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Review

Stir-bar sorptive extraction: A view on method optimisation, novel applications, limitations and potential solutions

A. Prieto[a], O. Basauri[a], R. Rodil[b], A. Usobiaga[a], L.A. Fernández[a], N. Etxebarria[a], O. Zuloaga[a,*]

[a] Department of Analytical Chemistry, University of the Basque Country, P.O. Box 644, 48080 Bilbao, Spain
[b] Department of Analytical Chemistry, Nutrition and Food Sciences, IIAA—Institute for Food Analysis and Research, University of Santiago de Compostela, 15782 Santiago de Compostela, Spain

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ABSTRACT

Introduced in 1999 as a novel solventless sample preparation method, stir-bar sorptive extraction (SBSE) has become a popular analytical technique for the pre-concentration of organic compounds into a polydimethylsiloxane (PDMS)-coated stir-bar. In the last 10 years, hundreds of applications in the environmental, food and biomedical fields can be found in the literature. However, only PDMS-coated stir-bars are commercially available, which reduces the applicability of SBSE to the extraction of the non-polar compounds due to the poor extractability of more polar analytes. In this review, a view on method optimisation, limitations, potential solutions such as in-house coatings and derivatisation and novel applications in multi-residue analysis and passive sampling are revised.

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* Corresponding author. Tel.: +34 94 601 32 69; fax: +34 94 601 35 00.
E-mail address: olatz.zuloaga@ehu.es (O. Zuloaga).

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1. Introduction

Determination of organic compounds in environmental, food or biomedical aqueous matrices requires of a pre-concentration step prior to chromatographic/electrophoretic separation and detection [1–4]. Historically, the sample preparation step has been considered the most polluting step of the whole analytical procedure. However, since the acceptance of the philosophy and ideas of green analytical chemistry in analytical laboratories, sample preparation techniques that minimise solvent consumption such as solid-phase micro-extraction (SPME), stir-bar sorptive extraction (SBSE), single-drop micro-extraction (SDME), liquid-phase micro-extraction (LPME), membrane-assisted solvent extraction (MASE), micro-porous membrane liquid–liquid extraction (MMLLE), membrane extraction with sorbent interface (MESI) or supported liquid membrane extraction (SLME) have substituted the more solvent consumer techniques such as liquid–liquid extraction (LLE) or solid-phase extraction (SPE) [5]. These new techniques miniaturise sample preparation and, thus, reduce organic solvent consumption. Besides, on-line coupling of extraction and analysis results in a higher sensitivity, a reduced potential of analyte loss and a reduction on the sample amount needed for analysis [1,2].

SBSE, as well as SPME, are solventless sample preparation techniques based upon sorptive extraction. In sorptive extraction the analytes are extracted from the matrix into a non-miscible liquid phase. The most widely used sorptive extraction phase is polydimethylsiloxane (PDMS). Inorganic adsorbents interact too strongly with trapped compounds and require very high desorption temperature, which leads to degradation reactions. Organic adsorbents such as Tenax often lead to poor blanks due to thermal decomposition and have significant catalytic activity, which prevents their use with chemically labile compounds. Additionally, PDMS is a well known stationary phase in gas chromatography (GC), is thermo-stable, can be used in a wide range of temperatures (220–320 °C) and has interesting diffusion properties [1–3,6].

SBSE was first introduced by Baltussen et al. [7] in 1999 as a new and improved sample preparation technique. In SBSE stir-bars (so-called "twisters") are coated with a PDMS layer (typically 0.5–1 mm thick). As can be observed in Fig. 1, the number of publications that use SBSE have linearly increased in the past 10 years, reaching up to 400 publications in September 2009. The extraction process is based on the PDMS–water equilibrium and many of the analytical applications have been thoroughly described in several reviews [1–4,6–8] and in hundreds of publications. The earliest published reviews [6–8] cover more deeply the physical–chemical features of PDMS and highlight the fact that the sorption process is essentially a liquid–liquid partition and, thus, not only the surface area but also the total amount of the extraction phase is important in sorptive extraction. On the contrary, the most recent reviews [1–4,8] cover in more detail the analytical applications in several

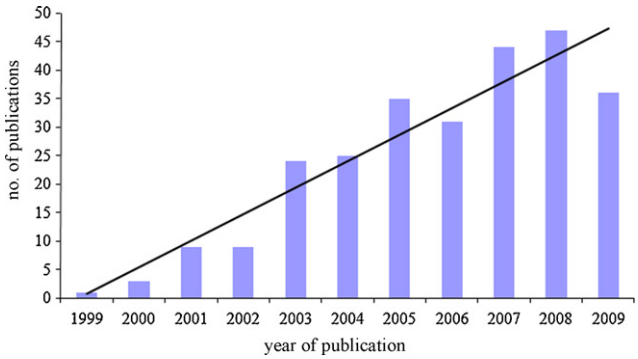

Fig. 1. Evolution of the number of publications on SBSE in the last decade.

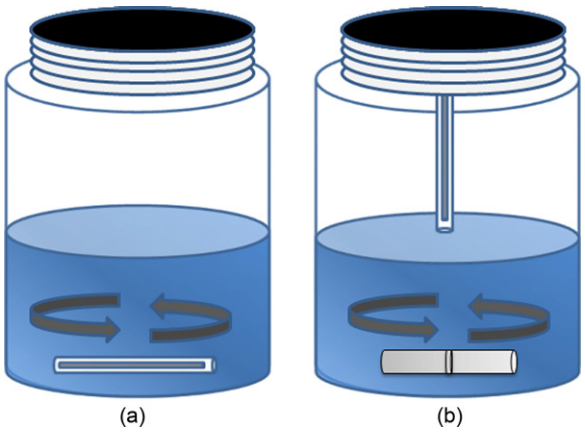

Fig. 2. Extraction modes in SBSE: immersion (a) and headspace (b).

fields like environmental analysis, biological fluids or food analysis, as well as novel SBSE methods, which include in situ and in-tube derivatisation, in situ de-conjugation and multi-shot mode [2].

At present only PDMS-coated stir-bars are commercially available and this represents one of the main SBSE drawbacks, since, due to the non-polarity of the PDMS polymer, polar compounds are poorly extracted.

In the present review article SBSE principles and modes will be briefly described and we will focus more deeply on other aspects of SBSE such as factors that need to be considered during SBSE optimisation, present limitations and potential solutions of SBSE drawbacks, as well as novel applications of the technique.

2. SBSE principles

Based on the general descriptions already given in many of the reviews mentioned above [1–3,6] and in those related to solid-phase micro-extraction (SPME) [9–11], it is quite simple to describe the basis of this type of pre-concentration process. Let us think that the extraction is taking place in a typical extraction vessel (~30 mL of total volume and ~20 mL of aqueous sample volume) as depicted in Fig. 2a, where the stir-bar can be, for convenience, that of 1 cm length and 24 μL of PDMS-phase volume.

As shown in Fig. 3 for certain persistent organic pollutants (naphthalene, Naph, biphenyl, Biphen, benzo[*a*]pyrene, B[*a*]P), we should keep in mind that, due to the chemical and hydrodynamical conditions at the solution/stir-bar interface, the process is kinetically governed until a steady state is attained, where the extraction

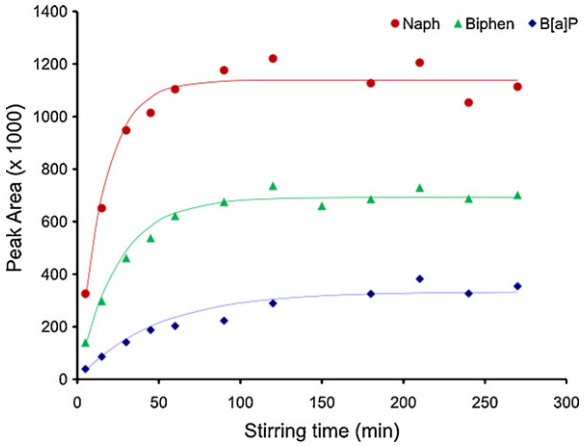

Fig. 3. Extraction time profile for certain persistent organic pollutants (naphthalene, Naph, biphenyl, Biphen, benzo[*a*]pyrene, B[*a*]P).

efficiency is governed by the distribution or partition coefficient of the target analyte between both phases ($K_{PDMS,w}$) and their respective volumes.

Starting from the kinetic step and considering a first-order one-compartment model, the following equation can be used:

$$C_{PDMS}(t) = C_{w,0} \times \frac{k_1}{k_2} \times (1 - e^{-k_2 \times \tau}) \quad (1)$$

where $C_{PDMS}(t)$ is the concentration of the target analyte in the stir-bar as a function of time, t, $C_{w,0}$ the initial concentration of the target analyte in the aqueous phase, and k_1 and k_2 are the uptake and the elimination rate-constants, respectively.

When chemical equilibrium is attained, the yield of the extraction can be estimated from the mass-balance equation and the partition coefficient as follows:

$$m_{w,0} = m_{PDMS} + m_w \quad (2)$$

$$K_{PDMS,w} = \frac{C_{PDMS}}{C_w} = \frac{m_{PDMS}}{m_w} \times \frac{V_w}{V_{PDMS}} = \frac{m_{PDMS}}{m_w} \times \beta \quad (3)$$

where $m_{w,0}$ is the initial mass of the target analyte in the aqueous phase that is distributed between PDMS (m_{PDMS}) and water (m_w). Additionally, the partition coefficient ($K_{PDMS,w}$) is defined as the ratio of the concentrations of the target analyte between the PDMS phase (C_{PDMS}) and the aqueous phase (C_w). Once the phase ratio ($\beta = V_w/V_{PDMS}$) is included, the volumes of each phase are considered as well.

Combining both Eqs. (2) and (3), and following the IUPAC suggestion of the term *recovery* [12], the theoretical recovery (R%) of a given SBSE setup can be calculated as follows:

$$R = \frac{m_{PDMS}}{m_{w,0}} = \frac{K_{PDMS,w}}{K_{PDMS,w} + \beta} \quad (4)$$

As it is shown in Fig. 4a and b, the recoveries are higher when low phase-ratios are used and highly non-polar compounds are extracted. In the case of SPME, the volume of the fibre is usually 0.5 μL, while for SBSE the smallest stir-bar has roughly 24 μL. This means that for the most common extraction setup, i.e.10 mL of aqueous solution, the phase ratio ranges from 400 (SBSE) to 20,000 (SPME). As a direct consequence of this physical difference between SPME and SBSE, the recoveries are much higher when SBSE is used (Fig. 4a).

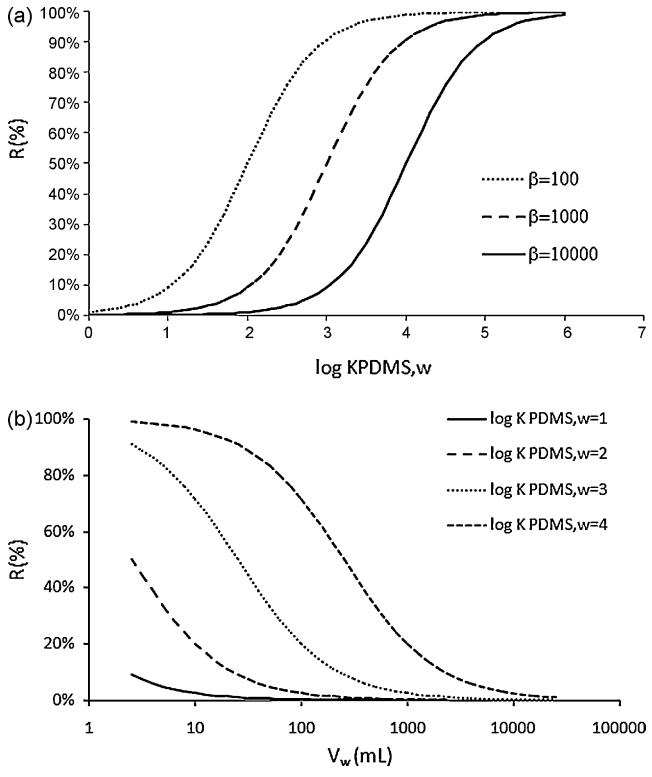

Fig. 4. Theoretical recovery in versus log$K_{PDMS,w}$ (a) and water phase volume (b) for PDMS-phase volume of 24 μL and initial analyte concentration in the water phase of 1 ng/mL.

Recent studies have correlated the $K_{PDMS,w}$ partitioning coefficient with the octanol–water distribution coefficient ($K_{o,w}$) and, although not exactly accurate, $K_{o,w}$ gives a good indication of whether and how well a given analyte can be extracted with SBSE [1,2]. Besides, the theoretical recoveries can be calculated using the KowWIN software program (Syracuse Research Corp., Syracuse, New York, USA) which is based upon a log$K_{o,w}$ calculator.

Additionally, this fact is also important when non-depletive extractions are expected, as it is the case of SPME and other passive sampling approaches [13]. In contrast to SPME, the use of SBSE as equilibrium sampling devices requires more stringent conditions (i.e. higher phase ratios and only polar analytes).

3. SBSE steps: extraction and desorption

SBSE consists of two major steps: extraction and desorption. These two principal steps in SBSE will be described.

3.1. Extraction step

During extraction the polymer-coated stir-bar is put in contact with the solutes by immersion (see Fig. 2a) or by headspace sampling (see Fig. 2b). This extraction step can be carried out under steady state conditions or in the absence of them.

