Spectrochimica Acta Part B 64 (2009) 1–15

Contents lists available at ScienceDirect

Spectrochimica Acta Part B

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

Review

Miniaturized preconcentration methods based on liquid–liquid extraction and their application in inorganic ultratrace analysis and speciation: A review

Francisco Pena-Pereira, Isela Lavilla, Carlos Bendicho *

Departamento de Química Analítica y Alimentaria, Area de Química Analítica, Facultad de Química, Universidad de Vigo, Campus As Lagoas-Marcosende s/n, 36310 Vigo, Spain

ARTICLE INFO

Article history:
Received 27 May 2008
Accepted 24 October 2008
Available online 6 November 2008

Keywords:
Miniaturization
Sample preparation
Liquid-liquid microextraction
Ultratrace elemental analysis
Speciation

ABSTRACT

Liquid–liquid extraction (LLE) is widely used as a pre-treatment technique for separation and preconcentration of both organic and inorganic analytes from aqueous samples. Nevertheless, it has several drawbacks, such as emulsion formation or the use of large volumes of solvents, which makes LLE expensive and labour intensive. Therefore, miniaturization of conventional liquid–liquid extraction is needed. The search for alternatives to the conventional LLE using negligible volumes of extractant and the minimum number of steps has driven the development of three new miniaturized methodologies, i.e. single-drop microextraction (SDME), hollow fibre liquid-phase microextraction (HF-LPME) and dispersive liquid–liquid microextraction (DLLME). The aim of this paper is to provide an overview of these novel preconcentration approaches and their potential use in analytical labs involved in inorganic (ultra)trace analysis and speciation. Relevant applications to the determination of metal ions, metalloids, organometals and non-metals are included.

Contents

* Corresponding author. Tel.: +34 986 812281; fax: +34 986 812556.
E-mail address: bendicho@uvigo.es (C. Bendicho).

0584-8547/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.sab.2008.10.042

1. Introduction

Liquid–liquid extraction (LLE), based on transfer of analyte from the aqueous sample to a water-immiscible solvent, is being widely employed for sample preparation. Nevertheless, some shortcomings such as the emulsion formation, the use of large sample volumes and toxic organic solvents and hence, the generation of large amounts of pollutants makes LLE expensive, time-consuming and environmentally unfriendly.

Miniaturization of this extraction technique can be achieved by a drastic reduction of the extractant phase volume. Based on this premise, three new methodologies have arisen, i.e., single-drop microextraction (SDME), hollow fibre liquid-phase microextraction (HF-LPME) and dispersive liquid–liquid microextraction (DLLME).

SDME is a preconcentration technique based on the use of a microdrop of extractant exposed to the sample solution (Direct-SDME or continuous-flow microextraction (CFME)), to a thin organic extraction phase (of lower density than water) layered over the aqueous sample (liquid–liquid–liquid microextraction, LLLME), or to the headspace above the sample when analytes are volatile or semi-volatile (headspace single-drop microextraction, HS-SDME). In HF-LPME using the two-phase sampling mode, a hydrophobic hollow fibre is used to protect and expose a certain volume of extractant to the sample. The extraction process occurs in the pores of the hollow fibre, where the solvent is immobilised. In the three-phase sampling mode (hollow fibre liquid–liquid–liquid microextraction, HF-LLLME), the analytes are extracted into an organic layer which fills the pores of the hollow fibre and then back-extracted into an aqueous phase placed inside the fibre. Although HF-LPME has been widely applied to the determination of organic compounds, especially in biological and environmental samples, the use of this technique in the inorganic field is still scarce. DLLME is based on the cloudy solution formed when an appropriate mixture of an extraction solvent and a disperser solvent is quickly injected into the aqueous sample. The water-immiscible extractant solvent should have higher density than water, while the disperser solvent should be miscible in the extractant solvent and the aqueous sample. The fine droplets of extraction solvent are dispersed throughout the aqueous sample, allowing its interaction with the analyte.

The development of the different modes of SDME along with HF-LPME and DLLME offers new possibilities over the classical liquid–liquid extraction. So far, no reviews have been published specifically addressing applications of miniaturized extraction techniques to the inorganic field.

Researchers have named the microextraction techniques discussed here in very different ways. For instance, SDME is also known as 'solvent drop microextraction', '(static) liquid-phase microextraction', '(immersed) solvent microextraction', 'single drop extraction' and 'single drop liquid phase microextraction'. Moreover, in some cases the same name has been given to different microextraction techniques. This is the case of the term 'liquid-phase microextraction (LPME)', which has been used to refer to SDME and to HF-LPME. In order to unify the nomenclature and avoid any misunderstanding, we will refer to 'single-drop microextraction' when the acceptor phase displays a drop configuration and to 'liquid-phase microextraction' when immiscible liquid films are employed for the acceptor phase. In the same way, we will refer to 'extractant phase' recognizing that organic solvents are not the only means to extract the analytes of interest.

Determination of the total amount of an element at ultratrace level is relevant, but knowledge of the concentrations of individual species is needed for assessing its toxicity and bioavailability. Speciation analysis refers to the activity of identifying and measuring species including isotopic composition, conformation, oxidation or electronic state, inorganic compounds and complexes, organometallic compounds and organic and macromolecular complexes [1].

In this review, an overview of modern liquid–liquid microextraction techniques to ultratrace inorganic analysis and elemental speciation is provided, covering relevant applications appeared over the last five years.

2. Miniaturization of conventional liquid–liquid extraction

The development of simplified and miniaturized methods of LLE based on the use of drops was not as trivial as could be initially thought because of the difficulty to incorporate the drop in an analytical system. Liu and Dasgupta developed the first drop-based extraction approach to the determination of NH_3 and SO_2 content in air samples [2]. The method was based on the natural ability of the rain drops to collect soluble gases. The determination of NH_3 was carried out after its collection into an acidic aqueous drop and post-derivatization to form indophenol blue, while a conductivity detector allowed the determination of SO_2 in the drop after its conversion to sulphuric acid using Mn-catalyzed oxidation by H_2O_2. In the last years, several microlitre systems such as liquid droplets at the tip of a capillary [3–7], supported liquid films/droplets [8] and continuous forming and falling drop systems [9,10], have been developed for determination of trace gases in air samples. An appropriate review chapter discussing these approaches can be found in the literature [11]. In 1996, Liu and Dasgupta developed another extraction system based on the use of a microdrop of chloroform suspended in a larger aqueous drop of sample to extract sodium dodecyl sulphate (SDS) after the formation of a coloured ion pair with methylene blue [12]. At almost the same time, Jeannot and Cantwell introduced a system based on the use of a Teflon rod to expose a drop of 8 μL of n-octane containing n-dodecane as internal standard in a stirred aqueous solution in order to extract 4-methylacetophenone [13]. After the extraction for a prescribed time, a 1 μL aliquot of the organic phase was taken with a microsyringe and injected into the GC for quantification. In 1997, Jeannot and Cantwell proposed for the first time a technique now known as single-drop microextraction, which involved an improvement over the previous attempts due to its technical simplicity [14].

2.1. Single-drop microextraction (SDME)

SDME is a simple, low-cost, fast and virtually solvent-free sample preparation technique based on a great reduction of the extractant phase-to-sample volume ratio. SDME is not exhaustive, and only a small fraction of analyte(s) is extracted/preconcentrated for analysis. From its first publication in 1997 [14], SDME has been used an extraction technique for numerous analytes, although almost only in the organic field. In fact, the first publication of this methodology in the inorganic field appeared in 2003, when Chamsaz used the headspace mode to determine As(III) and total As by ETAAS [15]. Since then, the number of publications has significantly grown, and the great potential of SDME has been demonstrated. Four modes of SDME have been used to extract/preconcentrate inorganic analytes: direct single-drop microextraction (Direct-SDME), headspace single-drop microextraction (HS-SDME), liquid–liquid–liquid microextraction (LLLME) and continuous-flow microextraction (CFME).

2.1.1. Direct single-drop microextraction (Direct-SDME)

Direct single-drop microextraction (Fig. 1A) is based on the exposure of a microdrop of water-immiscible extractant phase suspended from the tip of a microsyringe needle to a stirred aqueous sample. After extracting for a prescribed period of time, the drop is retracted back into the microsyringe needle and finally injected into the detector to obtain the corresponding analytical signal.

Since two liquid phases are in direct contact with each other, in the absence of any porous solid support at the interface, then when one of the phases is mechanically stirred (i.e. directly convected), the other will also experience convective mixing. This occurs because the first phase transfers momentum to the second phase as a result of frictional

drag at the LL interface. This is true regardless of whether the second phase is layered over (or under) the first or whether it has the form of a microdrop suspended in the first phase, as it happens with Direct-SDME [16].

Mass transfer of the analytes from the aqueous to extraction microdrop continues until thermodynamic equilibrium is attained or extraction is stopped. A theoretical model based on film theory of convective-diffusive mass transfer has been developed by Jeannot and Cantwell for Direct-SDME [14]. Film theory convective–diffusive mass transfer assumes no movement of the solution at the layer immediately adjacent to the interface and a gradually increasing vigorousness of convection of the solution at location further away from the interface. Considering the film theory under this condition, instantaneous and complete convective mixing exists in the bulk solution to some distance δ, the Nernst diffusion film, away from the liquid–liquid interface. The liquid layer of thickness δ, called the Nernst diffusion film, is postulated to be completely stagnant and nonconvected, so that analytes cross it by pure diffusion only. At faster stirring rates, δ decreases causing the increase of the extraction rate [16].

