists	Pork, liver and feed	Ractopamine, isoxsuprine, clenbuterol and fenoterol	Liquid	HPLC-UV HPLC-FLD	MIP with ractopamine	[69]
Herbicides (sulfonylurea herbicides)	Environmental water	Nicosulfuron	Liquid	HPLC-UV	MIP	[70]
Emerging pollutants (polar pharmaceuticals and personal care products)	River water, effluent and influent waste water	Paracetamol, caffeine, antipyrine, propranolol, carbamazepine, ibuprofen, diclofenac, methylparaben, ethylparaben, propylparaben, triclocarban, DHB, DHMB and BP3	Liquid	LC–MS/MS	Hydrophilic polymer based on poly(N-vinylpyrrolidone-co-divinylbenzene)	[71]
Phenyl arsenic compounds and their possible transformation products	Chicken tissues	cMMA,DMA,p-ASA,4-OH,3-NHPAA,PA,4-NPAA	Liquid	HPLC–ICP-MS	TiO_2-PPHF	[72]
Industrial residues	Wastewater	Benzothiazole	Thermal	GC–MS	PA	[60]
Drugs	Pork, liver and chicken samples	Sulfamethazine, sulfachloropyridazine, sulfamethizole, sulfathiazole, sulfameter and sulfamethoxazole	Liquid	HPLC-UV	MIP	[73]
Polar pharmaceuticals	Environmental water	Paracetamol, caffeine, antipyrine, propranolol, carbamazepine, naproxen and diclofenac	Liquid	LC–MS/MS	poly(MAA-co-DVB)	[74]
Chemical warfare agents and degradation products	Environmental water	EMPA, PMPA and MPA	Liquid	CE	ZrO_2-PDMS	[75]
Seleno-amino acids and seleno-oligopeptides	Biological samples	SeCys2, MeSeCys, SeMet, SeEt, γ-GluMeSeCys, GS-Se-SG	Liquid	HPLC-ICP-MS	PSP-TiO_2	[76]
Drugs	Human serum	Carvedilol	Liquid	HPLC-UV	Poly(methyl-PA-EG) and PDMS	[77]
Hormones	Water samples	Estriol, estradiol, ethynylestradiol, estrone, progesterone, medroxyprogesterone, levonorgestrel, northindrone	Liquid	LDTD-APCI-GC–MS/MS	PDMS/PTS/β-cyclodextrin	[78]
Drugs	Pork meat	Ractopamine	Liquid	ECL	MIP	[79]
Antibacterials synergist and sulfonamides	Urine, plasma and milk	Trimethoprim, sulfamether, sulfamethazine and sulfamerazina	Liquid	HPLC-UV	MIP	[80]
Drugs	Milk and milk powder	SDZ, SMR, SMZ, SMT, SMX and SDM	Liquid	LC–MS/MS	C_{18}-PDMS	[81]
Bisphenols	Personal care products	BPA, BPF and BPZ	Thermal	GC–MS	EG-Silicone	[82]
Organophosphorus pesticides	Environmental waters	Phorate, fenitrothion, malathion, parathion and quinalphos	Liquid	GC-FPD	PDMS/PTH	[83]
Metals	Drinking water	Copper	Liquid	FAAS	MIP, Cu-morin based	[84]
Estrogens	Environmental water	17-β-estradiol, dienestrol, diethylstilbestrol, estrone, 4-t-OP, BPA and 17α-ethynylestradiol	Liquid	LC-UV	Metal-organic frameworks (MOF) combined with PDMS (PDMS/MOF-5, PDMS/MOF-199 and PDMS/IRMOF-3)	[85]
Volatile compounds	Green Tea	32 VOCs present in beverages	Thermal	GC–MS	EG-Silicone	[60]
Alkyl phenols and metals	Water samples	APs, Cu(II), Cr(III) and Ni(III)	Liquid	GC/MS and ICP-OES	Silica gel modified with ketamine groups	[11]
Drugs	Urine	(+)-(S)-citalopram	Liquid	LC–MS/MS	Chiral-MIP	[86]
Drugs	Food samples	Vardenafil, tadalafil and sildenafil	Liquid	HPLC-UV	Endrimer-based MIP	[87]
Preservatives	Beverages (cola, orange juice and herbal tea)	BA, SA, MP, EP, PP and, BP	Liquid	HPLC-UV	APTES/OH-TSO and C_{18}-PDMS	[44]
Wine taint compounds	Wine	CPs and CAs	Thermal	GC–MS	EG–Silicone and PA	[62]