In the immersion mode, which is usually abbreviated simply as SBSE, the polymer-coated stir-bar is added to a headspace vial that contains the liquid sample and the sample is stirred under controlled physical and chemical conditions. After extraction, the stir-bar is removed, rinsed with distilled water in order to remove salts, sugars, proteins or other sample components, dipped on a clean paper tissue to remove water, and submitted to desorption. The rinsing step is extremely important when analytes are thermally desorbed in order to avoid the formation of non-volatile material that can clog the desorption unit. Besides, rinsing does not cause solute loss since, when PDMS is used, the solutes are sorbed in the polymer phase [14]. Most applications in the literature are performed in the immersion mode (see Tables 1–3).

The use of SBSE was extended almost immediately to sampling in vapour phase (headspace mode) by Bicchi et al. [15] and is known as headspace solvent extraction or HSSE. In HSSE, sampling is performed by suspending the coated stir-bar in the headspace vial and the polymer is in static contact with the vapour phase of a solid or liquid matrix. The sample is usually stirred in order to favour the presence of the solutes in the vapour phase. After headspace sampling it is also recommended to rinse the coated stir-bar with distilled water and to dip it on a clean paper tissue. Despite the selectivity of this approach, not many works using HSSE are found in the literature (see Tables 1–3). Working on the HSSE mode preserves the polymer from the absorption of non-volatile species and increases the lifetime of the stir-bar. During the simultaneous determination of methylmercury (MeHg) and butyltins (BTs) from environmental matrices, Prieto et al. worked in the HSSE mode since the signal of a derivatisation by-product hindered the determination of BTs when working in the immersion mode [16].

3.2. Desorption step

The extraction step is followed by a thermal or liquid desorption before chromatographic or electrophoretic separation and detection.

Table 1
Environmental applications of SBSE.

Analyte	Matrix	Sample amount	Mode	Addition	Derivatisation	Phase/dimension	Time	Desorption	Analysis	LODs	Repeatability (%)	Ref.
17β-Estradiol	Water (river)	10 mL	SBSE	–	In situ acylation: AAA; K_2CO_3 +In-tube silylation: BSTFA	PDMS 10 mm × 0.5 mm	120	TD	GC–MS	0.5 ng/L	0.8–1.4	[108]
24 Priority substances (WFD2000/60/EC)	Water	100 mL	SBSE	NaCl	–	PDMS	720 min	TD	GC–MS (SIM)	0.1–7.3 ng/L	2.9–11.8 Estuarine water 3.2–13.2 Sea water	[154]
35 Priority semi-volatile compounds	Water	100 mL	SBSE	NaCl	–	PDMS 20 mm × 0.5 mm	840 min	TD	GC–MS	0.04–10.7 ng/L	0.8–12.8 (ground water) 1.2–23.7 (tap water) 0.8–18.9 (surface water)	[33]
NP 4tOP	Water	2 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	0.002–0.02 ng/L	3.6–6.6%	[141]
Acidic pharmaceuticals	River, sea and wastewater	25 mL	SBSE	pH 2	–	PU	6 h	LD	LC-DAD	0.1–0.5 ng/mL	<15	[100]
APs	Water (river)	2 mL	SBSE	–	In-tube sylilation: BSTFA	PDMS 10 mm × 0.5 mm	60	TD	GC–MS	0.2–10 ng/L	3.6–14.8	[28]
APs BPA	Water	10 mL	SBSE	–	In situ acylation: AAA; K_2CO_3	PDMS 10 mm × 0.5 mm	60	TD	GC–MS	0.1–3.2 ng/L	1.6–11.0	[104]
Aromatic amines	Water	50 mL	SBSE	15% NaCl, pH 11	–	VI-DVB	2 h	LD	HPLC-DAD	0.98–2.57 μg/L	0.74–8.34	[97]
Benzophenone and its derivatives	Water (river)	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	120 min	TD	GC–MS	0.5–1 ng/L	1.5–5.1	[155]
Benzophenone and its derivatives	Water (river)	10 mL	SBSE	–	In situ: AAA K_2CO_3	PDMS 10 mm × 0.5 mm	120	TD	GC–MS	0.5–2 ng/L	4.5–15.4	[156]
Brominated flame retardants	Soil Dust	0.1500 g (soil) 0.015 g (dust)	SBSE	Use extract Acetone NaCl	–	PDMS-β-CD	10 min	LD	HPLC–UV	2.9–4.2 μg/L	3.5–16.6%	[92]
Chemical components of tobacco flavour	Tobacco flavour	0.500 g	SBSE	Water	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	–	<14.9	[32]
Chlorophenols	Sediment	0.5 g	SBSE	Use extract MeOH ACN	In situ: AAA	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	1.8–3.8 ng/g	6.8–13.6	[136]
Chlorophenols BPA 4tOP NP	Soil	1 g	SBSE	Use extract	In situ: AAA K_2CO_3	PDMS 20 mm × 0.5 mm	6 h	TD	GC–MS	0.2–0.9 ng/g 1.7 ng/g 0.3 ng/g 0.2 ng/g	13–19%	[140]
EDCs Pesticides PAHs PEs APs	Environmental water samples	10 mL	SBSE	NaCl MeOH	–	PDMS 10 mm × 0.5 mm	30 min	LD	LVI-GC–MS	5–60 ng/L	1–17	[53]
EDCs	Water	10 mL	SBSE	NaCl	–	PDMS	60 min	LD	LVI-GC–MS	0.01–0.24 μg/L	2–13	[157]

Table 1 (*Continued*)

Analyte	Matrix	Sample amount	Mode	Addition	Derivatisation	Phase/dimension	Time	Desorption	Analysis	LODs	Repeatability (%)	Ref.
EDCs (herbicides, pesticides, PAHs, PCBs, biocides, PEs and APs.)	Water	30 mL	SBSE	MeOH	–	PDMS 20 mm × 0.5 mm	60 min	LD	LVI-GC–MS (SIM)	–	0.1–18.4	[158]
Estrogens	Water (river)	10 mL 50 mL	SBSE	–	In situ: Na_2CO_3 and AAA	PDMS 10 mm × 0.5 mm	5 h	TD	GC–MS	0.2–1 ng/L	1.3–9.3	[26]
Estrogens, BPA	Water (drinking)	2 mL	SBSE	30% NaCl	–	PDMS-βCD	15 min	LD	LVI-GC-FPD	13–81 ng/L	2.5–7.5	[81]
EtHg, MeHg, Hg (II), DiEtHg	Water (drinking)	10 mL	SBSE	–	In situ alkylation $NaBPr_4$; pH 6	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	0.01–0.2 ng/L	2.6–11.5	[39]
Explosives (TNT, RDX)	Water	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	30 min	TD	IMS	0.1–1.5 μg/L	7–9	[34]
Food packaging migration	Water	–	SBSE	–	–	–	–	TD	GC–MS	–	–	[159]
Glyoxal Methylglyoxal	Water Beer Yeast cells extracts	15 mL 5 mL 150 μL	SBSE	NaCl	In situ DAN and $HClO_4$	PDMS 20 mm × 0.5 mm	18 h	LD	HPLC-DAD	15–25 ng/L	6.4–7.9	[115]
Insect repellent	Water (lakes and pools)	250 mL	SBSE	–	–	PDMS 20 mm × 1 mm	overnight	TD	GC–MS	25 μg/L	11	[178]
Malodorous compounds	Water (drinking)	–	SBSE	–	–	–	–	–	GC–MS	<1 ng/L	–	[160]
Malodorous compounds	Water (animal waste)	–	SBSE	–	–	PDMS 10 mm × 3.2 mm	60 min	TD	GC–MS	–	–	[161]
MeHg, Hg (II)	Water (river and tap)	10 mL	SBSE	–	In situ $NaBEt_4$; and NaOAc	PDMS 10 mm × 0.5 mm	15 min	TD	GC–MS	2–5 ng/L	7–9	[114]
Methylmercury BTs	Water	10 mL	HSSE	–	In situ: HOAc/NaOAc $NaBEt_4$	PDMS 20 mm × 0.5 mm	5 h	TD	GC–MS	0.4–5 ng/L	4–17	[16]
Methylmercury BTs	Sediment Biological tissue	0.1–1 g 0.1 g	HSSE	Use extract Buffer $NaBEt_4$	In situ: $NaBEt_4$	PDMS 20 mm × 0.5 mm	5 h	TD	GC–MS	10–42 pg/g 12–32 pg/g	5–19	[16]
MIB, geosmin	Water	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	45 min	TD	GC–MS	<0.3 ng/L	9.2	[162]
MIB, geosmin, haloanisoles	Water (drinking)	100 mL	SBSE	–	–	PDMS 20 mm × 0.5 mm	120 min	TD	GC–MS	0.1–1 ng/L	7–16	[179]
n-Alkanes, PAHs, OPPs	Water	50 mL	SBSE	–	–	Sol–gel PDMS	90 min	TD	GC-FID	0.19–20 ng/L	–	[91]
OCP	Soil	10 g	SBSE	PSWE extract ACN	–	PDMS 10 mm × 0.5 mm	180 min	TD	GC–MS	0.02–4.7 ng/g	20	[134]
OCPs PCBs PAHs PBDEs	Soil	1 g	SBSE	Use extract MeOH	–	PDMS 20 mm × 0.5 mm	14 h	TD	GC–MS	0.03–2.0 ng/g <0.5 ng/g <0.5 ng/g <0.5 ng/g	11–20 11–19 10–18 10–19	[137]
Off-flavour compounds	Water (drinking)	20–60 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	480 min	TD	GC–MS	0.030–0.16 ng/L	0.80–3.7	[61]
OH-PAHs	Water	10 mL	SBSE	–	In situ acylation: AAA + $NaHCO_3$	PDMS 10 mm × 0.5 mm	360 min	TD	GC–MS	0.27–25 ng/L	1.97–7.52	[110]
OPPs	Water	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	4.5 h	TD	CGC-FPD	–	–	[67]

OPPs	Soil	10 g	SBSE	ASE extract	–	MIP-coated	60 min	LD	GC/NPD	12–24 ng/g	3.5–6.1	[142]
Organic compounds	Water		SBSE	–	–	–	–	–	–	<1 ng/L		[84]
OCPs	Seawater	50 mL	SBSE	–	–	PPESK	20 min	LD	HPLC-DAD	0.11–0.26 ng/mL	2.1–10.2	[163]
OPPs	Water	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	50 min	TD	CGC-AED	0.8–15.4 ng/L	2.5–15	[73]
Orgnotin	Water	30 mL	SBSE	–	In situ $NaBEt_4$	PDMS 10 mm × 1 mm	15 min	TD	GC-ICPMS	0.1 pg/L	12	[18]
PAHs	Water	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	LD	LC-FLD	0.3–2 ng/L	–	[164]
PAHs	Seawater	200 mL	SBSE	–	–	PDMS 20 mm × 0.5 mm	60 min	TD	GC–MS	0.14–1200 ng/L	1–48	[165]
PAHs	Water	10 mL	SBSE	MeOH hyamine	–	PDMS 10 mm × 0.5 mm	210 min	TD	GC–MS	0.2–2.0 ng/L	3–15	[76]
PAHs PCBs PEs NPs	Water (seawater)	20 mL	SBSE	NaCl MeOH	–	PDMS 10 mm × 0.5 mm	12 h	TD	GC–MS	0.05–3.3 ng/L	4–20	[66]
PAHs	Drinking water	10 mL	SBSE	ACN	–	PDMS 10 mm × 0.5 mm	140 min	LD	HPLC-Fl	0.2–1.5 ng/L	1.9–12.8	[64]
PAHs	Water Sediment Fish bile	30 mL 1 g 1 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	90 min	LD	MEKC-DAD	2–11 μg/L	4.4–7.1	[59]
PAHs	Water	10 mL	SBSE	–	–	PDMS	60 min	LD	LC-fluorescence detection	0.2–2 ng/L	4.7–13.5	[166]
PAHs	Soil	10 g	SBSE	Use extract MeOH	–	PDMS 10 mm × 0.5 mm	4 h	TD	GC–MS	–	1.8–21.0	[135]
PAHs	Water (rainfall water)	10 mL	SBSE	–	–	PDMS 10 mm × 1 mm	140 min	LD	LC-FLD	0.2–1.5 ng/L	5.3–12.8	[48]
PAHs	Seawater	–	SBSE	–	–	–	–	TD	GC–MS	2.74–13.5 ng/L	–	[167]
PAHs	Water	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm × 6	60 min	LD	LC-FLD	0.4–5.0 ng/L	4.7–13.5	[168]
PAHs, PASHs	Water	50 mL	SBSE	–	–	PDMS-βCD-DVvB	90 min	TD	GC-FID	0.19–20 ng/L	6.3–12.9	[74]
PBDE	Environmental sample	30 mL	SBSE	MeOH	–	PDMS 20 mm × 0.5 mm	240 min	LD	LVI-GC–MS	0.3–203.4 ng/L	3.6–11.9	[47]
PBDE	Sediment	5 g	SBSE	Use extract MeOH	–	PDMS 20 mm × 0.5 mm	240 min	LD	LVI-GC–MS	0.3–203.4 ng/L	3.6–11.9	[47]
PBDEs	Water	100 mL	SBSE	MeOH	–	PDMS 20 mm × 0.5 mm	25 h	TD	GC–MS	0.3–9.6 ng/L	5–18	[169]
PCBs	Water	100 mL	SBSE	–	–	Various	4 h	TD	GC–MS	0.3–2 ng/L	2–7	[170]
PCBs	Water	8 mL	SBSE	MeOH	–	PDMS 10 mm × 0.5 mm	120 min	TD	GC–MS	0.05–0.15 ng/L	3.3–10.6	[65]
PES	Drinking water	30 mL	SBSE	–	–	PDMS 20 mm × 0.5 mm	60 min	LD	LVI-GC–MS (SIM)	3–40 ng/L	2.2–14.8	[60]
Pesticide residue	Surface water	50 mL	SBSE	NaCl	–	PDMS 10 mm × 1 mm	1 h	–	LC–MS–MS (QqQ)	0.01–1.0 μg/L	10–16	[52]
Pesticides	Water	–	SBSE	–	–	–	–	TD	GC–MS	–	–	[171]