Direct-SDME requires the use of a water-immiscible extractant phase and analytes more soluble in the extractant phase than in the sample solution [17].

The main drawbacks of Direct-SDME are due to the instability of the drop at high stirring rates or temperatures, especially when samples are not perfectly clean. Moreover, solvents with relatively high water solubility and low boiling points are not suitable for Direct-SDME because of their high rate of dissolution or evaporation. Acidic samples such as digests obtained upon acid digestion procedures or the presence of large non-polar species that can saturate the organic phase could be troublesome when applying this microextraction mode.

2.1.2. Headspace single-drop microextraction (HS-SDME)

HS-SDME (Fig. 1B), introduced by Theis et al. for the first time [18], is a sample preparation technique which allows extraction and preconcentration of volatile or semi-volatile compounds into a microdrop exposed to the headspace above the sample. Microextraction, preconcentration and derivatization in a single drop can be performed by exposing a hanging drop containing the derivatizing agent to the gaseous phase [19]. Mass transfer in the headspace is a fast process owing to the large diffusion coefficients in the gas phase (~10^4 greater than corresponding diffusion coefficients in condensed phases). Agitation of the sample solution improves mass transfer in the aqueous phase and induces the convection in the headspace. Therefore, thermodynamic equilibrium between the aqueous and vapour phases can be achieved rapidly. The overall rate of mass transfer is limited by both the aqueous-phase stirring rate and the diffusion of analytes within the extraction phase [18]. Nevertheless, mass transfer in the sample aqueous phase unequivocally is not a slow step when microextraction and derivatization are performed in the drop, as reported Fiamegos and Stalikas [19]. This microextraction mode, valid for the analysis of complex samples, can achieve a high degree of extract clean-up because non-volatile compounds and high molecular weight species are not extracted in the drop placed in the headspace. Aqueous drops and organic solvents with high boiling point have been used as extractant phases for inorganic analytes when HS-SDME is applied. This microextraction mode has been mostly used to determine metalloids, organometals and non-metals. For clean and compatible matrices, either HS-SDME or Direct-SDME can be used. Volatile analytes or suitable derivatization procedures yielding volatile species are required for the successful application of HS-SDME. Unlike the typical use of HS-SDME in combination with GC for applications in the organic field, solvents do not need to have high vapour pressure when this microextraction mode is employed in conjunction with atomic detectors without prior GC separation.

2.1.3. Liquid–liquid–liquid microextraction (LLLME)

LLLME (Fig. 1C) is a mode of microextraction suitable for ionisable analytes, which was developed by Ma and Cantwell in 1999 [20] under the name "solvent microextraction with simultaneous back-extraction". LLLME is based on the extraction of analytes from the aqueous stirred sample into an organic layer or membrane with lower density than water and simultaneous back-extraction into an aqueous microdrop. Direct convection (stirring) in one phase (aqueous sample) results in indirectly induced convection in the other two phases (organic layer and aqueous microdrop) as a result of momentum transfer across both LL interfaces [16]. The pH of the aqueous solution and the aqueous microdrop can be adjusted to obtain firstly the neutral form of the analyte, extractable by the organic solvent, and then ionise it. Finally, the ionised analyte is extracted into the drop. Another possibility could be the use of two different complexants, one added to the sample solution and the other dissolved in the aqueous drop. In this way, the formation of a neutral complex allows its extraction into the organic layer and, if the aqueous microdrop contains a complexant which forms a stronger complex with the analyte, its back-extraction into the drop. Although LLLME is more difficult to accomplish compared to other SDME modes, separation

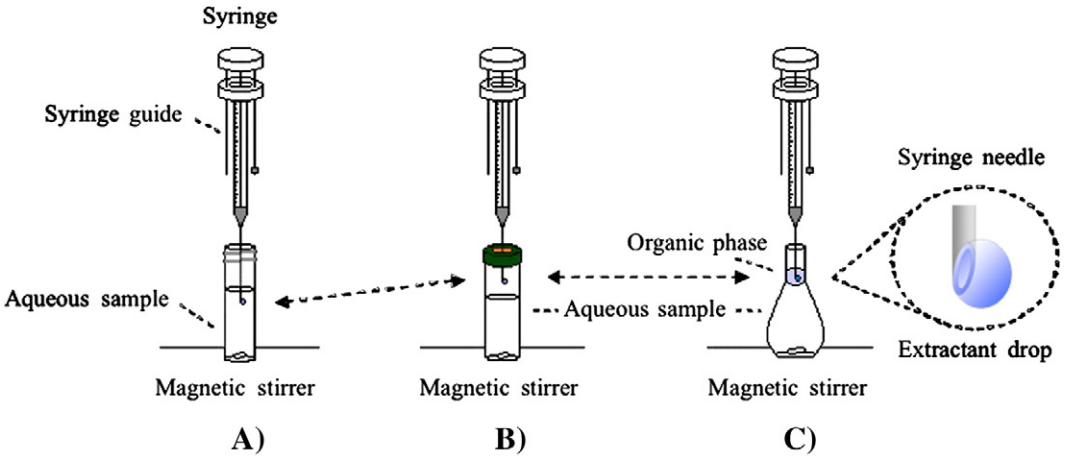

Fig. 1. Schematic representation of (A) direct single-drop microextraction (Direct-SDME), (B) headspace single-drop microextraction (HS-SDME) and (C) liquid–liquid–liquid microextraction (LLLME).

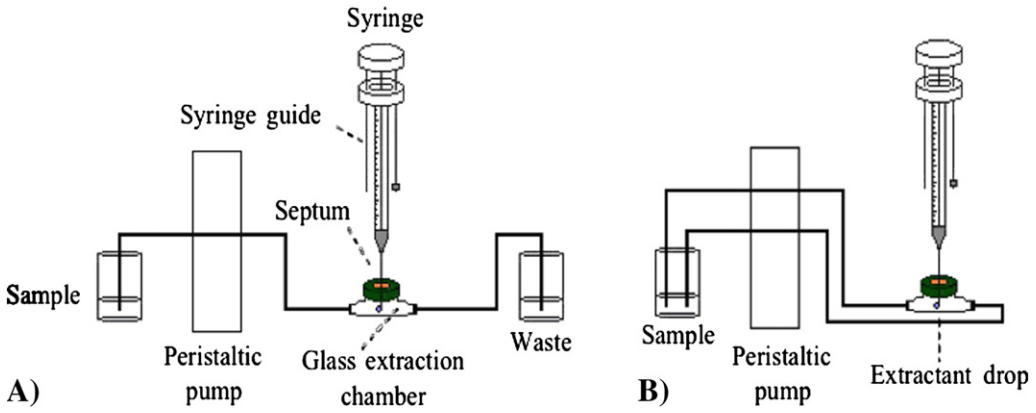

Fig. 2. Schematic representation of (A) continuous-flow microextraction (CFME) and (B) cycle-flow microextraction.

techniques such as RP-HPLC or CE can be used after preconcentration with LLLME, given that the extract has aqueous nature.

2.1.4. Continuous-flow microextraction (CFME)

Continuous-flow microextraction (Fig. 2A) is another mode of SDME, first reported by Liu and Lee [21], wherein the extraction is carried out in a glass extraction chamber instead of a vial. The sample, instead of being stirred, is pumped continuously at a constant flow rate and, when the extraction chamber is full of sample, a drop is formed at the tip of a microsyringe needle. In contrast to the above SDME microextraction modes, a solvent drop makes contact with a fresh and flowing sample solution. In CFME the flow induces mass transfer in the drop via momentum transfer (the extraction phase indirectly experiences convection as a consequence of convection of the aqueous sample). The rate of extraction increases with increasing flow rate of the aqueous solution, consistent with a decrease in thickness of the Nernst diffusion films [16]. This mode facilitates mass transfer and high preconcentration factors can be achieved.

Sample flow rate should ensure an effective microextraction of analytes without drop dislodgement or bubble formation. Like Direct-SDME, samples should be perfectly clean to enhance the stability of the drop at the tip of the needle. Xia et al. [22] reported a modification of this microextraction mode, called cycle-flow microextraction (Fig. 2B), with its introduction into the waste outlet tube from the sample reservoir. CFME has been used to extract transition metals by in-drop complexation of metal ions, although the conceivable possibilities for Direct-SDME can be applied to CFME. A revision of the different modes of SDME, including CFME, and their combination with different analytical techniques, can be found in a recent review [23].

2.2. Hollow fibre liquid-phase microextraction (HF-LPME)

Hollow fibre liquid-phase microextraction [24] is a technique which allows extraction and preconcentration of analytes from complex samples in both a simple and inexpensive way. In the two-phase LPME sampling mode (HF-LPME), the analyte is extracted from an aqueous sample to a water-immiscible extractant immobilised in the pores of a hollow fibre [25], typically made of polypropylene and supported by a microsyringe (Fig. 3A). In this sampling mode, the acceptor phase is organic, i.e., compatible with atomic detectors for total determination as well as GC and HPLC for the coupling of chromatographic separation techniques to atomic detectors.