AMP: amphetamine; APCI: atmospheric chemical ionization; APs: alkyl phenols; APTES: 3-aminopropyltriethoxysilane; BA: benzoic acid; BP: butyl p-hydroxybenzoate; BP3: benzophenone-3; BPA: bisphenol A; BPF: bisphenol F; BPZ: bisphenol Z; CAs: chloroanisoles; CPs: chlorophenols; DHB: 2,4-dihydroxybenzophenone; DHMB: 2,2-dihydroxy-4-methoxy benzophenone; ECL: electrochemiluminescence; EG: ethyleneglycol; EMPA: ethyl methylphosphonic acid; EP: ethyl p-hydroxybenzoate; γ-GluMeSeCys: γ-glutamyl-Se-methyl-selenocysteine; GS-Se-SG: selenodiglutathione; LDTD: laser diode thermal desorption; mAMP: methamphetamine; MIP: molecularly imprinted polymer; MOF: metal-organic frameworks; MP: methyl p-hydroxybenzoate; MPA: methylphosphonic acid; MeSeCys: methylseleno-cysteine; OF: organic frameworks; OH-TSO: hydroxy-terminated silicone oil; PA: polyacrilate; PDMS: polydimethylsiloxane; PMPA: pinacolyl methylphosphonate; poly(MAA-co-DVB): copolymer of methacrylic acid and divinylbenzene; PP: propyl p-hydroxybenzoate; PSP-TiO_2: partially sulfonated polystyrene-titania; PTH: polythiophene; PTS: phenyltrimethylsiloxane; SA: sorbic acid; SDM: sulfadimethoxine; SDZ: Sulfadiazine; SeCys2: selenocystine; SeEt: selenoethionine; SeMet: selenomethionine; SMR: sulfamerazine; SMT: sulfamethizole; SMX: sulfamethoxazole; SMZ: sulfamethazine; TiO_2-PPHF: high polar extraction phase of titania immobilized polypropylene hollow fiber; titania-OH-TSO: titania-hydroxy-terminated silicone oil; 4-t-OP: 4-t-octylphenol; VOCs: volatile organic compounds; ZrO_2: zirconia.

3.4. New coating materials

In recent years, researchers have focused on the development of new coatings [59] but despite this fact, there are only three commercially available coatings for SBSE: PDMS, Polyacrylate (PA) and ethylene glycol/silicone (EG/silicone). The last two coatings were introduced by Gerstel GMbH (Mülheim an der Ruhr, Germany) in 2011 for the extraction of polar and medium-polarity compounds. Since EG/silicone is a silicone-based compound, it will also extract non-polar compounds. Few papers on the use of PA and EG/silicone have been published [60–62], and in all cases, authors have reported higher extraction efficiency of these new sorbents for polar compounds than PDMS. However, Ochiai et al. [61] have reported some mechanical instability of EG-silicone coatings. This coating degraded quickly and each stir-bar could be used only about 20 times but to solve this issue, they modified the stirring of the sample. The EG-silicone bar is placed on the wall of the extraction jacket while the sample is stirred by a magnetic stir bar or a conventional PDMS-coated sorptive bar.

The development of new coatings is, in fact, the most relevant improvement to expand the applicability of SBSE, allowing the analysis of polar compounds. Nonetheless, these compounds generally cannot be analyzed using gas chromatography, and thermal desorption cannot be used. Table 5 shows a total of 21 methods that use liquid desorption, while only four that use thermal desorption.