Table 1 (*Continued*)

Analyte	Matrix	Sample amount	Mode	Addition	Derivatisation	Phase/dimension	Time	Desorption	Analysis	LODs	Repeatability (%)	Ref.
Pesticides	Water sample	5 mL	Sequential SBSE	NaCl	–	PDMS 10 mm × 0.5 mm (×2)	60 min	TD 2 stir-bars simultaneously	GC–MS	2.1–74 ng/L	1.4–13	[153]
Pesticides	Water (river)	10 mL	HSSE	NaCl	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	0.2–20 ng/L	1.4–20.2	[30]
Pesticides PCBs PAHs Organic acids PEs	Atmospheric aerosols	0.01–1 g	SBSE	MAE extract acetone	–	PDMS 10 mm × 0.5 mm	45 min	TD	GC–MS	3–60 ng/L 100 ng/L 10–90 ng/L 70–100 ng/L 20–90 ng/L	3–2 29 4–38 16–46 5–19	[80]
Pesticides	Water (river)	1.25 g	SBSE	NaCl	–	PDMS	60	TD	LTM-GC–MS	<10 ng/L	–	[172]
Pesticides, PAHs and PCBs	Water	100 mL (seawater) 10 mL (interstitial marine water)	SBSE	–	–	PDMS 20 mm × 0.5 mm	840 min	TD	GC–MS	0.1–7.5 ng/L	1.1–16.3%	[35]
Pesticides OCPs Carbamates OPPs Pyrethroids Other	River water Brewed green tea	40 mL	Dual SBSE	NaCl	–	PDMS 10 mm × 0.5 mm	60 min	TD 2 stir-bars simultaneously	LTM-GC–MS	1.4–6.0 ng/L 1.9–60 ng/L 0.83–9.4 ng/L 3.1–100 ng/L 0.90–19 ng/L	4.1–7.3 6.5–14 4.5–14 6.5–12 4.6–11	[72]
Phenolic estrogens amine-based estrogens Acid estrogens Trialkyltins Apolar estrogens	Aqueous samples	40 mL	Multi-shot SBSE	MeOH	In situ: AAA (phenolic compounds) In situ: ECF (amine-based and acidic estrogens) In-tube: BSTFA (17β-estradiol) In situ: $NaBEt_4$ (trialkyltins)	PDMS 10 mm × 0.5 mm	60 min	TD 4 twister	GC–MS	0.04–0.57 ng/L 3–22 ng/L 0.21–3.6 ng/L 0.01–4.55 ng/L	6–10 4–14 4–15 8–14	[152,180]
Phenolic estrogens Amine-based estrogens Acid estrogens Trialkyltins Apolar estrogens	Wastewater	10 mL	Multi-shot SBSE	MeOH	In situ: AAA (phenolic compounds) In situ: ECF (amine-based and acidic estrogens) In-tube: BSTFA (17β-estradiol) In situ: $NaBEt_4$ (trialkyltins)	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	–	–	[173]
Phenolic xenoestrogens	Water	10 mL	SBSE	–	In situ acylation: AAA; Na_2CO_3; $NaHCO_3$	PDMS 10 mm × 0.5 mm	90 min	TD	GC–MS	0.5–5 ng/L	3.3–7.2	[24]
Phenols	Water (lake and sea)	50 mL	SBSE	pH 8	–	VP-EDMA	1.5 h	LD	HPLC-DAD	62–380 ng/L	1.3–5	[95]

Phenols	Water	10 mL	SBSE	NaCl	In situ acylation: 250 μL AAA; 0.5 g K_2CO_3	PDMS 10 mm × 0.5 mm	45 min	TD	GC–MS	0.1–0.4 μg/L	6–27	[29]
Phenoxy acid herbicides Phenolic compounds	Water	15 mL	SBSE	NaCl	In-extract: MTBSTFA	PDMS 10 mm × 0.5 mm	240 min	LD	LVI-GC–MS	1–800 ng/L	7–20	[54]
Pyrethoid pesticides	Water	30 mL	SBSE	5% MeOH	–	PDMS 20 mm × 0.5 mm	60 min	LD	LVI-GC–MS	1.0–2.5 ng/L	<13.8	[51]
Pyrethroids	Water	10 mL	SBSE	MeOH	–	PDMS 10 mm × 0.5 mm	60 min	LD TD	GC–MS (SIM)	0.02–1.4 ng/L (TD) 0.02–1.4 ng/L (LD-1 μL) 0.9–32.5 ng/L (LD-10 μL)	3.8–14.7 (TD) 3.1–10.4 (LD)	[174]
Semi-volatile compounds	Water	100 mL	SBSE	NaCl	–	PDMS 20 mm × 0.5 mm	840 min	TD	GC–MS	5–50 ng/L	<20	[175]
Sex hormones	Water urine	30 mL	SBSE	NaCl	–	PDMS 20 mm × 0.5 mm	2 h or 4 h	LD	HPLC-DAD	0.3–1.0 μg/L	4.0–10.4	[50]
Steroid hormones	Water	50 mL	SBSE	6% NaCl, pH 11	–	VP-EDMA	2.5 h	LD	HPLC-DAD	0.09–0.28 μg/lL	0.5–4.37	[98]
Triazines	Underground waters	20 mL	SBSE	NaCl	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	0.2–3.4 ng/L	1.8–7	[176]
Triazinic herbicides	Water	4 mL	SBSE	5% MeOH	–	PU	30 min	LD	LC–UV	–	<7	[45]
Triclosan	River water	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	120 min	TD	GC–MS	5 ng/L	4.0–7.0	[41]
UV filters	Water	20 mL	SBSE	MeOH	–	PDMS 10 mm × 0.5 mm	3 h	TD	GC–MS	0.2–63 ng/L	6–16	[68]
VOCs, SVOCs	Water	10–200 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm 10 mm × 1 mm	30–75 min	TD	GC–MS	1 ng/L	–	[7]
Wine volatiles	Wine	30 mL	SBSE	EtOH	–	PDMS 10 mm × 0.5 mm	60 min	LD	LVI-GC–qMS (SIM)	0.05–161 μg/L	6–12	[177]

AAA: anhydride acetic acid, APs: alquilphenols, ASE: accelerated solvent extraction, BPA: bisphenol-A, BSTFA: bis(trimethylsilyl)-trifluoroacetamide, BTs: butyltins, CE (MEKC): capillary electrophoresis (micellar electroquinetic chromatography), CGC-AED: capillary gas chromatography with atomic emission detection, CGC-FPD: CGC-flame photometric detection, CS-LC–MS: column-switching-LC–MS, DAN: 2,3-diaminonaphthalene, ECF: ethyl chloroformate; EDCs: endocrine disrupting chemicals, GC-AES: GC-atomic emission spectrometry, GC-FID: GC-flame ionisation detector, GC-ICPMS: GC-inductively coupled plasma MS, GC–MS/OD: GC–MS/olfatometry detection, GC–MS: gas chromatography–mass spectrometry, GC-NPD: GC-nitrogen phosphorus detector, HPLC–UV: high-pressure liquid chromatography with UV detector, HSSE: headspace sorptive extraction, IBMP: 2-isobutyl-3-methoxypyrazines, IMS: integrated modelling system, LC-APCI-MS: LC-atmospheric pressure chemical ionisation tandem MS, LC-LFD: liquid chromatography-lateral flow devices, LC–MS: liquid chromatography–MS, LC–MS–MS (QqQ): LC–MS–MS-triple quadrupole, LC–UV: LC–ultraviolet detection, LD: liquid desorption, LTM-GC–MS: low thermal mass-GC–MS, LVI-GC-qMS: large volume injection, MAE: microwave-assisted extraction, MASE-EDMA: poly(methacrylic acid stearyl ester–ethylene dimethacrylate), MDGC-MS: multi-dimensional GC–MS, MIB: 2-methylisoborneol, MIP: molecular-imprinted polymer, MTBSTFA: N-(t-butyldimethylsilyl)-N-methyltrifluoroacetamide, NP: nonylphenol, NPG: nonylphenol glucuronide, NPs: nonylphenols, OCPs: organochlorine pesticides, OP: octylphenol, 4tOP: 4-tertoctylphenol, OPG: octylphenol glucuronide, PSWE: pressurised subcritical water extraction, OPPs: organophosphorus pesticides, PAHs: polycyclic aromatic hydrocarbons, PBDEs: polybrominated diphenyl ethers, PCA: pentachloroacetic acid, PCBs: polychlorinated biphenyls, PDMS: polydimethylsiloxane, PDMS-βCD: polydimethylsiloxane-β-cyclodextrine, PDMS-βCD-DVB: polydimethylsiloxane-β-cyclodextrine-divinylbenzene, PEs: phthalate esters, PFBHA: o-(2,3,4,5,6-pentafluorobenzyl)-hydroxylamine hydrochloride, PPESK: poly(phthalazine ether sulfone ketone), PU: polyurethane, RAM: restricted access materials, RDX: 1,3,5-trinitro-1,3,5-triazine, RTL: retention time locking, SBSE: stir-bar sorptive extraction, SVOCs: semi-volatile organic compounds, TBA: thiobarbituric acid, TBSA: tuberculostearic acid, TCA: trichloroacetic acid, TD: thermal desorption, TeCA: tetrachloroacetic acid, TNT: trinitrotoluene, USE: ultrasound-assisted solvent extraction, VI-DVB: vinylimidazol-ethylene dimethacrylate, VP-EDMA: vinylpyridine-ethylene dimethacrylate, VOCs: volatile organic compounds, WFD: water framework directive.

Table 2
Food and flavour applications of SBSE.

Analyte	Matrix	Sample amount	Mode	Addition	Derivatisation	Phase/dimension	Time	Desorption	Analysis	LODs	Repeatability (%)	Ref.
(E)-α(β)-Ionone	Raspberries	500–700 g	SBSE	–	–	PDMS	180 min	TD	Enantio-MDGC-MS	–	–	[146]
4tOP	Laboratory animal feed	5 g	SBSE	USE extract	–	PDMS	120 min	LD	LC–MS	0.2–1 ng/g	4.3–5.8	[23]
NPs						10 mm × 0.5 mm						
Aroma compounds	Coffee, herbs	–	HSSE	–	–	Dual phase	–	TD	GC–MS	–	–	[87]
Aroma compounds	Wine	–	SBSE	–	–	–	–	TD	GC–MS	–	–	[183]
Aroma compounds	Wine	5 mL	SBSE	–	–	PDMS 20 mm × 0.5 mm	60 min	TD	GC–MS	–	–	[184]
Aroma compounds	Sake	–	SBSE	NaCl	–	PDMS	30 min	TD	GC-olfatometry	–	<6	[185]
Aroma compounds	Wine	25 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	90 min	LC	GC–MS	–	0.22–9.11	[79]
Aroma-active compounds	wines	10 mL	SBSE	H_2O	–	PDMS	12 h	TD	GC–MS	–	2.5–9.9	[186]
				NaCl		10 mm × 0.5 mm						
Chemical components of tobacco flavour	Tobacco flavour	0.500 g	SBSE	H_2O	–	PDMS	60 min	TD	GC–MS	–	<14.9	[32]
						10 mm × 0.5 mm						
Chloranisoles	Cork	2 g	SBSE	USE extract	–	PDMS	60 min	TD	GC–MS	0.81–956 ng/L	3–17	[138]
Chlorophenols				EtOH AAA (pH 3.6)		10 mm × 0.5 mm						
Dicarboximide fungicides	Wine	10 mL	SBSE	–	–	PDMS	40 min	TD	cGC–MS(SIM)	2–50 ng/L	2–5	[117]
						10 mm × 0.5 mm		LD	LC-APCI-MS			
Essential oil	Plant material	–	SBSE	–	–	–	–	TD	MDGC-MS	–	–	[87]
Essential oil	Grapes	–	SBSE	–	–	PDMS 10 mm × 1 mm	30 min	TD	MDGC-MS	–	–	[187]
Essential oil	Plant material	–	SBSE	–	–	–	–	TD	MDGC-MS	–	–	[149]
Flavour and fragrance compounds	Vinegar and whisky	20–100 mL	SBSE	–	–	PDMS	–	TD	GC–MS	–	–	[188]
Food packaging migration	Water	–	SBSE	–	–	–	–	TD	GC–MS	–	–	[159]
Fungicides	Grapes	5 g	SBSE	NaCl	–	PDMS 10 mm × 1 mm	120 min	LD	LC–MS	10 ng/g (LOQ)	8–19 (SBSE)	[189]
Glyoxal	Water	15 mL	SBSE	NaCl	In situ DAN and $HClO_4$	PDMS	18 h	LD	HPLC-DAD	15–25 ng/L	6.4–7.9	[115]
Methylglyoxal	Beer Yeast cells extracts	5 mL 150 μL				20 mm × 0.5 mm						
Haloanisoles, halophenols	Cork	3.5 g	HSSE	–	–	PDMS	60 min	TD	GC–MS	3–31 ng/g	4.9–12.7	[190]
						10 mm × 0.5 mm						
Hop bitter acids	Beer	20 mL	SBSE	HCl	–	PDMS	60 min	LD	CE (MEKC)	0.02–3 ng/L	2–6	[57]