In the three-phase sampling mode (HF-LLLME), limited to analytes with ionisable functionalities, the analyte is extracted from an aqueous sample through the water-immiscible extractant immobilised in the pores of the hollow fibre and ultimately into an aqueous phase inside the lumen of the hollow fibre (Fig. 3B). As the acceptor phase is aqueous in this microextraction mode, the technique should be compatible not only with atomic detectors for determination of totals, but also with hyphenated techniques involving HPLC or CE separations for speciation.

Solvent impregnation of the fibre is essential since extraction occurs on the surface of the immobilised solvent. The pores of a porous hydrophobic polymer membrane are filled with an organic liquid, which is held by capillary forces [26]. The extractant should have a polarity matching that of the hollow fibre to be easily immobilised within its pores. In general, the extraction efficiency achieved with HF-LPME is higher than with Direct-SDME, since hydrophobic hollow fibres allow the use of vigorous stirring rates to accelerate the extraction kinetics. Moreover, the contact area between the aqueous sample and the extractant phase is higher than in the case of SDME, favouring the mass transfer rate. The use of the hollow fibre provides protection of the extractant phase and hence, the analysis of dirty samples is feasible. Moreover, the small pore size allows microfiltration of the sample, thus yielding very clean extracts.

However, it should be noted that this technique suffers from some drawbacks since the manipulation of the hollow fibre at the time of placing it at the tip of the needle of the microsyringe before the microextraction process could be a source of contamination. Two reviews [25,27] describe this interesting technique in detail.

2.3. Dispersive liquid–liquid microextraction (DLLME)

Dispersive liquid–liquid microextraction (DLLME) (Fig. 4), introduced by Rezaee et al. [28] is a simple and fast microextraction technique based on the use of an appropriate extractant, i.e., a few microlitres of an organic solvent with high density such as tetrachlorometane, chloroform, carbon disulphide, nitrobenzene, bromobenzene, chlorobenzene or 1,2-dichlorobenzene, and a

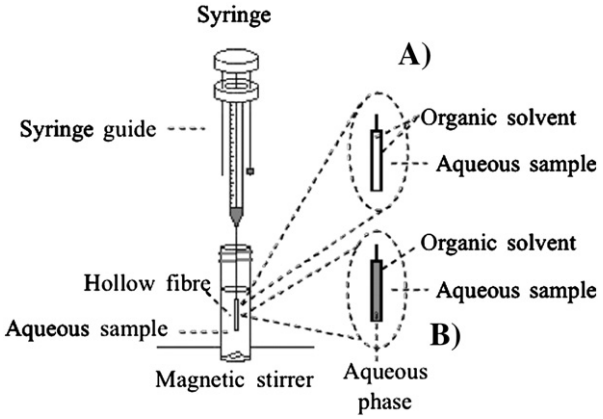

Fig. 3. Schematic representation of (A) hollow fibre liquid-phase microextraction (HF-LPME) and (B) hollow fibre liquid–liquid–liquid microextraction (HF-LLLME).

disperser solvent with high miscibility in both extractant and aqueous phase such as methanol, ethanol, acetonitrile or acetone. When the mixture of extractant phase and disperser is rapidly injected into the sample high turbulence is produced. This turbulent regimen gives rise to the formation of small droplets, which are dispersed throughout the aqueous sample. Emulsified droplets have large interfacial area. The nature of the emulsifier (disperser solvent) can also have an influence on droplet size distribution, the mean droplet size, and also on emulsion viscosity [29]. Liquid–liquid dispersions play an essential role in separation processes and reaction systems. This is because the large interfacial area due to dispersion facilitates mass transfer and reaction rate [30]. Turbidity is formed in the aqueous phase owing to the fine dispersion of the extractant distributed throughout the aqueous sample, which is facilitated by the disperser solvent. After formation of the cloudy solution, the surface area between extraction solvent and aqueous sample is very large, so the equilibrium state is achieved quickly and therefore the extraction time is very short. In fact, this is the principal advantage of DLLME. After centrifuging the cloudy solution, the sedimented phase at the bottom of a conical tube is recovered and used with the most appropriate analytical technique. In DLLME, dislike SDME, the syringe is not used as drop holder during the extraction process but in the collection and injection of the extract, thus avoiding problems such as drop dislodgment. Nevertheless, this technique is limited to a small number of extractants, which should efficiently extract the analytes of interest, since the required conditions, i.e., to have higher density rather than water, form a stable cloudy solution and be easily removed from the bottom of the conical vial after centrifugation, are met by a few organic solvents. In addition, this microextraction technique appears to be difficult to automate.

Very recently, Shemirani et al. developed a modification of the DLLME approach called “cold-induced aggregation microextraction” (CIAME) [31]. The procedure involves addition of an ionic liquid (IL), a non-ionic surfactant and a derivatizing reagent, if necessary, to an aqueous sample placed into a conical-bottom centrifuge tube. The dissolution of the IL in the sample is achieved by heating the centrifuge tube in a thermostated bath. After that, the centrifuge tube is placed in an ice bath, and like DLLME, a cloudy solution is obtained. The subsequent procedure is similar to that for DLLME. As the solubility of the IL increases with increasing salt content in the sample, the common ion effect can be employed by addition of another IL to decrease the solubility of the extractant phase, owing to the saline nature of ILs. Hence, two different ILs are needed to carry out the extraction of analytes in samples with high content of salt. Compared to DLLME, CIAME uses ILs instead of organic solvents as extractant phases, thus avoiding the use of a disperser solvent. Nevertheless, this methodology introduces several steps before centrifugation, so it is time consuming and, because of the high viscosity of ILs, the addition of a non-ionic surfactant to the sample as anti-sticking agent is needed since ILs adhere to the wall of the tube after centrifugation.

3. Extractant phases

Like LLE, the selection of an appropriate extractant phase is of major importance in SDME, HF-LPME and DLLME. The final choice should be made after comparing their different physical properties in order to achieve good sensitivity, precision and selectivity. A low extractant phase-to-sample ratio and a high distribution ratio, K, defined as the ratio of the concentrations of analyte in the extractant and aqueous phase at equilibrium, are needed to achieve high enrichment factors (i.e. ratio between the analyte concentration in the extractant phase and the initial concentration in the sample solution) and extraction efficiencies. Therefore, the K parameter, which depends to a large extent on the type and nature of the extractant phase, is a key variable, so it is necessary to emphasize the different extractant phases that can be used. Physical properties of the extractant phases to be used in SDME, HF-LPME and DLLME, such as boiling point, vapour pressure, water solubility, density, viscosity, surface tension, dipole moment and dielectric constant are given in Table 1.

In the two modes of SDME where the drop is immersed into the aqueous solution, i.e., Direct-SDME and CFME, the selection of the extractant should be based on a comparison of selectivity, extraction efficiency, incidence of drop loss, rate of drop dissolution (especially for faster stirring rates and extended extraction times) and level of toxicity [17]. A high boiling point reduces evaporative looses, while bubble formation can take place inside the drop when a solvent with a low boiling point such as benzene is used. A high surface tension increases the cohesive forces at the interface, hence reducing solvent solubilization. Ionic analytes can be complexed during the micro-extraction process within the drop by exposing a microdrop of extractant containing a complexing agent to the sample, or prior to SDME, by addition of the complexing agent to the sample and exposure of a drop of extractant to the pre-treated sample. In contrast to these two modes of SDME, it is possible with HS-SDME to use a microdrop of water or water-miscible organic solvents to extract volatile or semivolatile analytes. In principle, any extractant could be chosen when HS-SDME is employed, but in practice the extractant should have a high boiling point, and hence, a low vapour pressure, besides the ability to extract the analytes.

In the case of HF-LPME, the extractant should have a low solubility in water to avoid its dissolution and low volatility to reduce evaporation of the solvent during extraction. Additionally, the extractant should have a polarity matching that of the polypropylene

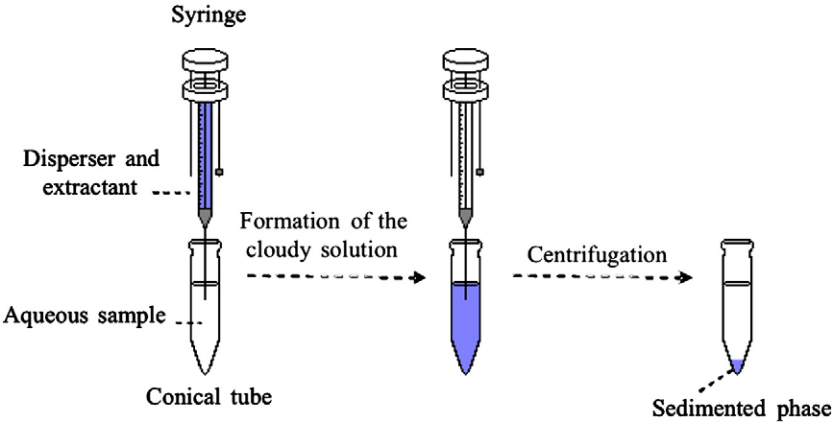

Fig. 4. Schematic representation of the dispersive liquid–liquid microextraction (DLLME) procedure.

fibre typically used in HF-LPME, so that it can be strongly immobilised within the pores of the hollow fibre to prevent leakage and, of course, high extraction efficiency for the target analytes. As in the case of Direct-SDME and CFME, air bubble formation should be avoided because they adhere to the hollow fibre surface, promoting solvent evaporation and low precision.