The new coatings are typically manufactured using two technologies: Molecular Imprinting Technology (MIT) and sol–gel processes. MIT is a technique to create artificial receptors or ligands with a predetermined selectivity and specificity for a given analyte. These materials are known as Molecularly Imprinted Polymers (MIPs). MIPs are robust molecular recognition elements, such as antibodies or biological receptors, and they are useful to separate and analyze complex samples such as biological fluids and environmental samples [63]. MIPs applied to SBSE allow the selective extraction of the analyte based on its tridimensional structure or functional groups. On the other hand, the sol–gel process is a method for producing advanced solid materials from small molecules. The method is used for the creating organic-inorganic hybrids materials, mainly metal oxides of silicon, titanium and zirconium. In general, the sol–gel process involves the transition of a solution system from a liquid “sol” (mostly colloidal) into a solid “gel” phase. Using the sol–gel process, it is possible to manufacture advanced materials in a wide variety of forms: ultrafine or spherical shaped powders, thin film coatings, fibers, porous or dense materials. These materials can be applied onto a magnetic rod for the production of new sorptive bars with new physical and chemical properties [64,65].

4. Some outstanding issues

4.1. Stir bar status control

One of the most common issues that researchers are faced with when they start working with SBSE is the maximum number of analysis that can be made with one sorptive bar before degradation. Obviously, this number depends on several factors including the matrix properties, extraction conditions, but particularly on the desorption conditions. High desorption temperature, long desorption times, extreme sample pH, oxidation of the adsorbent and irreversible adsorption of matrix components are some of the most common factors which decrease the useful life of the adsorbent.

In this regard, it is important to know how the degradation of the adsorbent affects the analytical results. The degradation of the coating bar generally is progressive and results in gradual decrease of the stationary phase volume. As previously discussed, the extraction efficiency strongly depends on the volume of adsorbent, and this effect is different for each analyte depending on the physicochemical properties. Therefore, the effect of the degradation of the sorptive bars will not be equal for all analytes, even to the extent that bars that show an extraction efficiency similar to new bars for some analytes will show total inefficiency for the extraction of others. The selection of the IS will play an essential role in the accuracy of the results. The effects of the aging of the adsorbent on the recovery of analytes must be studied in the validation step of any SBSE-based method. The maximum number of extractions that can be made with each sorptive bar and the maximum correction of the internal standard for each analyte must be established. A control of each batch of sorptive bars or an individual control of each one must be made in order to obtain adequate results in a long period of time. This procedure can be made by setting a minimum recovery of the internal standards or, in a simpler way, by recording the number of extractions made with each bar or batch.

4.2. Stir bar conditioning

An important factor that must be taken into account during SBSE is the “memory effect” of the adsorbent after sample desorption. Stir bars are reusable and as any other laboratory material, they must be cleaned and properly conditioned before the next use. Compounds with high boiling points, such as PAHs, PCBs and PBDEs, are the most critical when thermal desorption is used. Typical thermal desorption instruments do not reach more than 300–350 °C and PDMS cannot be heated to temperatures higher than 300 °C because it is degraded. Although desorption is performed under an intense flow of inert gas (50–200 mL min^{-1}) and for long desorption times (5–15 min), the total desorption of compounds with high boiling point is no easy to obtain. In addition, incomplete desorption can be more marked when liquid desorption is used because a thermodynamic equilibrium is established between the coating and the extraction solvent, but since the coating is selected to have a high affinity for the analyte, the equilibrium seldom is completely displaced to the solvent, and a portion of the total amount in the sorbent could not be extracted. This fact has many implications including false positives, blank issues, loss in reproducibility, as well as a reduction of the concentration range of the method.

Therefore, extreme care should be taken in the conditioning of bars and adequate procedures should be established when a method is developed in order to avoid cross contamination between uses. Stir-bar conditioning can be performed in two ways, thermal desorption or a solvent conditioning procedure. The former can be carried out in the same thermal desorption instrument that is coupled to the gas chromatograph or using a specific equipment. This procedure has several disadvantages, the specific equipment is expensive and the use of the gas chromatograph is highly time-consuming and the instrument can be contaminated by previous processes. Residues of coating or non-volatile matter from the matrix can enter into the thermal desorption unit or into the gas chromatograph. The shelf life of the coating can be dramatically reduced if very high temperatures are applied. Solvent conditioning could be the best approach, but the solvent must be carefully selected in order to avoid coating damages. Acetonitrile and mixtures of this solvent with dichloromethane are the most common solvents used for this purpose. Methanol is not recommended since it is a protic solvent.