						10 mm × 0.5 mm						
Linalool	Coffee	–	SBSE	–	–	PDMS 10 mm × 0.5 mm	–	–	MD-GC DCS-GC–MS	–	1.6–1.7	[191]
Monoterpenes	Grapes	–	SBSE	–	–	PDMS 10 mm × 1 mm	30 min	TD	MDGC-MS	–	–	[192]
Monoterpenes	Essential oil	10 mL	SBSE	–	–	PDMS	20 min	TD	–	–	–	[193]
OCPs	Vegetables	25 g	Dual SBSE	MeOH	–	PDMS	60 min	TD	GC–MS	0.83–3.0 ng/g	–	[75]
Carbmate pesticides OPPs Pyrethroid pesticides Other pesticides	Fruit Green tea					10 mm × 0.5 mm				1.0–26 ng/g 0.63–20 ng/g 163–349 ng/g 119–364 ng/g		
OCPs, chlorobenzenes	Fruit, vegetables	10 g	SBSE	Water suspension	–	PDMS 10 mm × 1.0 mm	60 min	TD	GC–MS	<5 ng/g	<25	[194]
Odour compounds	Fruit (snake fruit)	–	SBSE	–	–	–	–	TD	GC–MS	–	–	[187]
Odours	Mouth	–	HSSE	–	–	–	–	TD	GC–MS/OD	–	–	[195]
Off-flavours IBMP EP Geo TCA TeCA TBA PCA	Wine	10 mL	SBSE	–	–	PDMS 10 mm × 1 mm	60 min	TD	GC–MS	0.1–3.3 ng/L	0.8–6.3	[82]
OPPs	Juice	30 mL	SBSE	–	–	PPESK	30 min	TD	GC-ECD	0.05–2.53 ng/L	1.6–11.9	[73]
Organic compounds	Wine	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	90 min	TD	GC–MS	–	–	[196]
Organophosphorous pesticides	Honey	10 mL	SBSE	NaCl	–	PDMS-PVA	20 min	LD	HPLC–UV	7–103 ng/L	5.3–14.2	[56]
PAHs	Mate tea	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	120 min	LD	HPLC-FLD	0.1–8.9 ng/L	6.0–10.1	[63]
PAHs, OCP, OPPs triazines	Saffron spice	0.1 g	SBSE	MeOH	–	PDMS	840 min	TD	GC–MS/MS	0.04–1.2 ng/g	2.9–22.7	[197]
				Na_2SO_4		20 mm × 0.5 mm						
Pesticides, benzo[*a*]pyrene	Sugarcane juice	–	SBSE	–	–	PDMS 10 mm × 0.5 mm	3 h	TD	GC–MS	2–710 ng/L	–	[198]
Pesticides	Honey	2.5 g	SBSE	H_2O	–	Sol–gel PDMS/PVA	120 min	LD	LVI-GC-FPD	0.01–0.1 ng/g	5–9	[56]
Pesticides	Vegetables	10 g	SBSE	–	–	–	30 min	TD	GC-NPD	0.2 ng/g	5–31	[199]
Pesticides	Strawberries	Homogenate	SBSE	Water suspension	–	PDMS 10 mm × 0.5 mm	–	TD	GC–MS	–	–	[200]

Table 2 (*Continued*)

Analyte	Matrix	Sample amount	Mode	Addition	Derivatisation	Phase/dimension	Time	Desorption	Analysis	LODs	Repeatability (%)	Ref.
Pesticides	Fruit, vegetables	5 g	SBSE	H_2O	–	PDMS 10 mm × 1 mm	4 h	LD	CE (MEKC)	<1 ng/g	3–17	[58]
Pesticides	Tobacco and tea leaves	15 g	SBSE	MeOH	–	–	60 min	TD	GC–MS	3.3–11.4 ng	5.3–8.6	[139]
Pesticides	Tea	15 g	SBSE	MeOH	–	–	60 min	TD	GC–MS	4.2–10.5 ng	5.0–9.6	[139]
Pesticides	Herbal teas	1 g	SBSE	–	–	PDMS	30 min	TD	GC–MS		2.7–8.0	[122]
Pesticides	Pear pulp	1 g	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	1.2–3.9 ng/g	2.6–12.9	[143]
Pesticides	Vinegar	40 mL	SBSE	–	–	PDMS 20 mm × 0.5 mm	150 min	TD	GC–MS	0.13–0.81 μg/L	2.06–22.22	[69]
Pesticides	Orange	5 g	SBSE	NaCl	–	PDMS 10 mm × 1 mm	120 min	LD	LC–MS	0.001–0.05 ng/g (LOQ)	4–16% (SBSE)	[201]
Pesticides	Fruits and vegetables	15 g	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	–	–	[202]
Pesticides	Vegetables, fruits and baby food	15 g	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	cGC-MS	–	–	[203]
Pesticides	Food	25 g	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	–	–	[75]
Pesticides	Fruits and vegetables	15 g	SBSE	Use extract	–	PDMS	60 min	TD	RTL-GC	–	–	[202]
Pesticides	River water	40 mL	Dual SBSE	NaCl	–	PDMS	60 min	TD 2 stir-bars simultane-ously	LTM-GC–MS	1.4–6.0 ng/L	4.1–7.3	[72]
OCPs	Brewed green tea					10 mm × 0.5 mm				1.9–60 ng/L	6.5–14	
Carbamates										0.83–9.4 ng/L	4.5–14	
OPPs										3.1–100 ng/L	6.5–12	
Pyrethroids										0.90–19 ng/L	4.6–11	
Other												
Preservatives	Beverages, vinegar, aqueous sauces and quasi-drug drinks	10 mL	SBSE	NaCl	–	PDMS 10 mm × 0.5 mm	120 min	TD	GC–MS	0.015–3.3 mg/L	0.86–6	[62]
Stale-flavour carbonyl compounds	Beer	30 mL	SBSE	–	In situ: PFBHA	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	0.021–0.032 μg/L	2.4–7.3	[116]

TCA	Floor of sake and rice	1 g	SBSE	EtOH H_2O	–	PDMS	60 min	TD	GC–MS	–	4.8–20.5	[204]
TCA and phenols	wine	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	0.34–61.56 pg/L	1.5–3.5	[205]
Terpenes	Raspberry fruit	1 g	SBSE	Buffered suspension	–	PDMS	30	TD	Enantio-MDGC-MS	–	–	[206]
Terpenoids	Beer	30 mL	SBSE	–	–	PDMS 20 mm × 0.5 mm	120 min	TD	CG–MS	0.013–0.278 μg/g	2.0–8.2	[207]
VOCs	Plant material	Variable	HSSE	–	–	Variable	Variable	TD	GC–MS	nmol/L range	–	[150]
VOCs	Malt whiskey	10 mL	SBSE	–	–	PDMS 10 mm × 1 mm	30–60 min	TD	GC–MS	–	–	[208]
VOCs	Fungi	Culture	HSSE	–	–	PDMS 10 mm × 1 mm	60 min	TD	GC–MS	–	–	[209]
VOCs	Wines	30 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	LD	LVI-GC-qMS	0.18–416.5 μg/L	9–18	[210]
VOCs	Vinegar	25 mL	SBSE	NaCl	–	PDMS 10 mm × 0.5 mm	130 min	TD	GC–MS	0.03–8.60 μg/L	2.88–9.80	[70]
VOCs	Truffle	1 g	HSSE	–	–	PDMS 10 mm × 3.2 mm (×2 or/3)	180 min	TD	GC–MS	–	–	[151]
VOCs (plant emission)	Living plants	–	HSSE	–	–	–	–	–	–	–	–	[211]
VOCs	Wine	0.5 mL	SBSE	H_2O and HCl	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	–	2.3–9.8	[212]
VOC	Red raspberries	10 g	SBSE	$CaCl_2$ NaCl	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	–	–	[213]
VOC	Raspberries	10 g	SBSE	$CaCl_2$ NaCl	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	–	–	[214]
VOC	Oak-aged wine	25 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	90 min	TD	GC–MS	0.01–3.26 ng/L	0.1–5.5%	[215]
VOCs	Grapes	200 g	SBSE	–	–	PDMS 10 mm × 0.5 mm	360 min	TD	GC–MS	–	–	[216]
VOCs	Vineyard grapes	20 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	120 min	TD	GC–MS	–	–	[217]

Table 2 (*Continued*)

Analyte	Matrix	Sample amount	Mode	Addition	Derivatisation	Phase/dimension	Time	Desorption	Analysis	LODs	Repeatability (%)	Ref.
Volatile metabolites	Fungi	Culture	HSSE	–	–	PDMS 10 mm × 0.5 mm	30 min	TD	GC–MS	–	–	[218]
VOCs	Grape juice	20 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	120 min	TD	GC–MSD	-	1.3–63.9	[219]
Volatile phenols	Wine	25 mL	SBSE	–	–	PDMS	60 min	TD	GC–MS	0.006–0.373 mg/L	3.77–4.67	[220]
Volatile terpenoids	Carrots	0.2 g	SBSE	–	–	PDMS	30 min	TD	GC–MS	–	–	[144]
VOCs	Pinotage wines	0.5 mL	HSSE	NaCl	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	50 pg/L–281 ng/L	6–7	[221]
VOCs (chemical signals)	Plant material	–	SBSE	–	–	–	–	TD	GC–MS	–	–	[222]
VOCs	Wine	30 mL	SBSE	EtOH	–	PDMS 10 mm × 0.5 mm	60 min	LD	LVI-GC-qMS(SIM)	0.05–161 μg/L	6–12	[177]

AAA: anhydride acetic acid, APs: alquilphenols, ASE: accelerated solvent extraction, BPA: bisphenol-A, BSTFA: bis(trimethylsilyl)-trifluoroacetamide, BTs: butyltins, CE (MEKC): capillary electrophoresis (micellar electroquinetic chromatography), CGC-AED: capillary gas chromatography with atomic emission detection, CGC-FPD: CGC-flame photometric detection, CS-LC–MS: column-switching-LC–MS, DAN: 2,3-diaminonaphthalene, ECF: ethyl chloroformate; EDCs: endocrine disrupting chemicals, GC-AES: GC-atomic emission spectrometry, GC-FID: GC-flame ionisation detector, GC-ICPMS: GC-inductively coupled plasma MS, GC–MS/OD: GC–MS/olfatometry detection, GC–MS: gas chromatography–mass spectrometry, GC-NPD: GC-nitrogen phosphorus detector, HPLC–UV: high-pressure liquid chromatography with UV detector, HSSE: headspace sorptive extraction, IBMP: 2-isobutyl-3-methoxypyrazines, IMS: integrated modelling system, LC-APCI-MS: LC-atmospheric pressure chemical ionisation tandem MS, LC-LFD: liquid chromatography-lateral flow devices, LC–MS: liquid chromatography–MS, LC–MS–MS (QqQ): LC–MS–MS-triple quadrupole, LC–UV: LC–ultraviolet detection, LD: liquid desorption, LTM-GC–MS: low thermal mass-GC–MS, LVI-GC-qMS: large volume injection, MAE: microwave-assisted extraction, MASE-EDMA: poly(methacrylic acid stearyl ester–ethylene dimethacrylate), MDGC-MS: multi-dimensional GC–MS, MIB: 2-methylisoborneol, MIP: molecular-imprinted polymer, MTBSTFA: N-(t-butyldimethylsilyl)-N-methyltrifluoroacetamide, NP: nonylphenol, NPG: nonylphenol glucuronide, NPs: nonylphenols, OCPs: organochlorine pesticides, OP: octylphenol, 4tOP: 4-tertoctylphenol, OPG: octylphenol glucuronide, PSWE: pressurised subcritical water extraction, OPPs: organophosphorus pesticides, PAHs: polycyclic aromatic hydrocarbons, PBDEs: polybrominated diphenyl ethers, PCA: pentachloroacetic acid, PCBs: polychlorinated biphenyls, PDMS: polydimethylsiloxane, PDMS-βCD: polydimethylsiloxane-β-cyclodextrine, PDMS-βCD-DVB: polydimethylsiloxane-β-cyclodextrine-divinylbenzene, PEs: phthalate esters, PFBHA: o-(2,3,4,5,6-pentafluorobenzyl)-hydroxylamine hydrochloride, PPESK: poly(phthalazine ether sulfone ketone), PU: polyurethane, RAM: restricted access materials, RDX: 1,3,5-trinitro-1,3,5-triazine, RTL: retention time locking, SBSE: stir-bar sorptive extraction, SVOCs: semi-volatile organic compounds, TBA: thiobarbituric acid, TBSA: tuberculostearic acid, TCA: trichloroacetic acid, TD: thermal desorption, TeCA: tetrachloroacetic acid, TNT: trinitrotoluene, USE: ultrasound-assisted solvent extraction, VI-DVB: vinylimidazol-ethylene dimethacrylate, VP-EDMA: vinylpyridine-ethylene dimethacrylate, VOCs: volatile organic compounds, WFD: water framework directive.

Table 3
Biomedical and pharmaceutical applications of SBSE.