In DLLME, on the one hand, the extractant phase should have higher density than water, efficiently extract the targeted compounds, form a stable cloudy solution and have low solubility in water. On the other hand, the disperser solvent should be miscible in both the extraction solvent and aqueous sample.

3.1. Organic solvents

Organic solvents are, by far, the most used extractant phases with the three methodologies described in this review. In general terms, the choice of a proper organic solvent is based on the old principle 'like dissolves like' (*similia similibus solvuntur*), although it is advisable to take into account the physical properties of organic solvents according to the microextraction methodology (and the selected mode) applied, as explained above.

Atomic spectrometric detection techniques, i.e., electrothermal-atomic absorption spectrometry (ETAAS), electrothermal vaporization-inductively coupled plasma-mass spectrometry (ETV-ICP-MS) and electrothermal vaporization-inductively coupled plasma-optical emission spectrometry (ETV-ICP-OES) have been used for the determination of the majority of the analytes after their preconcentration by the microextraction techniques discussed here. Several aspects should be carefully studied when organic solvents are injected into a graphite furnace, especially in the case of chlorine containing organic solvents. The formation of volatile chlorides of analytes in the presence of chlorinated solvents seems to be the explanation for the significant losses of some analytes. Moreover, losses increase with increasing chlorine content in the organic solvent, being the highest with tetrachloromethane [32]. Furthermore, organic solvents can penetrate deeply into the graphite and their removal requires a high ashing temperature and a long pre-treatment step [33]. Permanent modifiers, such as Rh or Ir, have been used to minimize these problems when chloroform was selected as the extraction phase. Nevertheless, permanent modifiers also suffer from some drawbacks, such as: poorly reproducible treatment technologies, impaired efficiency compared with modifier addition to each sample aliquot; relatively short lifetimes; limitations imposed on temperature programs; applicability to relatively simple matrices, etc. [34].

3.2. Ionic liquids (ILs)

Room temperature ionic liquids (RTILs) are interesting alternatives to organic solvents because of their unique physicochemical properties, which depend on the nature and size of their cationic and anionic

Table 1
Physical properties of the extractants used in SDME, HF-LPME and DLLME

Extractant	Boiling point (°C)	Vapour pressure (Torr)	Water solubility (mg/L)	Density (g/cm^3)	Viscosity (cP)	Surface tension (dyn cm^{-1})	Dipole moment (D)	Dielectric constant
Organic solvents								
Cyclohexane	80.7	97.8	55	0.78	0.90	24.65	0.00	2.02 (20 °C)
n-Hexane	68.7	151.3	1.2	0.65	0.29	17.94	0.08	1.88
Octane	125.7	14.0	6.6×10^{-3}	0.70	0.51	21.18	0.00	1.95 (20 °C)
Iso-octane	99.2	49	2.4	0.69	0.50 (20 °C)	18.8	0.00	1.94 (20 °C)
Decane	174.2	1.3	0.05	0.73	0.86	23.37	0.00	1.99 (20 °C)
Benzene	80.1	95.2	1791	0.87	0.60	28.2	0.00	2.27
Toluene	110.6	28.5	515	0.86	0.55	27.92	0.31	2.38
o-Xylene	144.4	6.6	175	0.88	0.76	29.49	0.45	2.57 (20 °C)
m-Xylene	139.1	8.3	146	0.86	0.58	28.10	0.30	2.37 (20 °C)
p-Xylene	138.4	8.7	156	0.86	0.60	27.76	0.02	2.27 (20 °C)
Ethylbenzene	136.2	9.6	152	0.86	0.64	28.48	0.37	2.40 (20 °C)
Methanol	64.5	127.0	∞	0.79	0.55	22.30	2.87	32.66
Ethanol	78.3	59.0	∞	0.79	1.08	22.32 (20 °C)	1.66	24.55
1-Octanol	195.2	0.08	538	0.82	7.36	26.92	1.76	10.34 (20 °C)
Benzyl alcohol	205.4	0.11	800	1.04	4.65 (30 °C)	39.44	1.66	13.1 (20 °C)
Ethylene glycol	197.5	0.09	∞	1.11	13.76	48.49 (20 °C)	2.31	37.7
Acetone	56.1	231.1	∞	0.78	0.30	22.68	2.69	20.56
4-Methyl-2-pentanone (MIBK)	117.4	18.8	17000	0.80	0.55	23.64 (20 °C)	–	13.11 (20 °C)
α,α,α-Trifluorotoluene	102.0	38.5	–	1.18	0.57 (19.8 °C)	23.41 (20 °C)	2.56	9.03
Chlorobenzene	131.7	11.7	327	1.10 (20 °C)	0.72 (30 °C)	31.98 (30 °C)	1.62	5.62
Dichlorometane	39.6	435.8	1980	1.32	0.39 (30 °C)	26.54 (30 °C)	1.14	8.93
Chloroform	61.2	194.8	8500	1.48	0.54	26.53	1.15	4.81 (20 °C)
Tetrachloromethane	76.6	115.2	770	1.58	0.90	26.13	0.00	2.23
1,2-Dichloroethane	83.5	83.3 (20 °C)	8100 (20 °C)	1.25	0.73 (30 °C)	30.84 (30 °C)	1.83	10.37
1,2-Dichlorobenzene	180.5	1.3	156	1.30	1.32	26.48 (20 °C)	2.14	9.93
Tetrachloroethylene	121.1	18.5	150	1.61	0.80 (30 °C)	31.30	0.00	2.28
Bromobenzene	155.9	4.2	424	1.48	1.01 (30 °C)	35.09 (30 °C)	1.55	5.40
Nitrobenzene	210.8	0.28	1900 (20 °C)	1.20	1.62 (30 °C)	42.17 (30 °C)	4.00	34.78
Acetonitrile	81.6	88.81	∞	0.78	0.34	28.25	3.53	35.94
Pyridine	115.2	20	∞	0.98	0.88	36.33	2.37	12.91
N′N″-dimethylformamide	153.0	3.7	∞	0.94	0.80	36.42	3.24	36.71
Carbon disulfide	46.2	361.6	2100 (20 °C)	1.29	0.36 (20 °C)	32.25 (20 °C)	0.06	2.64
Ionic liquids								
[C_4MIM][PF_6]	–	–	18800	1.36–1.37	148–450	48.8–49.8	–	–
[C_6MIM][PF_6]	–	–	7500	1.29–1.31	560–586	–	–	–
[C_8MIM][PF_6]	–	–	2000	1.20–1.23	682–710	34.2–36.5	–	–
[C_6MIM][Tf_2N]	–	–	3400	1.33	–	–	–	–
Water	100.0	23.8	∞	1.00	0.89	71.81	1.82	78.36

All data were extracted from reference [99], except for ionic liquids, obtained from reference [35]. These properties were measured at 25 °C unless otherwise stated.

constituents. These include negligible vapour pressure, good thermal stability, tunable viscosity and miscibility with water and organic solvents and thus an environmentally friendly extraction phase. Therefore, they are useful in microextraction techniques studied here, in addition to LLE and solid phase microextraction (SPME) [35]. It is worth mentioning that some additives used in LLE, such as crown ethers, diketonates or organophosphorous derivatives, also extract metallic cations into ILs with higher efficiency compared to organic solvents. The explanation of this may rely on the interface of the system, since an IL forms a well-defined interface larger than classical hydrophobic solvents, in addition to other aspects discussed in a recent molecular dynamics study [36].

1-alkyl-3-methylimidazolium hexafluorophosphates ($[C_n MIM][PF_6]$, $n=4, 6, 8$) have been used in SDME as extractants for several compounds in both direct and headspace modes, given that they have adequate viscosity and immiscibility in water as well as non-volatility. The unique properties of these ILs facilitate the use of larger drop volumes (even 10 μL) for longer extraction times than organic solvents [37] and, as a result of their negligible volatility and thermal stability, they can be exposed to the headspace of heated samples at high temperatures without loss [38]. 1-alkyl-3-methylimidazolium hexafluorophosphates ($[C_n MIM][PF_6]$, $n=4, 6, 8$) ILs have been used as extractants in the Direct-SDME of several environmental pollutants, including organomercury and organotin compounds [39] and in CIAME for inorganic mercury [31]. To date, these are the only two applications of RTILs in the inorganic field but they have very great potential for application, probably not only in SDME and CIAME, but all three methodologies, because of their properties (see Table 1).