4.3. Stability of new coatings

Although new coatings have been developed in recent years and their suitability for the extraction of a wide variety of compounds has been proved, their quality must be further

assessed beyond extraction efficiency. New coatings must be physically stable and have good mechanical properties that ensure they do no break or degrade after their use. Bonding of the coating to the cover of the magnetic rod, generally glass, is one of the difficulties. Bars are subjected to several processes during the extraction and analysis that can damage the coating. During the stirring, the surface of the coating is continuously rubbing the bottom surface of the glass flask at a very high stirring rate (usually up to 1000–2000 rpm) and these frictions can break the union between the coating and the supporting surface where is attached, generally glass, and then the coating will break away. The bonding must be strong enough to allow an intense friction between the coating and the surface of the sample recipient without material losses. Some authors have employed a metal-organic framework in order to increase the mechanical resistance of the bar [85]. These frameworks consist of metal ions or clusters coordinated to increase the rigid properties of organic molecules. In addition, the coating must also be thermally stable in order to tolerate the high temperature needed for desorption.

The coatings must be also chemically inert. The coating material will be in constant contact with oxygen, both atmospheric and dissolved in the water samples. Consequently, it could be quickly and easily oxidized and will lead to a modification of the coating structure and properties which can result in loss of extraction capabilities. Furthermore, coatings could be damaged by a large number of compounds including matrix modifiers such as acids, bases or organic solvents, major components of the sample (proteins or lipids) that may obturate the surface of the coating, or any substance that could permanently bind to the coating.

The most critical step in which the coating can be damaged is desorption (liquid and thermal). New developed materials must be able to tolerate the high temperatures used in thermal desorption without degrading or losing extraction efficiency. When liquid desorption is used, the material should not be damaged or dissolved by the organic solvent. The coating must be chemically stable and it should not dissolve into the extraction solvent. All these challenges must be solved and the performance parameters presented before claiming that a new coating is valid for SBSE. An assessment of the robustness, chemical, physical and thermal resistance would be mandatory every time a new coating is proposed.

5. Conclusions

It has been ten years since SBSE was first applied. Since then, there has been a steady increase in the number of published methods that propose the use of SBSE. Although environmental have been the most studied matrices, SBSE has been successfully applied to almost all types of matrices, covering all the fields of analytical chemistry research. The main limitation of SBSE in the early stages of development was that there was only one available coating material, which allowed only the extraction of compounds with high $K_{o/w}$. This limitation was partially overcome by the use of matrix modifies. However, compounds with low $K_{o/w}$ values, or relative low values, could not be successfully extracted with PDMS stationary phases. SBSE was developed as an improvement to SPME and it was therefore designed for thermal desorption coupled to a gas chromatograph only. Later, liquid desorption of the stir-bars was proposed in order to use liquid or gas chromatography without using expensive thermal extraction units.

Current trends in research related to SBSE are focused toward the development of new coating materials for the stir-bars, which extend the versatility and applicability of the technique. These new materials are divided in two main groups: coating for the extraction of polar compounds (i.e., PA and EG-based coatings), and coating for selective extractions (i.e., MIPs). But besides the extraction performance, these proposed new coatings still have to prove their robustness and quality in order to claim that they are valid for their intended purpose. It is worth noting that most of the new proposed materials are desorbed by liquid desorption, and this could be due to the fact that polar compounds are not susceptible to thermal desorption, or the coating cannot tolerate high temperatures. The number of extractions that can be made with a new material, before its performance begins to decrease, could be a good reference to evaluate its robustness.

Despite the continuous development and evaluation of new coatings, there are others limitations that must be overcome, like the automation of liquid desorption, the impossibility of re-analysis after thermal desorption, the control of coating status after several uses and the mixing up of used twisters with new ones. Taking into account that stir-bars are expensive and must be reused for several extractions as long as the coating is in appropriate conditions, SBSE has not the best precisions (RSD) when compared to other extraction techniques such as SPE. Therefore, SBSE may be the best choice for ultra-trace analysis, but probably not the best technique for small sample volumes or when high precision is required.

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