Analyte	Matrix	Sample amount	Mode	Addition	Derivatisation	Phase/dimension	Time	Desorption	Analysis	LODs	Repeatability (%)	Ref.
1-Hydroxypyrene	Urine	10 mL	SBSE	–	In situ AAA; $KHCO_3$	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	2 ng/L	5.0–6.3	[111]
4-Hydroxynonenal	Urine	1 mL	SBSE	H_2O; pH 5.5	Pre-in situ PFBHA in pyridine +On-Twister AAA; pyridine	PDMS 10 mm × 0.5 mm	50 min (42 °C)	TD	GC–MS	22.5 ng/L	3.3–7.2	[112]
NPs 4tOP	Human urine and plasma	1 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	0.004–0.04 ng/mL	1.5–3.9%	[23]
NPG	Human urine	1 mL	SBSE	Hydrolysis	–	PDMS 10 mm × 0.5 mm	90 min	TD	GC–MS	0.2 μg/L	7.1–9.2%	[14]
Antidepressant drugs	Plasma	1 mL	SBSE	Borate buffer	–	PDMS 10 mm × 0.5 mm	45 min	LD	HPLC–UV	15–40 μg/L LOQ	2.6–14.2	[49]
Banned azo dyes	Leather	–	SBSE	Alkaline hydrolysis	–	PDMS	–	LD	LC–UV	–	–	[223]
Barbiturates	Urine	5 mL	SBSE	–	–	PDMS 20 mm × 1 mm	30 min	TD	GC–MS	12 ng/L	–	[224]
Basic drugs	Forensic samples	–	SBSE	–	–	PDMS	–	TD	GC–MS	–	–	[225]
BPA	Water; body fluid samples	2–50 mL water 0.2–1 mL fluids	SBSE	–	In situ AAA; Na_2CO_3 or $NaHCO_3$ (pH 10.5)	PDMS 10 mm × 0.5 mm	45–120 min	TD	GC–MS	1–5 ng/L water 20–100 ng/L fluids	3.8–9.6	[107]
Caffeine and metabolites	Biological fluids	1 mL	SBSE	10% MeOH	–	RAM	40 min	LD	LC–UV	5–20 ng/mL	<10%	[101]
Caffeine, theophylline	Human blood	–	SBSE	–	–	PDMS	–	–	GC–MS	0.06–0.4 mg/L	–	[226]
Chlorophenols	Water; urine	10/2 mL	SBSE	–	In situ acylation: AAA; Na_2CO_3	PDMS 10 mm × 0.5 mm	120/60 min	TD	GC–MS	1–2 ng/L 10–20 ng/L	1.5–21.7 4.7–14.7	[103]
Drugs of abuse	Biological fluids	5 mL	SBSE	Hydrolysis	In situ: ECF, in situ: AAA	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	<5 μg/L	–	[22]
Estrone; 17β-estradiol	Urine	1 mL	SBSE	–	Pre in situ: AAA; Na_2CO_3 +Post HS acylation: AAA; pyridine	PDMS 10 mm × 0.5 mm	60 min (40 °C)	TD	GC–MS	0.02–0.03 μg/L	1.6–4.5	[105]
Fluoxetine	Human plasma	1 mL	SBSE	Borate buffer	–	PDMS 10 mm × 0.5 mm	30 min	LD	LC–MS (MIM)	3 μg/L	4.8	[227]
Fluoxetine	Plasma	1 mL	SBSE	H_2O	In situ carbamate formation: ethyl chloroformate (ECF); EtOH:pyridine	PDMS 10 mm × 0.5 mm	30 min	TD or LD	GC–MS	TD: 0.46 ng/L LD: 10 ng/L	7–14	[113]

Table 3 (*Continued*)

Analyte	Matrix	Sample amount	Mode	Addition	Derivatisation	Phase/dimension	Time	Desorption	Analysis	LODs	Repeatability (%)	Ref.
Glycine	Maillard reaction	1 mL	SBSE	Phosphate buffer NaCl	–	–	60 min	TD	GC–MS	–	–	[228]
NPG; OPG	Urine	1 mL	SBSE	–	In-tube BSTFA	PDMS 10 mm × 0.5 mm	90 min (37 °C)	TD	GC–MS	0.01–0.11 μg/L	2.5–7.3	[229]
Odour-active, volatile constituents	Human milk	5 mL	SBSE	–	–	PDMS 20 mm × 0.5 mm	60 min	TD	GC–MS	–	–	[195]
Odours	Mouth	–	HSSE	–	–	–	–	TD	GC–MS/OD	–	–	[195]
OPPs	Water	10 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	50 min	TD	CGC-AED	0.8–15.4 ng/L	2.5–15	[181]
PCBs	Sperm	1 mL	SBSE	H_2O:MeOH	–	PDMS 10 mm × 0.5 mm	45 min	TD	GC–MS	0.1 ng/L	3–7	[17]
Pesticides	Breast milk	–	SBSE	–	–	–	–	TD	GC–MS	–	–	[230]
Pharmaceuticals	Urine	5 mL	SBSE	–	In situ: AAA, in situ: ECF	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	<1 μg/L	–	[21]
Phenolic xenoestrogens	Urine	1 mL	SBSE	–	Pre-in situ acylation: AAA; K_2CO_3	PDMS 10 mm × 0.5 mm	150 min	TD	GC–MS	10–50 ng/L	2.7–8.6	[103]
Phthalates, metabolites	Body fluids, infusates	5 mL	SBSE	–	–	PDMS 10 mm × 1 mm	60 min	TD	GC–MS	–	–	[231]
Sex hormones	Water Urine	30 mL	SBSE	NaCl	–	PDMS 20 mm × 1 mm	2 h or 4 h	LD	HPLC-DAD	0.3–1.0 μg/L	4.0–10.4	[50]
Steroid sex hormones	Urine	5 mL	SBSE	pH 4	–	MASE-EDMA	40 min	LD	HPLC–UV/fluorescence	8–10 ng/L	4.2–10	[94]
Steroids, drugs	Biological fluids	5 mL	SBSE	Hydrolysis	In situ: ECF In situ: AAA	PDMS 10 mm × 0.5 mm	–	TD	GC–MS	–	–	[19]
TBSA	Sputum samples	2 mL	SBSE	–	In situ: ECF; EtOH:pyridine (5:1)	PDMS 10 mm × 0.5 mm	30 min	TD	GC–MS	0.2 ng/mL	4.8	[31]
Testosterone, eepitestosterone	Human urine	15 mL	SBSE	NaCl	–	PDMS	60 min	TD	GC–MS	0.9–2.8 μg/L	2.5–7.6	[36]
Triclosan	Urine	1 mL	SBSE	1 mL water	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	0.05 μg/L	2.4–6.7	[41]
Triclosan	Saliva	1 mL	SBSE	–	–	PDMS 20 mm × 1.0 mm	2 h	LD	LC-DAD	0.1 μg/L	3.6	[182]
Triclosan	Toothpaste	25 mL	SBSE	–	–	PDMS 20 mm × 1.0 mm	2 h	LD	LC-DAD	0.1 μg/L	3.6	[182]
VOCs	Urine	0.5 mL	SBSE	H_2O	–	PDMS 10 mm × 0.5 mm	60 min	TD	CG–MS	–	–	[232]

VOCs	Anal gland secretion	5 mg	HSSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	CG–MS	–	–	[232]
VOCs	Hamster and mouse urine	1 mL	SBSE	–	–	PDMS 10 mm × 0.5 mm	60 min	TD	GC–MS	–	0.7–5.5	[233]
VOCs	Mouse urine	0.5 mL	SBSE	H_2O	–	PDMS 10 mm × 0.5 mm	60 min	–	GC–MS GC-AES	–	–	[234]

AAA: anhydride acetic acid, APs: alquilphenols, ASE: accelerated solvent extraction, BPA: bisphenol-A, BSTFA: bis(trimethylsilyl)-trifluoroacetamide, BTs: butyltins, CE (MEKC): capillary electrophoresis (micellar electroquinetic chromatography), CGC-AED: capillary gas chromatography with atomic emission detection, CGC-FPD: CGC-flame photometric detection, CS-LC–MS: column-switching-LC–MS, DAN: 2,3-diaminonaphthalene, ECF: ethyl chloroformate; EDCs: endocrine disrupting chemicals, GC-AES: GC-atomic emission spectrometry, GC-FID: GC-flame ionisation detector, GC-ICPMS: GC-inductively coupled plasma MS, GC–MS/OD: GC–MS/olfatometry detection, GC–MS: gas chromatography–mass spectrometry, GC-NPD: GC-nitrogen phosphorus detector, HPLC–UV: high-pressure liquid chromatography with UV detector, HSSE: headspace sorptive extraction, IBMP: 2-isobutyl-3-methoxypyrazines, IMS: integrated modelling system, LC-APCI-MS: LC-atmospheric pressure chemical ionisation tandem MS, LC-LFD: liquid chromatography-lateral flow devices, LC–MS: liquid chromatography–MS, LC–MS–MS (QqQ): LC–MS–MS-triple quadrupole, LC–UV: LC–ultraviolet detection, LD: liquid desorption, LTM-GC–MS: low thermal mass-GC–MS, LVI-GC-qMS: large volume injection, MAE: microwave-assisted extraction, MASE-EDMA: poly(methacrylic acid stearyl ester–ethylene dimethacrylate), MDGC-MS: multi-dimensional GC–MS, MIB: 2-methylisoborneol, MIP: molecular-imprinted polymer, MTBSTFA: N-(t–butyldimethylsilyl)-N-methyltrifluoroacetamide, NP: nonylphenol, NPG: nonylphenol glucuronide, NPs: nonylphenols, OCPs: organochlorine pesticides, OP: octylphenol, 4tOP: 4-tertoctylphenol, OPG: octylphenol glucuronide, PSWE: pressurised subcritical water extraction, OPPs: organophosphorus pesticides, PAHs: polycyclic aromatic hydrocarbons, PBDEs: polybrominated diphenyl ethers, PCA: pentachloroacetic acid, PCBs: polychlorinated biphenyls, PDMS: polydimethylsiloxane, PDMS-βCD: polydimethylsiloxane-β-cyclodextrine, PDMS-βCD-DVB: polydimethylsiloxane-β-cyclodextrine-divinylbenzene, PEs: phthalate esters, PFBHA: o-(2,3,4,5,6-pentafluorobenzyl)-hydroxylamine hydrochloride, PPESK: poly(phthalazine ether sulfone ketone), PU: polyurethane, RAM: restricted access materials, RDX: 1,3,5-trinitro-1,3,5-triazine, RTL: retention time locking, SBSE: stir-bar sorptive extraction, SVOCs: semi-volatile organic compounds, TBA: thiobarbituric acid, TBSA: tuberculostearic acid, TCA: trichloroacetic acid, TD: thermal desorption, TeCA: tetrachloroacetic acid, TNT: trinitrotoluene, USE: ultrasound-assisted solvent extraction, VI-DVB: vinylimidazol-ethylene dimethacrylate, VP-EDMA: vinylpyridine-ethylene dimethacrylate, VOCs: volatile organic compounds, WFD: water framework directive.

3.2.1. Thermal desorption

Most SBSE or HSSE applications involve the use of thermal desorption (TD) followed by GC to recover the analytes accumulated in the coated stir-bar [16–43] (Tables 1–3), which implies not using organic solvents and allows the complete introduction of the extracted solutes in the chromatographic system. TD is performed at temperatures in the 150–300 °C range and, in contrast with SPME, desorption can take long, up to 15 min. However, the high sensitivity of the TD requires the use of an expensive unit on the GC setup, the thermal desorption unit (TDU). The TDU consists of two programmable temperature vapourisers (PTVs). While the first PTV is heated in order to desorb the solutes from the coated stir-bar, the second PTV is kept cool (temperatures in the −150 and 40 °C range) in order to cryofocus the desorbed analytes before entering the GC. Cryogenic focusing guarantees quantitative transfer of the analytes previously trapped to the chromatographic column (with considerable increase in sensitivity) [6] and minimises chromatographic peak width. Although TD is the most straightforward desorption mode, it is limited to thermally stable volatile and semi-volatile solutes and GC [6].

3.2.2. Liquid desorption

Liquid desorption (LD) is an alternative to TD when thermally labile solutes are analysed, when the separation is carried out using liquid chromatography (LC) or capillary electrophoresis (CE) or when a TDU unit coupled to GC is not available. During LD mode, the polymer-coated stir-bar is immersed in a stripping solvent or solvent mixture for the chemical desorption of the extracted solutes. The minimum stripping solvent volume must guarantee the complete immersion of the coated stir-bar and, obviously, the solvents or mixtures used in this step must be compatible with the polymer. Acetonitrile (ACN), methanol (MeOH), mixtures of these solvents or mixtures with water or aqueous buffers are the most common desorption solvents [44–52], although isooctane [51,53] or ethyl acetate [54] have also been studied. Some authors have attributed the low recoveries obtained in isooctane to the strong partition of non-polar solvents into PDMS phase, resulting in a substantial increase of the stir-bar weight [51]. The recovery of the analytes during LD is strongly determined by the $K_{o,w}$ partition coefficient. Since polar stripping solvents are mainly used during LD, this desorption mode is mainly useful for non-volatile and thermo-labile compounds with an intermediate polarity ($\log K_{o,w} \sim 2$) that can be re-extracted from the PDMS-coated stir-bar with relatively high yields. LD is accelerated by means of mechanical shaking, increased temperature or sonication [45–47,49,52,53,55,56] and it has been combined with either GC or more often with LC (see Tables 1–3). In the case of GC analysis, large volume injection (LVI) is chosen since most of the desorption-extract can be injected into the chromatographic column, increasing method sensitivity. Compared to LC, few reports have been proposed to combine SBSE with CE [57–59], although CE offers the high resolution required in the analysis of complex matrices with a reduced amount of sample, reduced solvent, reagent consumption and waste generation.

LD can also be more suitable than TD in order to minimise contamination from PDMS phase that can interfere in the analysis of certain solutes (i.e. phthalate esters, PEs) [60]. Besides, LD offers additional interesting features such as cost-effectiveness, the opportunity for method development and possible re-analysis [60].

4. Factors affecting SBSE

The factors which affect the two previously described steps of the SBSE process (extraction and desorption) must be optimised, although in the literature the extraction step captures much more attention. Most of the works still use a one variable at time (OVAT)

methodology during the optimisation [45,46,49–52,56,61–65]. With this approach, all of the variables except one are fixed and the behaviour of the system is studied at several levels of that variable. This method may be effective in some situation, but it is very ineffective, since it takes too many experiments and it cannot identify interactions among the variables because it does not thoroughly explore the space of possible solutions. To overcome these limitations, Designs of Experiments (DoE) should be applied but this approach is only used by fewer authors [16,42,47,48,54,66–71]. This approach uses a series small of carefully designed experiments which allow a thorough exploration of the experimental space. Thus, the application of DoE methodology have made possible the identification of interaction among different variables of the SBSE extraction process, e.g. between the pH of the solution and the addition of an inert salt [68].