3.3. Aqueous drops

Aqueous drops can be used as extractants instead of organic solvents when HS-SDME, LLLME or HF-LLLME are used. This possibility is particularly useful when liquid chromatography or capillary electrophoresis is involved, since the extraction phase is totally compatible with the mobile phase or the electrolyte used in these separation techniques. The high surface tension of aqueous solutions allows the use of relatively large drop volumes in the case of HS-SDME.

3.3.1. Noble metal-containing aqueous drops

Our research group has used noble metal-containing aqueous drops (Pd(II) and Pt(IV)) as extraction agents for hydride-forming elements such as As, Se, Sb or $MeHg^+$ after their derivatization with $NaBH_4$ or by photoassisted vapour generation in the presence of organic acids [40–43]. Pd(II)- or Pt(IV)-containing aqueous microdrops can effectively extract and preconcentrate the analytes, acting as matrix modifiers in the furnace.

The proposed sequestration mechanism of the volatile compounds is based on the reduction of Pd(II) or Pt(IV) in the drop surface due to the hydrogen gas that evolves into the headspace after the decomposition of sodium tetrahydroborate (III) or after UV irradiation of organic acids. Subsequent catalytic decomposition of the volatile compounds occurs on the finely dispersed Pd^0 or Pt^0 formed in the drop [40].

HS-SDME with Pd(II) drops provides relatively high enrichment factors by using a short microextraction time when hydride generation is employed, thus improving sample throughput. In the presence of low-molecular weight organic acids, UV irradiation generates volatile Se species such as H_2Se, SeCO, Me_2Se or Et_2Se, which are trapped in the Pd-containing aqueous drop. The most likely explanation for the efficient sequestration of Se vapours generated without injecting $NaBH_4$ is the presence in the headspace of small amounts of H_2 formed upon UV irradiation of organic acids, which reduces Pd(II) to Pd^0.

The application of Pd(II)-containing aqueous drops for HS-SDME could be extended not only to hydride-forming elements but transition metals and noble metals, taking into account that the photoassisted vapour generation can be efficiently carried out, as proposed by Guo et al. in recent publications [44–47].

3.3.2. Acidic and alkaline aqueous drops

Zhang et al. [48] introduced the possibility of using an aqueous drop to extract volatile and semivolatile ionisable compounds. In this work, a 5-μL aliquot of sodium hydroxide (at a concentration of 1 mol/L) was used as the extraction phase for five phenols model compounds.

The most important parameter that should be optimized when a water-based HS-SDME methodology is utilized to extract volatile and semivolatile ionisable compounds is the pH of both the sample and the microdrop. The pH of the sample should ensure the formation of the volatile neutral form of the analyte, while the pH of the drop should be such as to be able to ionise the analyte and consequently reduce its volatility. Until now, basic aqueous droplets have been used in the inorganic field to extract cyanides after HCN formation by pH adjustment of the sample [49,50], whereas acidic aqueous drops have been used to extract ammonia after its deprotonation [51].

4. Application of SDME, HF-LPME and DLLME to ultratrace inorganic analysis

Tables 2 and 3 summarize the relevant applications of the microextraction techniques discussed above in inorganic analysis, including metals, metalloids, organometals and non-metals.

4.1. Metals

Three different Direct-SDME-ETAAS methods were proposed for the determination of Cd. Dithizone was used in two of them as complexant for Cd by addition to the sample and subsequent extraction of the resultant cadmium dithizonate by a microdrop of toluene [52] or chloroform [53]. In the first case, the same procedure is also valid for determining Pb [52]. A method based on the formation of a cadmium ion pair in a drop of nitrobenzene and ammonium tetraphenylborate after formation of a cationic complex in the sample solution by addition of 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol (5-Br-PADAP) [54] was also developed. A high enrichment factor (390) was achieved in 15 min of microextraction.

Lin and Whang [55] described a procedure for the gas chromatographic determination of Cr(III) in water samples based on Cr(III) conversion to volatile chromium trifluoroacetylacetonate ($Cr(tfa)_3$) by microwave-assisted derivatization (MAD) using 1,1,1-Trifluoroacetylacetone (Htfa) as derivatizing agent. After allowing the sample solution to cool, a microdrop of toluene was immersed into the sample solution for 30 min in order to extract $Cr(tfa)_3$. For determination of total chromium, sodium sulphite was used as reducing agent to convert Cr(VI) to Cr(III) prior to derivatization. Pena et al. [56] described a new semiautomated Direct-SDME-SIA-ETAAS method for determination of Cr(VI) in water samples based on the use of a microdrop of toluene to extract the complexes formed after derivatization with APDC.

A drop of 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone (PMBP) dissolved in benzene was also used for determination of lead in biological samples by Direct-SDME-ETAAS [57]. In this case, an enrichment factor of 16 is achieved in 20 min.

Xia et al. [22] proposed the use of continuous flow microextraction (CFME) combined with low-temperature electrothermal vaporization and inductively coupled plasma mass spectrometry (LTETV-ICPMS) for the determination of Be, Cd, Co and Pd using a microdrop of

Table 2
Application of SDME, HF-LPME and DLLME to the determination of metals

Analyte(s)	Analytical technique	Extraction phase	Extraction time (min)	Enrichment factor	LOD (ng/L)	RSD (%)	Ref.
Metals							
Labile Al and total Al	Cycle-flow microextraction-ETV-ICP-MS	8-HQ-Chloroform	8	210	3.3	10	[58]
Au	DLLME-ETAAS	Chlorobenzene /acetone	<3	388	5	4.2	[64]
Be	CFME-LTETV-ICP-MS	BZA-Benzene	10	260	0.072	16	[22]
	Cycle-flow microextraction-LTETV-ICP-MS	BZA-Benzene	10	160	0.12	16	[22]
Bi	HF-LPME-ETV-ICP-MS	Tetrachloromethane	15	43	1.6	11	[62]
Cd	Direct-SDME-ETAAS	Dithizone–Chloroform	10	65	0.7	7.4	[53]
	Direct-SDME-ETAAS	Tetraphenylborate-Nitrobenzene	15	390	6.5	6.4; 5.8	[54]
	Direct-SDME-ETAAS	Toluene	10	118	2	11	[52]
	CFME-LTETV-ICP-MS	BZA-Benzene	10	300	0.16	12	[22]
	Cycle-flow microextraction-LTETV-ICP-MS	BZA-Benzene	10	180	0.27	11	[22]
	CFME-ETV-ICP-MS	8-HQ-Chloroform	15	140	4.6	16	[59]
	HF-LPME-ETV-ICP-MS	Tetrachloromethane	15	29	4.5	9.4	[62]
	HF-LLLME-ETAAS	1-Octanol-Dithizone/HNO_3	30	387	0.8	2.5	[61]
	DLLME-ETAAS	Tetrachloromethane /methanol	<3	125	0.6	3.5	[65]
Co	CFME-LTETV-ICP-MS	BZA-Benzene	10	215	0.56	14	[22]
	Cycle-flow microextraction-LTETV-ICP-MS	BZA-Benzene	10	125	0.99	14	[22]
	DLLME-FO-LADS	1,2-Dichlorobenzene/ethanol	<3	165	200	<4	[71]
	DLLME-UV-VIS	Chloroform/ethanol	<3	125	500	2.5	[72]
	DLLME-ETAAS	Tetrachloromethane/acetone	<3	101	21	7.5	[66]
Cr(III) + Total Cr	MAD-Direct-SDME-GC-FPD	Toluene	30	48	500	7.8	[55]
Cr(VI)	Direct-SDME-SIA-ETAAS	Toluene	5	20	20	7	[56]
Cu	HF-LPME-ETV-ICP-MS	Tetrachloromethane	15	305	12	8.8	[62]
	DLLME-FAAS	Chloroform/methanol	<3	42	3000	5.1	[69]
Hg	HF-LPME-ETV-ICP-MS	Tetrachloromethane	15	20	3.3	10	[62]
	CIAME-UV-VIS	$[C_6MIM][PF_6]/[C_6MIM][Tf_2N]$	~20	35	300	1.3	[31]
Ni	DLLME-ETAAS	Tetrachloromethane/acetone	<3	200	33	8.2	[66]
Pb	Direct-SDME-ETAAS	PMBP/Benzene	20	16	25	6.1	[57]
	Direct-SDME-ETAAS	Toluene	10	90	90	12.8	[52]
	CFME-ETV-ICP-MS	8-HQ-Chloroform	15	190	2.9	12	[59]
	CFME-ETAAS	PMBP/benzene	15	45	12	6.8	[60]
	HF-LPME-ETV-ICP-MS	Tetrachloromethane	15	73	4.8	6.1	[62]
	DLLME-ETAAS	Tetrachloromethane/acetone	<3	150	20	2.5	[67]
	DLLME-FAAS	Tetrachloromethane/methanol	<3	450	500	2.0	[70]
Pd	CFME-LTETV-ICP-MS	BZA-Benzene	10	70	0.83	14	[22]
	Cycle-flow microextraction-LTETV-ICP-MS	BZA-Benzene	10	40	1.5	14	[22]
	HF-LPME-ETV-ICP-MS	Tetrachloromethane	15	24	7.9	7.1	[62]
	DLLME -FO-LADS	1,2-Dichlorobenzene/ethanol	<3	162	250	<4	[71]
V(V) + total V	HF-LPME-ETV-ICP-OES	Tetrachloromethane	8	74	86V(IV); 71V(V)	5.3	[63]
Zn	HF-LPME-ETV-ICP-MS	Tetrachloromethane	15	284	29	6.9	[62]