4.1. Factors affecting extraction

Regarding the extraction step, the most studied variables are extraction time, pH adjustment, addition of an inert salt, addition of an organic modifier and stirring speed, followed by extraction temperature, sample volume and the volume of the acceptor phase, but some minor variables such as the dilution of the sample have also been investigated [70]. Some of these variables, such as sample pH or addition of an inert salt, modify the analytes or sample conditions and affect the equilibrium and other group of variables accelerate the process affecting its kinetics, such as stirring speed. Next, some of the main variables affecting the extraction step are studied in detail.

Sample pH is an important variable during SBSE for those analytes with acidic or basic properties and, in that case, pH is adjusted in order to obtain the solute partially or totally in the non-ionic form leading to the maximum extraction efficiency [44,46,49,62,68]. However, too acidic (pH < 2) or too basic (pH > 9) conditions are not recommended in order to avoid PDMS-phase degradation and extend PDMS-coated stir-bar lifetime [44,54]. In some cases, however, and although solutes with dissociation capability were studied, i.e. organophosphorus pesticides (OPPs) [56], explosives (trinitrotoluene, TNT, 1,3,5-trinitro-1,3,5-triazine, RDX) [34] or steroid sex hormones [50], no significant effect of sample pH was observed.

Inert salts such as sodium chloride are added during SBSE in order to modify the ionic strength of the sample solution. In general, it has been observed that for hydrophobic analytes ($\log K_{o,w} > 3.5$) the addition of an inert salt does not improve, but even reduces, the extraction efficiency [49,54,63,68,69,72]. On the contrary, for polar analytes the response increases with the addition of inert salts [54,62,72]. To explain the decreased response obtained for non-polar solutes after salt addition, various hypotheses are given. According to some authors [59,63,64] the salt addition causes an "oil effect" that promotes the movement of non-polar compounds to the water surface, minimising the interaction with PDMS-coated stir-bar. Similarly, other authors attribute such a decrease for hydrophobic analytes as a result of the increase of viscosity, which slows down the extraction kinetics of the compounds [54]. Some authors have explained this fact by the occupation of superficial area of the polymeric phase with salt ions, which decreases the superficial area available to interact with the analytes [45]. Finally, other authors [49] attribute the reduction of the extraction efficiency of non-polar analytes to electrostatic or ion-pairing interactions between the solutes and the salt, which reduce the ability of the analytes to move. In the case of polar analytes, the addition of an inert salt reduces water solubility and improves extraction efficiency [52]. However, discrepancies to these general rules can also be observed. For instance, in the case of polycyclic aromatic hydrocarbons (PAHs), while some authors have observed a decrease in extraction efficiency at high ionic strengths [59,63], others observed the opposite effect [53,66]. Similarly for OPPs, negative [73] and positive effect [74] after salt addition have been observed. Ochiai et al. [61] showed a different behaviour for off-flavour compounds in drinking water depending on whether the stir-bar was immersed or located in the headspace. Salt addition increased responses for HSSE but was not significant for SBSE. In summary, it could be concluded that salt addition must be carefully optimised in each case.

Organic modifiers such as MeOH, ACN or hyamine are tested as additives during SBSE in order to minimise analyte adsorption to the glass walls [75] but, above all, MeOH is the most used. However, the addition of such modifiers can also increase the solubility of the solutes in the water phase and, therefore, minimise extraction efficiency [50,51,67,75]. Broadly speaking, for compounds with high $\log K_{o,w}$ (>5.0) MeOH avoids adsorption of the analytes onto the glass of the vial, while for compounds with lower $\log K_{o,w}$ (<2.5) MeOH increases solubility of the compound in the solution, decreasing the partition into the PDMS phase [76]. When MeOH was added higher recoveries were observed during the determination of UV-filters [68], PEs [53,66], alkylphenols (APs) [53,66], PAHs [53], polybrominated diphenyl ethers (PBDEs) [42,47] or polybrominated biphenyls (PBBs) [42]. On the contrary, lower recoveries were observed for the most polar OPPs [67] or steroid sex hormones [50]. Finally, no significant differences were observed for triazinic herbicides [45]. In fact, some studies have also shown that the amount of the organic modifier has to be carefully optimised. For instance, in the case of pyrethroid pesticides, MeOH contents up to 5% increased extraction efficiency but higher contents showed a the opposite effect [51]. The same pattern was observed when ACN was used as modifier for the determination of PAHs and a lower recoveries were observed for high ACN contents [48,64].

Another key variable is the extraction temperature. At elevated temperatures the extraction equilibrium is reached faster [44,46,49,77] but the $K_{o,w}$ partition coefficient of the analytes and, thus, the extraction efficiencies become lower [77]. Besides, some authors claim that the lifetime of PDMS extraction phase can be remarkably reduced at temperatures above 40 °C [77]. In this sense, most of the works in the literature that study extraction temperature have observed an increase of extraction efficiency up to 40–60 °C [44,46,49,78–80] and a decrease due to a decrease of sorption distribution coefficient at higher temperatures (70 °C) [44,46,49,80]. However, Hu et al. observed a decrease on extraction efficiency with the increase of extraction temperature in the 15–50 °C range during the determination of OPPs using sol–gel PDMS/poly(vinylalcohol)-coated stir-bars [81]. Besides, Brossa et al. [53] observed an increase of extraction efficiency at temperatures up to 70 °C when analysing different endocrine disruptor compounds (some pesticides, PAHs, PEs, and APs) but the reproducibility was poor. Finally, Boudat-Deschamps et al. [48] observed no significant influence of extraction temperature for the determination of PAHs in rainfall water, attributing this fact to the narrow temperature range studied (23–40 °C).

The stirring rate is also often studied since it can accelerate the extraction and, thus, increase responses at a fixed extraction time. This fact is explained by the decrease of the thickness of the boundary layer between the stir-bar and the solution bulk. However, increasing stirring rate may cause physical damage to the extraction phase due to the direct contact of the stir-bar with the bottom of the sample vial [77]. Some authors have found that the stirring rate increases responses up to values in the 500–750 rpm range but that higher values have little or no effect [54,56]. In such cases a lack of homogeneity in agitation and bubble formation at high values are attributed to the lack of improvement or to the negative effect [54]. However, other results have also been observed. Serodio and Nogueira [51] observed a decrease in the signal when stirring

above 750 rpm, while high stirring rates (1000–1250 rpm) showed better results in some of the works of the literature [45,69,70].

As shown in Section 2 (see Eqs. (1) and (2)), the total amount of extracted solute in SBSE depends on the phase ratio. In the case of sample volume, higher sample volumes decrease extraction efficiency [48,61] but, however, chromatographic response can increase due to an increase on the mass of the analyte [61]. Leon et al. [20] observed that higher sample volumes increased chromatographic responses for non-polar analytes ($\log K_{o,w} > 3.5$), whereas for polar analytes sample volume had little effect. Guerrero et al. observed a positive effect of sample volume for pesticides [69], while Giordano et al. [52] observed the opposite even when some of the pesticides studied were the same (i.e. hexythiazox, chlorpyriphos or malathion), which may be due to the different sample volume ranges studied (10–44.3 and 20–100 mL, respectively). Sample volume increased chromatographic response for both SBSE and HSSE of off-flavour compounds in drinking water [61] or PEs and nonylphenols (NPs) in environmental waters [66]. In the case of off-flavours in wine, an increase up to 35 mL was observed but far beyond the increase was negligible [82]. Small differences were observed in the 10–60 mL range for the determination of preservatives in beverages, vinegars, aqueous sauces and quasi-drug drinks [62], PAHs and polychlorinated biphenyls (PCBs) in environmental waters [66].

Following the same argument, the volume of the PDMS phase influences extraction efficiency. Leon et al. [20] studied two different stir-bars (10 mm × 0.5 mm, 24 μL PDMS and 20 mm × 0.5 mm, 47 μL of PDMS) during the determination of 35 priority semi-volatile compounds and higher amounts were extracted with the 20 mm × 0.5 mm stir-bars. Prieto et al. [42] observed no significant differences during the determination of PBBs and PBDEs when using the four commercially available PDMS-coated stir-bars (10 mm × 0.5 mm, 20 mm × 0.5 mm, 10 mm × 1.0 mm, 20 mm × 1.0 mm). Franc et al. [82] noticed that the highest increase in sensitivity when using higher PDMS volumes were observed for the more polar (lower $\log K_{o,w}$) compounds, while the increase was less significant for compounds with higher $\log K_{o,w}$ values.

Finally, the extraction time is one of the most studied variables. However, this variable is studied at different stages of the optimisation. Typically, this variable is studied once the values of the rest of the parameters have been fixed, and the time profiles are studied in order to obtain the equilibration time [16,20,42,54,61,63–66,73]. However, in some cases extraction time profiles are studied at different values of variables that can alter equilibration conditions, such as extraction temperature [44,46,49]. Working under equilibrium guarantees maximum sensitivity but above all better precision. However, sometimes, in order to minimise analysis time, authors sacrifice sensitivity and precision and work under non-equilibrium conditions [20,44,54,63–65,73]. Some other works study the extraction time before the optimisation of other parameters [45,50–52,74] that affect extraction equilibrium and that can obviously modify optimum extraction time or together with them [47,48,67,69,70] and in those cases it cannot be assured whether equilibrium or non-equilibrium conditions are being attained.

4.2. Factors affecting desorption

4.2.1. Thermal desorption

During TD the desorption time, the desorption temperature and the cryofocusing temperature are the most studied variables but vent pressure and desorption (or vent) flow are also studied in several works [16,42,66,67,83].

The desorption temperature is normally evaluated in the 150–300 °C range. Generally, a positive effect of the desorption temperature is observed [34,66,70], although some authors decide not to work under the highest recommended temperature values in order to increase the lifetime of the stir-bars, as well as to minimise the baseline disturbances observed at high temperatures [34].

Similarly, the desorption time usually shows either a positive effect [66] or it is not significant [67] but it is often fixed at high values in order to minimise carryover effect [68]. Working desorption times are usually in the range of 1–15 min. Besides, some authors prefer the use of long desorption times at lower desorption temperatures with the aim of preserving the lifetime of the PDMS-coated stir-bars [68].

The cryofocusing temperature is also one of the key variables during this step since it guarantees the focusing of the analytes during desorption before entering the chromatographic column. In the analysis of MeHg and BTs from environmental matrices [16], it was observed that temperatures as low as −140 °C were necessary in order to observe the MeHg peak. Guerrero et al. [70] also observed a negative effect of cryofocusing temperature during the determination of volatiles in vinegar and the variable was set at −140 °C. MacNamara et al. [67] observed that cryofocusing temperatures higher than −150 °C were necessary for the analysis or OPPs but no significant influence was observed in the −60 to −20 °C range. Therefore, as expected low cryofocusing temperatures are especially important for volatile analytes.

4.2.2. Liquid desorption

For LD, the stripping solvent nature, desorption time and desorption volume are the most frequently studied variables.

As mentioned before, ACN, MeOH, water, aqueous buffers or mixture of them are the most widely used solvents [44–52]. For the back extraction of triazinic herbicides from PU foams MeOH, ACN and MeOH:ACN (50:50) were studied under sonication and MeOH yielded the maximum efficiencies [45]. However, ACN gave better results for the extraction of pyrethroid pesticides [51] and steroid sex hormones [50] from PDMS phases.

The LD times at room temperature range from 15 to 30 min, although sometimes this time is reduced in order to minimise analysis time [44] using mechanical agitation or shaking [46,47,49,52,53], sonication [44,45,56] or increased temperatures (50–70 °C) [46]. For antiepileptic drugs [46] and antidepressants [49] better results were obtained under magnetic stirring at 50 °C than under ultrasounds at 25 °C. However, dirtier chromatograms and a loss of precision can sometimes be observed at higher temperatures [53]. Besides, sonication can result in solvent evaporation when vials are not properly closed [54].

The stripping solvent volume must guarantee the complete immersion of the stir-bar. In order to minimise the solvent volume several authors accomplished the liquid desorption into a vial containing a 250 μL glass insert [44,51,54]. Typical stripping solvent volumes range from 50 to 200 μL (using glass inserts) up to 5 mL. Brossa et al. [53] observed that recoveries were independent of the desorption volume (studied range 0.5–2 mL).

5. Present limitations and potential solutions

Although SBSE is widely applied in environmental, food and biomedical analysis, it has also some limitations or drawbacks that will be briefly described below, as well as, some potential solutions.

One of the drawbacks is related to the fact that the coated stir-bar cannot be directly desorbed in a simple split/splitless injection port of a gas chromatograph. Hence the analyte has to be back extracted into a fitting solvent, which adds an additional step to the overall analytical method, or a specially designed TDU needs to be used.

Moreover, operations like removing the stir-bar from the sample, rinsing and drying (optionally liquid desorption, if applied)

are usually performed manually, which is laborious and can introduce errors. Automation of these steps is possible but this increases the cost and complexity of the hardware involved. To overcome this limitation, new easily automatable procedures for enrichment, i.e. high-capacity sorption probe (HCSP) [84], sample enrichment probe (SEP) [85] or thin-film microextraction [86] have been introduced, which combine the advantages of the large volume of the stationary phase in SBSE with the simplicity of SPME.

However, the most important limitations of SBSE are related to the coating of stir-bars. The non-polar PDMS is at present the only polymer commercially available as a coating for stir-bars. Recovery of polar analytes is poor and often in situ derivatisation is applied to increase extraction yields. Stir-bars coated with materials with better affinity to polar compounds would improve SBSE flexibility and selectivity while maintaining its concentration capability. New approaches or concentrating materials are therefore required to overcome the above-mentioned limitation and to extend the range of applications. Up to now, developments of novel stir-bars were reported with limited references. One of the introduced solutions was dual-phase-coated stir-bars, which combine two or more sampling materials with different concentration capabilities [87]. These new stir-bars consist of a short PDMS tube at both ends with two magnetic stoppers, whose inner cavity is packed with different types of adsorbents such as activated carbons. Dual-phase stir-bars with carbon both in SBSE and in HSSE mode have shown to improve the recovery of volatile and polar compounds compared to the conventional PDMS stir-bar. Moreover, in-house procedures for stir-bar coating are reported in the following sub-section.

Several materials were evaluated as simple and inexpensive approaches for the concentration of analytes in water samples. PDMS rods presented recoveries comparable to stir-bars, together with several advantages such as a lower cost and a higher feasibility [88,89]. Polypropylene (PP) microporous membranes as solid adsorbents were also evaluated both in SBSE and in HSSE modes [90]. PP was shown as a promising material for the concentration of medium and low polarity compounds.

Physical damage of the coating due to the direct contact with the bottom of the sample vial has also been claimed by certain authors [74], although not observed in most cases. In this sense, Yu et al. [74] designed and manufactured a "dumbbell-shaped" stir-bar controlling the glass bubble on two tips of the glass stir-bar to prevent the direct contact of the coating with the bottom of the vessel and, thus, reduce the friction loss.

In the following sub-sections in-house coating and derivatisation with the aim of improving extractability of polar compounds and matrix effects in SBSE will be described in more detail.

5.1. In-house coatings

Several problems have been found for the preparation of SBSE coatings with different polarities directly onto the glass tube and to obtain a thick layer of extraction phase. In order to solve this problem, different in-house procedures for stir-bar coating have been reported.

The first approach was sol–gel technology. This technology is a suitable procedure for the preparation of thick film and to obtain phases with high thermal and solvent stability, low bleeding, good repeatability and long lifetime because of the strong adhesion between the coating and the surface of glass by chemical bounding. Using this procedure a compact and thermally stable porous hydroxyl-terminated sol–gel network with 30-μm film thickness was achieved [77,91]. The results demonstrated that this phase was suitable for both non-polar and polar analytes. Stir-bars with PDMS as coating layer prepared by the sol–gel technique have been applied to the extraction of n-alkanes, PAHs and OPPs [91]. The parameters affecting the preparation of the sorptive phase were evaluated and the temperature of the aging step was found to be of special importance to avoid cracking of the film. Novel stir-bars were also prepared using sol–gel technology by introducing different groups in the PDMS network such as β-cyclodextrin [81,92], divinylbenzene (DVB) [74] and poly(vinylalcohol) [56]. The results indicated that these novel stir-bars improved the extraction selectivity towards polar analytes (e.g. estrogens and bisphenol A, BPA). However, problems for cracking of the polymer layer were observed, leading to a gradual loss of coating over time.

The second approach was the use of monolithic material. The preparation of monolithic materials is very simple, by polymerisation of a monomer mixture with a porogen solvent, forming a porous polymer containing a network of interconnected pores with sizes in the low micrometer range. As a result, monolithic materials possess very good permeability, which speeds up the mass transfer. The main advantages are simplicity in the preparation, high permeability, favourable mass transfer characteristics and low cost. If suitable monolithic materials are chosen, non-polar and polar compounds could be concentrated effectively. For the extraction of polar compounds (e.g. steroid hormones, phenols, aromatic amines, ...) several monomer mixtures were prepared and evaluated successfully, i.e. octyl methacrylate (MAOE)-ethylene dimethacrylate (EDMA) [93], methacrylic acid stearyl ester (MASE)-EDMA [94], vinylpyridine (VP)-EDMA [95], vinylpyrrolidone (VPL)-DVB [96], vinylimidazole (VI)-DVB [97] and VP-EDMA [98]. However, the extraction efficiencies for strongly polar compounds were not as good as expected.

New materials such as poly(phthalazine ether sulfone ketone) (PPESK) and PDMS/polypyrrole (PPY) were also selected as SBSE coatings. The porous structures of these coatings provide large surface area that can enhance the extraction efficiency. The extraction mechanism is adsorption in the first one and both adsorption (PPY) and absorption (PDMS) in the later. PPESK stir-bars prepared by immersion precipitation technique exhibit high thermostability (290 °C) and long lifetime. However, the denser surface layer hinders the transfer of the analytes. The results showed that better enrichments were obtained for semi-polar and polar compounds with PPESK (evaluated for organochlorine pesticides, OCPs, and OPPs) than with PDMS stir-bar [73]. A PDMS/PPY stir-bar was evaluated for the extraction of antidepressants in plasma and it showed high extraction efficiency (sensitivity and selectivity) [44]. Polyurethane (PU) foams were also proposed as SBSE phases [99]. It was demonstrated that PU foams present remarkable thermal stability and excellent mechanical resistance to organic solvents. The PU foams proposed in the literature seem to be promising polymeric phases for SBSE, mainly to monitor the most polar analytes (e.g. triazinic herbicides and acidic pharmaceuticals) [45,100].

In addition, more selective stir-bars based on restricted access materials (RAM) and molecular imprinted polymers (MIP) have been synthesised and evaluated. Firstly, a biocompatible stir-bar was prepared by physically coating alkyl-diol-silica (ADS) RAM. This ADS-RAM stir-bar was able to simultaneously fractionate the protein component from a biological sample, while directly extracting the analytes (caffeine and its metabolites) [101]. Therefore, the sample preparation time was minimised and the potential sample preparation artefacts were eliminated since precipitation of proteins was not required. Secondly, a MIP-film was prepared by precipitation of the polymer, based on nylon-6, in the presence of the template molecule (an organophosphate insecticide: monocrotophos) and coated onto the surface of a stir-bar [102]. Compared with PDMS stir-bar, the MIP-coated film showed not only a high selectivity but also a rapid equilibrium adsorption.

Despite all these efforts, there is still the need for a polymeric material that allows better sensibility to recover a broad group of polar organic compounds, enlarging further SBSE applicability.

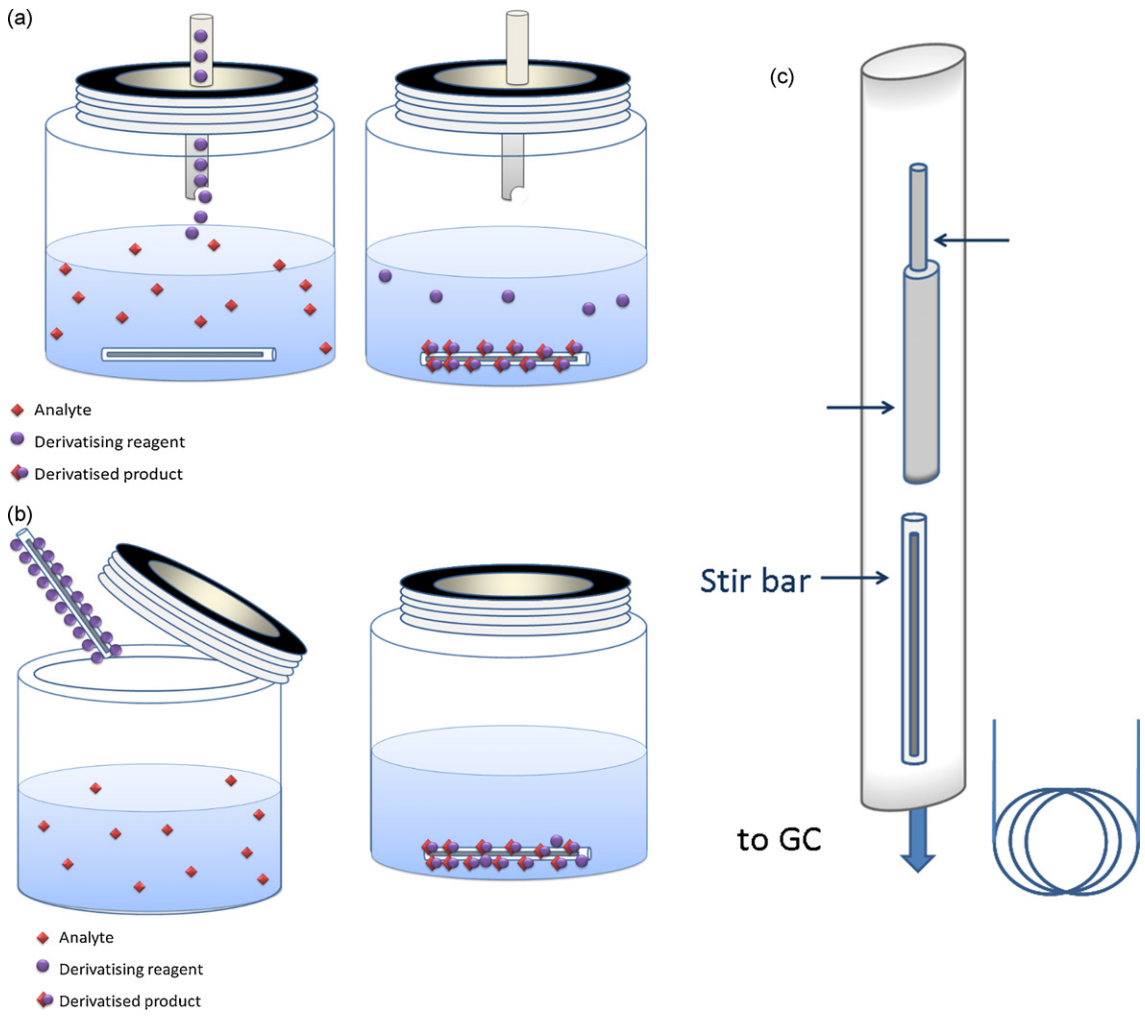

Fig. 5. Different derivatisation modes in SBSE: in situ (a), on-stir-bar with the derivatisation reagent preloaded before exposure to the sample (b) and in-tube derivatisation (c).

5.2. Derivatisation

Derivatisation of polar and thermally labile compounds is one of the most used alternatives to implement SBSE. Different derivatisation strategies can be employed in situ, on-stir-bar or post-extraction.

In situ derivatisation is the simplest approach. Derivatisation occurs in the aqueous sample before, or simultaneously, with the extraction step (see Fig. 5a). Thus, the desired derivatives are formed first and then extracted into the PDMS phase. It improves both the affinity of the analyte for the PDMS phase and the subsequent GC separation. However, the major limitation of the approach using direct derivatisation in the sample is that it is not applicable to moisture-sensitive reactions.

On-stir-bar derivatisation can be performed either by preloading the stir-bar with the derivatisation agent, so the reaction takes place as soon as analytes are incorporated in the PDMS phase (simultaneous extraction and derivatisation) (see Fig. 5b) or by first concentrating the analytes in the PDMS phase and then exposing the stir-bar to the vapour of the derivatisation agent (extraction followed by derivatisation).

The last strategy (post-extraction) can be performed with both thermal desorption (in-tube) and liquid desorption (in-extract). In the former case, a small glass capillary tube containing the derivatisating agent is placed with the stir-bar in the desorption chamber (see Fig. 5c). In the latter case, the derivatisation reagent is added to the organic solvent after stir-bar desorption. The most suitable approach depends on the properties of the analytes and the derivatisation reaction to be carried out.

Both in situ acylation (normally acetylation) and in-tube silylation are the most widely used derivatisation techniques. In the first approach (in situ acetylation with anhydride acid acetic at basic sample pH) the derivatisation of analytes containing phenolic moieties has been performed, e.g. chlorophenols and APs [28,29,103,104], estrogens and xenoestrogens [24,105–108], derivatives of benzophenone [109] and hydroxy-PAHs [110,111]. This approach improves both the extraction efficiency, because $\log K_{o,w}$ increases, and sensitivity in the GC analysis, e.g. the in situ derivatisation of BPA with anhydride acid acetic exhibited approximately a 100-fold higher sensitivity than the method without derivatisation [107]. In addition, anhydride acid acetic has been used in many studies for acylation of a hydroxyl group by on-stir-bar derivatisation after extraction [36,105,112].

Silylation can be used to derivatise a wide range of functional groups, such as aromatic and aliphatic alcohols, carboxylic acids, amines and amides. Since silylating agents are very sensitive to traces of water and other protic sorbents, derivatisation is performed post-extraction. N-(tert-butyldimethylsilyl)-N-methyltrifluoroacetamide (MTBSTFA) has been applied for in-extract derivatisation of phenolic compounds and acidic pharmaceuticals and herbicides [54]. Because of its high volatility, N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) was selected for

in-tube derivatisation [28]. The responses obtained for APs by SBSE and TD-GC-MS without derivatisation, with in situ acetylation and in-tube silylation have been compared by Kawaguchi et al. [28]. Both derivatisation approaches in situ acetylation and in-tube silylation improved the sensitivity as compared to without derivatisation. Among the two derivatisation approaches, in situ acetylation provided better sensitivity for the compounds with hydrophilic properties because the affinity of the compounds for the PDMS phase increases whereas in-tube silylation provided better results for the analytes with hydrophobic properties [28].