benzoylacetone (BZA) in benzene, in which BZA acts as both extractant and chemical modifier. Sample flow rate showed an important effect on the microextraction of the analytes. While the concentration of Be, Cd and Co in the organic microdrop showed an increase at high flow rates, the behaviour for Pd was inverse. The authors attributed this effect to the slower extraction kinetics of Pd-BZA-benzene compared to the others. The CFME method was compared to cycle-flow microextraction and finally applied to the determination of the analytes of interest in human hair and human urine biological standard reference materials. One year later, the same research group [58] employed cycle-flow microextraction combined with ETV-ICP-MS for the determination of different Al fractions (labile monomeric Al species ((free Al (Al^{3+}, $AlOH^{2+}$ and $Al(OH)_2^+$) and non-labile monomeric Al species (Al–citrate, Al–SO_4, Al–F, Al–EDTA, Al–humic) in natural waters and drinks. Total Al was determined using pneumatic nebulisation (PN)-ICP-MS, while the non-labile aluminium was obtained by subtraction of labile aluminium from the total aluminium. The extraction and preconcentration of labile aluminium were carried out by exposing a 4 μL droplet of 8-hydroxyquinoline (8-HQ) in chloroform to the sample, achieving an enrichment factor of 210 in 8 min. Labile monomeric Al and non-labile monomeric Al were identified from the total soluble Al in the analyzed samples (natural water, tea and coffee), but the method only provides method dependent speciation information for aluminium. Li et al. [59] described a CFME-ETV-ICP-MS method for the extraction of Cd and Pb based on the simultaneous chelation and extraction of these analytes by exposing an 8-HQ-chloroform drop to the aqueous sample for 15 min. Among the different extraction factors optimized in this work, the influence of sample flow-rate should be highlighted, since a low sample flow rate, i.e., 0.05 mL/min, provides the highest extraction efficiency. This fact emphasizes that the extraction kinetics are rather slow.

Cao et al. [60] also reported a CFME method for the determination of lead in water samples. In this case, a drop of PMBP in benzene was exposed to an aqueous sample pumped at a constant flow rate of 0.5 mL/min.

Peng et al. [61] used HF-LLLME in combination with ETAAS for the ultrasensitive determination of Cd in seawater samples. Cd was extracted into an acidic aqueous solution after its extraction into a mixture of 1-octanol and dithizone, which impregnated the pores of the fibre. A high enrichment factor was achieved under optimal conditions. Recently, Xia et al. [62] used HF-LPME prior to low temperature ETV-ICP-MS for detecting Cu, Zn, Pd, Cd, Hg, Pb and Bi in biological and environmental samples. Trace metals, complexed with diethyldithiocarbamate (DDTC), were extracted with tetrachlorometane and finally injected into the graphite furnace. Limits of detection of target elements were found in the low pg/mL level, meaning an improvement of 1 or 2 orders of magnitude as compared to traditional methods. Li and Hu applied HF-LPME coupled to ETV-ICP-MS to determine vanadium species in natural waters [63]. An 8-cm long polypropylene hollow fibre fixed into a U-shape was used to expose the suitable solvent, tetrachlorometane, to a 3.5 mL aqueous sample. The selective determination of V(V) was carried out at pH 5.0 after addition of ammonium pyrrolidine dithiocarbamate (APDC) as

Table 3
Application of SDME, HF-LPME and DLLME to the determination of metalloids, organometals and non-metals

Analyte(s)	Analytical technique	Extraction phase	Extraction time (min)	Enrichment factor	LOD (ng/L)	RSD (%)	Ref.
Metalloids							
As(III)+total As	HS-SDME-ETAAS	AgDDC-pyridine:benzyl alcohol	7	150	45	8.6	[15]
	HS-SDME-ETAAS	Pd(II) aqueous drop	1.5	70	100 As(III); 150 Total As	3.5 As(III); 2.2 Total As	[40]
Total Se	HS-SDME-ETAAS	Pd(II) aqueous drop	15	285	20	4	[42]
Se(IV)+total Se	HS-SDME-ETAAS	Pd(II) aqueous drop	1.5	25	150	3	[43]
	Cycle flow microextraction-ETV-ICP-MS	Tetrachloromethane	10	75	2.7 Se(IV); 3.0 Se(VI)	13.2 Se(IV); 13.9 Se(VI)	[74]
	HF-LPME-ETV-ICP-MS	Tetrachloromethane	20	410	0.50 Se(IV); 0.56 Se(VI)	7.1 Se(IV); 7.6 Se(VI)	[74]
	DLLME-ETAAS	Tetrachloromethane/ethanol	<3	70	0.05	4.5	[73]
Se(IV)	Direct-SDME-GC-FID	Tetrachloromethane	20	91	900	3.2–6.1	[75]
Sb(III) + total Sb	Direct-SDME-ETAAS	BPHA–Chloroform	8	96	8.0 Sb(III); 9.2 Total Sb	6.6 Sb(III); 7.1 Total Sb	[76]
Organometals							
Methylmercury	HS-SDME-ETAAS	Pd(II) aqueous drop	2	40	4000	7	[41]
	HF-LPME-ETAAS	Toluene	10	55	400	11	[82]
	HF-LLLME-ETAAS	Toluene/thiourea	10	204	100	13	[82]
Organomercury (5)	Direct-SDME-CVAFS	$C_4MIM][PF_6]$	15	5–40	–	–	[39]
	Direct-SDME-CVAFS	$[C_8MIM][PF_6]$	30	4–27	–	–	[39]
Organomercury (3)	HF-LLLME-HPLC-UV	Toluene/$Na_2S_2O_3$	25	120–350	300–3800	6.4–8.9	[81]
Organomercury (2)	LLLME-CE-UV	Toluene/L-Cysteine	40	210; 324	430; 940	6.1; 7.2	[80]
Organotin (8)	Direct-SDME-ETAAS	$[C_4MIM][PF_6]$	15	10–90	–	–	[39]
	Direct-SDME-ETAAS	$[C_8MIM][PF_6]$	30	11–161	–	–	[39]
Organotin (3)	HS-SDME-GC-MS	Decane	11	–	TBT: 3 (Sn)	3.6	[78]
Organotin (2)	Direct-SDME-GC-MS-MS	α,α,α-Trifluorotoluene	60	140 TBT; 92 TPT	0.36 TBT; 2.9 TPT	11 TBT; 10 TPT	[77]
	Direct-SDME-GC-MS-MS	α,α,α-Trifluorotoluene	60	48 TBT; 112 TPT	6.3 TBT; 0.85 TPT	17 TBT; 7.5 TPT	[77]
Organotin (6)	DLLME-GC-FPD	Tetrachloromethane/ethanol	<3	825–1036	0.2–1	2.3–5.9	[79]
MMT	HS-SDME-GC-MS	Octane	20	2100	53 (Mn)	8.4	[83]
Non-metals							
Free cyanide	HS-SDME-CE-UV	Ni(II)-NH_3 aqueous drop	20	58	2080	4.3–6.8	[49]
Weak acid dissociable cyanide	HS-SDME-CE-UV	Ni(II)-NH_3 aqueous drop	15	60	3900	2.7–5.8	[50]
Ammonia	HS-SDME-CE-UV	H_3PO_4 aqueous drop	15	14	27000	5.3–7.5	[51]
VSCs (5)	Direct-SDME-GC-FPD	N-hexane	5	6–30	10700–57100	4.6–16.7	[85]
	HS-SDME-GC-FPD	*N′N″*-dimethylformamide	5	98–1432	200–1900	6.4–12.3	[85]
Iodine	Direct-SDME-GC-MS	Iso-octane	15	–	10	<2.8	[84]
Bromate, iodate, bromide, iodide	Direct-SDME-GC-MS	Toluene	15	–	45–70	<7.5	[86]

complexant and 1,2-cyclohexanediamine-tetraacetic acid (CDTA) as masking agent for V(IV), since the two species of vanadium could not be separated merely by pH control. Total vanadium was extracted after its complexation with APDC at pH 5.0, while the content of V(IV) was calculated by subtraction of V(V) from the total V. The calculated enrichment factor was 74 with 8 min of microextraction.

Although DLLME was firstly described in 2006 [28], several methods for determination of metals have already been developed with this technique. In all cases, a complexant is added to the sample before the mixture of the extractant and the disperser solvent. DLLME has been mainly employed in combination with ETAAS for quantitation. For instance, Au [64], Cd [65], Co [66], Ni [66] and Pb [67] have been determined in different water samples by this analytical technique after extraction of the corresponding complex into a chlorinated organic solvent, generally tetrachlorometane. Owing to the problems associated with the use of chlorinated organic solvents with ETAAS [68], several strategies were applied, such as the injection of the extract into the graphite furnace 10 s after starting the drying step to avoid problems caused by the wetting of graphite with organic solvents [65] or the use of Pd as chemical modifier [64]. In a few cases, it was considered that the corresponding complexant provided sufficient analyte stabilization to work without a chemical modifier [66,67].