Other reagents have been used for in situ derivatisation, such as ethyl chloroformate (ECF) for carboxyl and amine groups [31,113], sodium tetraethylborate ($NaBEt_4$) [18,42,114] or tetrapropylborate ($NaBPr_4$) [39] for organomercury and organotin compounds and 2,3-diaminonaphthalene (DAN) for the determination of a-oxoaldehydes [115]. ECF acts as an acylating reagent and has been compared with anhydride acid acetic for the determination of acetaminophen in urine [21] and fluoxetine in plasma [113]. The carbonate or carbamate derivatives (products of the reaction with ECF) showed higher affinity for the PDMS coating than the acetylated ones. However, the addition of ethanol and pyridine to the aqueous sample, necessary for the ECF reaction, can decrease the distribution of the solutes into de PDMS phase. For that reason, the derivatisation mixture needs to be diluted with water after derivatisation and before SBSE sampling [21]. $NaBEt_4$ and $NaBPr_4$ act as alkylating reagents and have been used for the determination of MeHg [16] and organotin compounds [16,18]. Neng et al. [115] used DAN for the determination of glyoxal and methylglyoxal in environmental and biological matrices. In this case, chromophore and non-polar adducts 1,4-diazaantracene and 2-methyl-1,4-diazaantracene are formed. Furthermore, aldehydes and ketones can be converted into oximes by reaction with (2,3,4,5,6-pentafluorobenzyl)hydroxylamine (PFBHA), either directly in the sample (in situ) or on the stir-bar previously loaded with PFBHA (on-stir-bar), using the HSSE mode [112,116]. A comparison between these two modes revealed that the extraction efficiency of aldehydes from beer was slightly higher by in situ derivatisation [112,116].

Two of these approaches in situ and on-stir-bar or post-extraction derivatisation can be combined to improve sensitivity in the determination of compounds containing different functional groups. An example of this is the determination of estrogens [105,108] by in situ acetylation of the phenolic moiety, which increases the affinity of the compounds for the PDMS phase, followed by on-Twister acetylation or in-tube silylation of the aliphatic alcohol, which improves the peak shape and thus the minimum amount detectable by GC–MS. The combination of in situ acetylation and in-tube silylation exhibited approximately a 5-fold higher sensitivity than the in situ acylation method, 10-fold higher sensitivity than the in-tube silylation method, and 250-fold higher sensitivity than the method without derivatisation [108]. Another example is the determination of 4-hydroxynonenal, which first is converted into its oxime derivate by reaction in situ with PFBHA and later its aliphatic alcohols are acetylated by on-stir-bar reaction with anhydride acid acetic [112].

5.3. Matrix effect

Like in many other sample preparation techniques for trace analysis, the efficiency of SBSE can be strongly affected by the complexity of the matrix involved [17,117]. For instance, substantial levels of dissolved or suspended inorganic or organic matter contained in environmental matrices may interfere with the extraction of the target compounds by either PDMS or other phases and, therefore, the extraction yield may drastically change from sample to sample. In food analysis also, a significant extraction efficiency decrease is observed in comparison with pure water due to the large variability in ionic strength, pH or sugar and fat contents, among others [118].

One way to minimise matrix effect is based on the use of surrogates from the very beginning of the analytical procedure. If the extraction efficiency decrease for both the analyte and the surrogate are similar, the surrogate signal may compensate for the matrix effect [62,66,83]. In this sense, isotopically labelled surrogates are the ideal. However, in certain cases, the use of isotopically labelled surrogates does not compensate for matrix effect. For instance, the use of ^{2}H-labelled PAHs and ^{13}C-PCBs did not compensate for the organic matter presence in natural waters [66]. Besides, even if matrix effects can be compensated by the use of an appropriate standard, efforts should be made to eliminate these co-eluting compounds, since their presence will reduce method sensitivity. When analysing low concentrated samples, this can lead to false negative results [119].

Another way to compensate matrix effect is based on standard addition calibration and this method was preferred to the conventional external calibration in some studies [1,16,47,50,59,72,75,118,120–122] in order to provide the level of accuracy required for the trace analysis in a variety of environmental samples. However, the standard addition method can be tedious for routine analysis when a large number of samples must be processed and different standard additions must be performed in each sample.

6. Novel application fields

One overview of SBSE application in environmental, food and biomedical analysis is included in Tables 1–3. In a first attempt we considered to include information such as theoretical and apparent recoveries, due to the added value of these parameters. However, we had to discard this option since in many works the terms theoretical recovery and apparent recovery are mixed-up. In future works we recommend authors working on SBSE to clearly state whether theoretical or apparent recoveries are being calculated, following the guiding procedures of IUPAC [12].

In the following sub-sections we will describe in more detail some novel applications of SBSE: passive sampling, solid sample pre-concentration and multi-residue analysis.

6.1. Passive sampling

One of the fields where the use of SBSE, or more precisely PDMS-coated rods and films, is gaining interest is in passive sampling. In fact, passive sampling is one of the tools that is more thoroughly studied and used in long-term monitoring and also as a bio-mimetic extraction technique, as it has been deeply described in several recent reviews [123–125]. One of the key features of the sorptive techniques applied to passive sampling is that it allows the equilibrium sampling strategy, as it can be seen from the sorption time profile given in Eq. (1). Following this approach it is possible to overcome the drawbacks of sorption kinetics once the equilibrium state between the sampler and the media is assured [13]. This way, instead of measuring the total concentration of a given compound in a complex media, the freely dissolved concentration in that media is determined. As it has been shown in the literature [126], based on a truly partitioning of the analyte among the different compartments in which it can be associated with (freely dissolved, organic matter, fat content, particulate matter, headspace, etc.) and assuring a non-depletive sorption by the passive sampler (i.e. a recovery, as defined in Eq. (4), lower than 5%), it is possible to understand the distribution of chemicals in complex systems. As can be seen from Fig. 4a and b, in the case of the small-

est SBSE stir-bars (24 μL), sample volumes higher than 1 or 10 L are required to assure non-depletive extractions for many hydrophobic compounds ($\log K_{o,w} > 4$). In the literature, there are several fundamental works that describe the configurations and the calibration methods of these equilibrium sampling devices, essentially the SPME [127] and their applications in further environmental issues [128,129]. Additionally, in order to overcome the disadvantages of the low sampling rate as a consequence of the small surface area/diffusion path ratio of the SPME, membrane enclosed PDMS or silicone rods and stir-bars (MESCO) have been studied [86,130–133].

6.2. SBSE as pre-concentration of solid samples

Although most applications of SBSE are directed to the pre-concentration of aqueous matrices, applications to the determination of solid samples can also been found in the literature (see Tables 1–3). The use of SBSE after solid–liquid extraction is not only useful for pre-concentration but it also avoids clean-up and reduces matrix effects [80,134].

In most cases a solid–liquid extraction is performed using ultrasonic extraction (USE) [47,59,74,92,135–141], microwave-assisted extraction (MAE) [80], accelerated solvent extraction (ASE) [142] or pressurised subcritical water extraction (PSWE) [134]. In all the cases the solid–liquid extraction is performed in a water-miscible solvent (ethanol, MeOH, acetone, ACN, dichloromethane, . . .) or solvent mixtures in order to dilute the extract in water prior to SBSE. Once the extraction is performed, the organic extract is diluted in water before SBSE. The percentage of the organic solvent is usually the most influencing variable, since high organic solvent content can diminish the recovery obtained for SBSE [74,134,137,139] and can also damage the PDMS polymer [80].

In some other works that deal with solids, the sample is not previously extracted and a direct SBSE extraction is performed [143–150]. In those cases the solid sample is either suspended in an aqueous solution and the stir-bar is dipped into the suspension [143–145,147,150] or HSSE is performed [147,148,151].

6.3. SBSE for multi-residue analysis

In the case of multi-residue analysis, the problem arises when extraction conditions for the different solutes are different. This problem can be solved by adopting some consensus conditions [16,42,66,83]; however, this leads to a decrease in sensitivity. In the case of SBSE this can be solved either in the multi-shot or in the sequential modes.

6.3.1. Multi-shot or dual mode

In the multi-shot mode different sample aliquots are extracted under the same or different extraction condition using a coated stir-bar per sample and, then, the stir-bars are simultaneously desorbed in the TDU unit (see Fig. 6) [26]. When the different sample aliquots are extracted under the same chemical conditions, an increase in sensitivity is only searched for certain analytes that are best extracted under the same conditions. For instance, SBSE in the multi-shot mode was used for the determination of estrogens in river water samples [26]. The authors compared the limits of detection (LODs) obtained for 10 and 50-mL aliquots extracted in the single-shot mode and five 10-mL aliquots that were analysed in the multi-shot mode. LODs for estrone (E1), 17β-estradiol (E2) and 17α-ethynylestradiol (EE) were 1, 2 and 5 pg/mL, respectively, for 10-mL in the single-shot mode after in situ derivatisation. LODs improved for 50-mL down to 0.5, 1 and 2 pg/mL for E1, E2 and EE, respectively. The multi-shot mode using five stir-bars yielded LODs down to 0.2, 0.5 and 1 pg/mL for E1, E2 and EE, respectively.

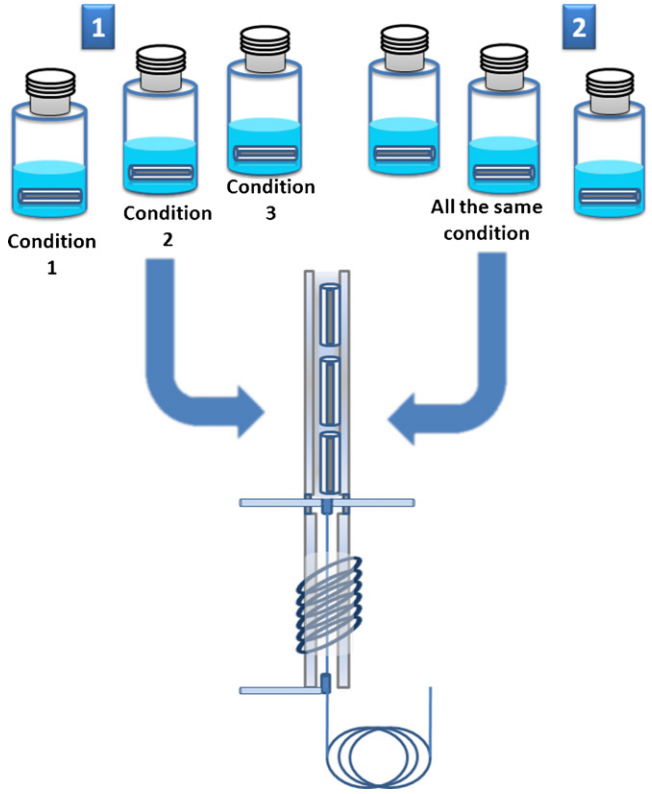

Fig. 6. SBSE in the multi-shot mode.

A different approach was developed by Splivallo et al. [151] who analysed volatile organic compounds (VOCs) produced by the fruiting of truffles by HSSE. In this case two or three stir-bars were suspended onto an iron pin which was placed in the headspace of the same sample. The stir-bars were then simultaneously desorbed.

However, when analytes are best extracted under different chemical conditions, in multi-residue analysis, for instance, where a large number of compounds are being targeted, different sample aliquots can be treated under different chemical conditions and the stir-bars can be simultaneously desorbed onto the gas chromatograph. In this sense, Ochiai et al. [75] developed a multi-residue screening method for the determination of 85 pesticides (organochlorine pestices, OCPs, carmabate pesticides, OPPs, pyrethroid pesticides and others) in food matrices (vegetables, fruit and green tea) using what they called dual SBSE combined with TD-GC-MS. The USE methanol extract was diluted in water before SBSE. One extraction was performed on a 2-fold diluted extract (mainly targeting compounds with high $\log K_{o,w}$) and another extraction was performed on a 5-fold diluted extract (targeting compounds with low and medium $\log K_{o,w}$ values). In a similar work, Ochiai et al. [72] optimised a dual SBSE method for the previously mentioned families of pesticides in aqueous samples (river water and brewed green tea samples). While recovery of more hydrophilic pesticides ($\log K_{o,w} < 3.5$) dramatically increased on increasing concentration of NaCl, recovery for more hydrophobic solutes ($\log K_{o,w} > 3.5$) decreased in the presence of NaCl. Thus, the authors proposed a dual SBSE where one 20-mL aliquot was extracted after the addition of NaCl at a 30% of concentration and the second aliquot was extracted unmodified. Similarly, Van Hoeck et al. [152] developed a multi-residue method for screening endocrine-disrupting compounds (EDCs) and pharmaceuticals in aqueous samples by multi-stir-bar sorptive extraction-single desorption–GC–MS. Four different sample aliquots were submitted to SBSE under different conditions in order to accomplish the determination of a wide range

of EDCs (phenolic EDCs, amine-based EDCs, acidic EDCs, organotin compounds and EDCs with $\log K_{o,w} > 5$). The four stir-bars and a glass wool plug with BSTFA were placed in a TD tube and were simultaneously analysed by GC–MS.

6.3.2. Sequential SBSE

In sequential SBSE, the extraction conditions of a single sample aliquot are modified depending on the analytes to be extracted [153] using one or more stir-bars. A single stir-bar only can be used when no organic modifier (MeOH, for instance) is added during the second extraction conditions.

Ochiai et al. [153] optimised a sequential SBSE method for the multi-residue analysis of pesticides. A single sample aliquot was sequentially extracted under different conditions using two different stir-bars. Firstly, a 5-mL sample aliquot was extracted without addition of NaCl. After the first extraction was accomplished, the first stir-bar was removed and 30% of NaCl was dissolved in the sample. A second stir-bar was then added and the second extraction was performed. The sequential approach eliminated the negative effect of the solutes with $\log K_{o,w}$ higher than 4.0, while maintaining an increased recovery for hydrophilic solutes with salt addition. Besides, a much higher recovery (39–109%) of a wider range of pesticides could be obtained using the proposed method compared to the previously mentioned dual SBSE procedures [72,75], even with a smaller sample volume (5 mL).

7. Concluding remarks

SBSE has already shown its maturity among the extraction techniques since it has been fully understood in terms of thermodynamical and kinetical features and since the development of analytical methods has covered many analytical requirements. There are, however, many issues that require further research in the methodology as well as in the automatisation.

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