DLLME-FAAS has been applied to the determination of Cu [69] and Pb [70] in water samples by complexation and subsequent extraction of the formed chelates with 8-HQ and DDTP, respectively. A microsample introduction system was employed for lead determination of lead.

Shokoufi et al. [71] proposed the use of fiber optic-linear array detection spectrophotometry (FO-LADS) combined with DLLME for the simultaneous determination of palladium and cobalt in water samples. Pd and Co were previously complexed with 1-(2-Pyridylazo)-2-naphtol (PAN) at pH 4.0. A mixture of ethanol plus 1,2-dichlorobenzene was used to form the necessary stable cloudy solution. After centrifuging the mixture, the extract was injected into a 50 µL cylindrical micro-cell located in a fiber optic-linear array detector spectrophotometer to obtain the corresponding spectra. Since the absorption spectra of Pd and Co complexes overlap, first derivative spectra at 692 and 650 nm, respectively, were used for their simultaneous determination. Gharehbaghi et al. [72] developed another DLLME-UV-VIS method to determine Co in water samples after its complexation with PAN. A binary mixture of chloroform and ethanol was used as extraction and dispersion solvent, respectively. It should be noted here that chloroform is generally rejected as an extraction phase when DLLME is used because it does not form a stable cloudy solution [64,65,67,73]. Moreover, dilution of the extract with 250 µL of acetone was performed prior to the spectrophotometric measurement, so a 50 mL sample volume is needed to achieve an enhancement factor of 125. In this case, acetylacetone was proposed as a masking agent for Pd, which otherwise interfered with the determination of Co (in addition to other ionic metals).

A new methodology, named as CIAME, derived from DLLME, was proposed by Shemirani et al. and applied to the determination of Hg(II) [31]. Two different ILs, [C_6MIM][PF_6] and [C_6MIM][Tf_2N], were needed to carry out the extraction of analytes in samples with high salt content. Michler thioketone (MTK) was used as complexant for Hg(II). Mercury, finally present in an 8 μL of ionic liquid phase at the bottom of the conical-centrifuge tube, was determined after dilution with 350 μL of ethanol, so the enrichment factor was partially lost.

4.2. Metalloids

Chamsaz et al. [15] employed HS-SDME for the determination of As(III) and total As after arsine generation using sodium tetrahydroborate ($NaBH_4$), followed by extraction of the formed AsH_3 in a pyridine:benzyl alcohol drop containing silver diethyldithiocarbamate (AgDDC) and Ni(II) as chemical modifier. Although pyridine is the most suitable medium for the reaction of arsine with AgDDC, it could not be used alone because of its high vapour pressure, so it was used together with benzyl alcohol in order to decrease the volatility of the extractant. The determination of total As was carried out after pre-reduction of As(V) with KI. A 150-fold enrichment factor was achieved in 7 min under the optimal conditions.

As mentioned above, HS-SDME using a Pd-containing aqueous drop has been used in combination with ETAAS in our research group. Fragueiro et al. [40] developed a method for the determination of As(III) and total As based on the use of a Pd microdrop exposed to the headspace of a closed vial as extractant for the generated hydride. The selective determination of As(III) was carried out using citric acid as sample medium, while the medium used for the determination of total As was HCl. The method provided an enrichment factor of 70 for As(III) in only 90 s. This method was also tested with other hydride forming elements, achieving enrichment factors of 25 and 20 for Se(IV) and Sb(III), respectively. Figueroa et al. [42] used UV irradiation in the presence of low-molecular weight organic acids in order to generate volatile Se compounds (hydrides and alkyl-Se) at the pg/mL level, and their subsequent extraction into an aqueous microdrop containing 75 μg/mL of Pd(II). Acetic acid showed the best performance of the five different short chain organic acids used as sample medium, i.e. formic, citric, oxalic, ethylenediaminetetraacetic and citric acids. An enrichment factor of 285 is achieved in 15 min with a limit of detection of 20 pg/mL Se. In later work, Fragueiro et al. [43] used UV irradiation to pre-reduce Se (VI) to Se(IV), prior to determination of total inorganic Se and Se(IV). Thus, for the determination of total inorganic Se, a sample containing 1.5 mol/L HCl was subjected to UV irradiation for 45 min in order to convert Se(VI) into Se(IV) and, finally, a Pd drop was exposed to the headspace of the vial to extract the H_2Se generated after addition of $NaBH_4$ to the sample. For the selective determination of Se(IV), the HS-SDME was carried out for 90 s without UV treatment. UV irradiation allows the pre-reduction of Se(VI) to Se(IV) thus providing safer conditions than typically used i.e., prereduction of Se(VI) performed by boiling with 5–6 mol/L HCl for 15–30 min under reflux.

Xia et al. [74] made a comparative study between HF-LPME and cycle-flow microextraction for the ETV-ICP-MS determination of Se (IV) and Se(VI) in aqueous samples. The method is based on the complexation of Se(IV) with APDC and subsequent microextraction of the complex using tetrachloromethane as extraction phase in both cases. APDC was used as both the extractant and the chemical modifier for ETV-ICP-MS detection. The total inorganic Se content (Se (IV)+Se(VI)) was determined after pre-reduction of Se(VI) to Se(IV) by gentle boiling in 5 mol/L HCl medium for 50 min. The results showed that HF-LPME-ETV-ICP-MS is more precise and robust than cycle-flow microextraction-ETV-ICP-MS.

Sarkouhi et al. [75] reported a study on the combination of Direct-SDME with GC-FID to determine Se(IV) based on the reaction of selenious acid (Se(IV)) with 1,2-diaminobenzene in acid medium, and extraction of the piazselenol complex formed by exposure to a microdrop of tetrachloromethane for 20 min. The derivatization of Se(IV) needs at least 15 min at 90 °C to be quantitative.

Bidari et al. [73] combined DLLME with iridium-modified graphite tube atomizer atomic absorption spectrometry for determination of selenium species in water samples. The stable cloudy solution was formed by injection of a mixture of APDC, tetrachloromethane and ethanol into a water sample. The effect of several interferents was not significant on the extraction recovery of selenium (as selenite), except Ni(II), Al(III) and, especially Cu(II). These could be alleviated by adding EDTA to the sample. Total inorganic selenium was determined in water samples after pre-reduction of selenate to selenite by gentle boiling in 5 mol/L HCl for 50 min.

Fan [76] studied the determination of Sb(III) and total Sb by Direct-SDME combined with ETAAS. The selective determination of Sb(III) was achieved by simultaneous complexation and extraction in a chloroform microdrop containing N-benzoyl-N-phenylhydroxylamine (BPHA), using Rh as permanent modifier. The total antimony content was determined after pre-reduction of Sb(V) to Sb(III) by L-cysteine at pH 2.0 for 15 min. The enrichment factor was 96 using an 8 min collection time.

4.3. Organometals

Shioji et al. [77] employed the Direct-SDME mode for the determination of tributyltin and triphenyltin by GC-MS-MS after two different derivatization reactions, i.e., with sodium tetrakis(4-fluorophenyl)borate and with sodium tetraethylborate, using hexyl TBT as internal standard dissolved in the extraction solvent. Both derivatization reactions were optimized and their analytical performances were compared. α,α,α-trifluorotoluene was selected as extractant in both cases. The stability of the drop was strongly dependent of the temperature and the stirring rate. Thus, although there are several papers where high temperatures are used to improve the mass transfer rate, high temperatures cause the solvent drop to be unstable due to undesirable bubble formation. A decrease of the sample temperature made it possible to raise the stirring rate.

Colombini et al. [78] compared HS-SDME, headspace solid-phase microextraction (HS-SPME) and liquid–liquid extraction (LLE) for the extraction of three organotin compounds (monobutyltin (MBT), dibutyltin (DBT) and tributyltin (TBT)) after their ethylation with sodium tetraethylborate ($NaBEt_4$). HS-SDME was performed by exposing a microdrop of decane to the headspace of the sample for 10 min.

DLLME combined with GC-FPD was developed by Birjandi et al. [79] for determining monobutyltin (MBT), dibutyltin (DBT), tributyltin (TBT), monophenyltin (MPhT), diphenyltin (DPhT) and triphenyltin (TPhT) in water samples after derivatization with sodium tetraethylborate and its extraction with tetrachlorometane and ethanol. High enrichment factors, between 825 and 1036, were achieved.

Gil et al. [41] used HS-SDME to extract and preconcentrate methylmercury onto a noble metal-containing aqueous drop after generation of its hydride into a closed vial prior to its determination by ETAAS. Both Pd(II) and Pt(IV) could be used as efficient extractants of MeHgH. Based on the affinity of mercury for binding thiol groups, L-cysteine and diethyldithiocarbamate were tried as trapping agents in this work, but did not provide efficient trapping of MeHgH.

LLLME combined with CE-UV has been developed by Fan and Liu [80] for the determination of methylmercury and phenylmercury in water samples. Analytes complexed with PAN were first extracted into toluene, and back-extracted simultaneously into an aqueous drop of L-cysteine. The enrichment factor was 324 for methylmercury and 210 for phenylmercury after 40 min of microextraction.

Recently, Xia et al. [81] proposed a modification of the Westöö method for the simultaneous determination of methylmercury, ethylmercury and phenylmercury by combination of HF-LLLME with

HPLC-UV. Organomercury compounds are first extracted by a thin layer of toluene immobilised in the pores of the polypropylene hollow fibre and immediately back-extracted from the toluene phase to an aqueous $Na_2S_2O_3$ solution inside the lumen of the fibre. The aqueous extract is finally injected into the HPLC system for separation, using 2-mercaptoethanol in the mobile phase as complexing agent, given that 2-mercaptoethanol reacts with organomercury thiosulphate complexes to form the more stable neutral 2-mercaptoethanol complexes.

A comparison of the two hollow fibre-based modes (HF-LPME and HF-LLLME) has been proposed by Jiang et al. [82] for the determination of methylmercury in human hair and sludge samples by ETAAS, using Pd as a permanent modifier. In the two-phase mode (HF-LPME), toluene was used as the extraction phase, while in the three-phase mode (HF-LLLME) the analyte was first extracted into toluene impregnated within the pores of the hollow fibre, and then back-extracted into an acidic aqueous solution of thiourea placed inside the hollow fibre. HF-LLLME achieved a better enrichment factor for methylmercury compared to the HF-LPME device.

Liu et al. [39] studied the extractability of 45 environmental pollutants, including several organometallic compounds of mercury and tin, using two room temperature ionic liquids, 1-alkyl-3-methylimidazolium hexafluorophosphate ($[C_nMIM][PF_6]$, $n=4$, 8). The organomercury and organotin compounds (methylmercury, ethylmercury, phenylmercury, dimethylmercury and diethylmercury; monomethyltin, dimethyltin, trimethyltin, monobutyltin, dibutyltin, tributyltin, triphenyltin and dioctyltin) were extracted for 15 min with $[C_4MIM][PF_6]$ or for 30 min with $[C_8MIM][PF_6]$ prior to their determination. Atomic absorption and cold-vapour atomic fluorescence spectrometry were employed to determine organotin and organomercury compounds, respectively. Taking into account the enrichment factors achieved using SDME in its direct mode (between 4 and 161), ionic liquids can be considered an attractive alternative to organic solvents for extracting inorganic analytes. $[C_4MIM][PF_6]$ proved to be more effective than $[C_8MIM][PF_6]$ for the preconcentration of the studied compounds, probably due to the hifger viscosity of $[C_8MIM][PF_6]$ (see Table 1) [39], which generates a greater resistance of the analytes to diffuse across the laminar film of the extractant phase.

Pena et al. [83] combined headspace single-drop microextraction with gas chromatography-mass spectrometry (GC-MS) for the determination of methylcyclopentadienylmanganese tricarbonyl (MMT), a gasoline fuel additive. The proposed method provides high extraction efficiency without derivatization. An application to analysis of wastewater taken from a car wash unit was made.

4.4. Non-metals

Das et al. [84] established a comparison between Direct-SDME and SPME (in its immersed mode) combined with gas chromatography-mass spectrometry to determine iodine in pharmaceuticals, iodized salt, milk powder and vegetables. The derivatization procedure relies on a rapid sequence of oxidation and iodination using 2-iodosobenzoate as an oxidizing agent and *N*,*N*-dimethylaniline as an iodine scavenger at pH 6.4. The SDME procedure was then carried out for 15 min by exposing 1 μL of iso-octane to the stirred sample (300 rpm). For SPME, a 100 μm PDMS fibre was directly exposed to the analyte solution for 15 min with a stirring rate of 300 rpm. Direct-SDME proved more efficient than SPME, as it is evident from the detection limits (25 ng/L by SPME, 10 ng/L by Direct-SDME) and precision (2.5–5.2% by SPME, 1.7–2.8% by Direct-SDME) achieved.

Xiao et al. [85] compared three different extraction methods (Direct-SDME, HS-SDME and HS-SPME) for the GC-FPD determination of five volatile sulphur compounds (VSCs) (dimethyl sulphide (DMS), diethyl sulphide (DES), dimethyl disulphide (DMDS), dipropyl disulphide (DPrDS) and dipropyl trisulphide (DPrTS)) in beer and beverages. *N*,*N*′-dimethylformamide was the most suitable extractant phase for HS-SDME, while n-hexane was selected for the Direct-SDME mode. HS-SPME of VSCs was carried out with a 100 μm PDMS fibre. Detection limits ranging from 0.2 to 1.9 ng/mL by HS-SDME, from 10.7 to 57.1 ng/mL by direct-SDME, and from 0.5 to 208.1 ng/mL by HS-SDME were obtained. In terms of repeatability, SDME modes were found to be not as good as HS-SPME. Headspace techniques (SDME and SPME) were finally applied to the analysis of VSCs in beer and beverages.

Jermak et al. [49] extracted free cyanide from the headspace of physiological samples (urine and saliva from non-smoker and smoker) using an aqueous microdrop (5 μL) containing $NiCl_2$ (as derivatization agent), NH_4OH, sodium carbonate and ammonium pyromellitate (as internal standard) as the acceptor phase. Cyanide extraction was performed by adjusting the sample pH between 4.5 and 7.5 to promote protonation of the cyanide, taking into account the weak acidity of hydrogen cyanide ($pK_a=9.21$) and using an aqueous alkaline solution (pH 11) containing a derivatizing agent as extractant to ionise the analyte and consequently reduce its volatility. The extracted cyanide forms the $Ni(CN)_4^{2-}$ complex with Ni^{2+} in ammoniacal medium, which is introduced into the CE microvial for subsequent analysis.

This research group [50] used the same aqueous extraction phase (with a slight change of the proportions of their components) to determine weak acid dissociable cyanide (WAD cyanide), which constitutes the toxicologically significant form of cyanide in industrial effluents, by HS-SDME-CE-UV. WAD cyanide includes free cyanide (CN^-+HCN) and moderately and weakly complexed metal cyanides, such as $Zn(CN)_4^{2-}$, $Cd(CN)_4^{2-}$, $Cu(CN)_3^{2-}$, $Ag(CN)_2^-$, $Ni(CN)_4^{2-}$ and $Hg(CN)_4^{2-}$. Three different ligand-displacing reagents (ethylenediamine, dithizone and polyethyleneimine) were tested for decomposition of the metal-cyanide complexes, which is the most important feature of WAD cyanide analysis. An appropriate mixture of ethylenediamine and dithizone was finally selected, as none of the three reagents alone was able to decompose all WAD cyanide complexes.

Pranaityte et al. [51] established a new water-based headspace SDME method combined with capillary electrophoresis for the determination of ammonia in environmental and biological samples. In this case, since the ammonium cation is weakly acidic ($pK_a=9.25$), an acidic aqueous drop containing H_3PO_4 and KH_2PO_4 as internal standard (pH 3–7) was exposed to the headspace of a sample at alkaline pH (pH 12) to extract NH_3. Since the analyte does not exhibit any significant absorbance in the UV range, indirect detection at 214 nm using conventional imidazole containing carrier electrolyte was employed for CE separations. This technique provides an enrichment factor of approximately 14 after a 15 min microextraction time.

Reddy-Noone et al. [86] used two different microextraction techniques for the GC-MS determination of bromate, iodate, bromide and iodide in sea water and table salt. The determination of iodide and bromide was based on their oxidation with 2-iodosobenzoate (iodide is oxidized at pH 6.4 (10 min) while bromide is oxidized at pH 2–3 (1 min)) and electrophilic substitution reaction of 2,6-dimethylaniline to yield 4-halo-2,6-dimethylaniline. Determination of bromate and iodate was based on their reduction to halides by ascorbic acid after removal of free bromide and iodide by anion exchange with AgCl. Direct-SDME was carried out exposing 2 μL of toluene to the aqueous stirred solution for 15 min, while a LPME method was performed adding 50 μL of toluene to a sample placed into a 5 mL standard flask and shaking it vigorously for 1 min. Once the phase separation was achieved, 2 μL of the organic phase (upper layer) was withdrawn by a microsyringe and injected into the GC. A comparison of both methods established that the LPME method was more sensitive than Direct-SDME.

5. Related microextraction techniques

Apart from the techniques described above, other microextraction techniques such as solid-phase microextraction (SPME) and stir bar

sorptive extraction (SBSE) rely on the same principles when a small volume of a high molecular weight polymeric liquid material such as polydimethylsiloxane (PDMS) is employed as extractant phase [87].

5.1. Solid phase microextraction (SPME)

SPME has grown to currently become one of the most successful microextraction techniques, being widely applied to the determination of inorganic analytes. In fact, there are several reviews where its theoretical and practical aspects, as well as its uses to determine inorganic analytes are revised in depth; so interested readers are referred to literature for more details about this well-known microextraction technique [88–91].

SPME is a microextraction technique introduced by Arthur and Pawliszyn in 1990 [92], where a sorbent coated on a fused silica fibre (which fits inside the needle of a syringe-like SPME holder) is used to extract and preconcentrate target analytes by immersion of the fibre into the sample (Direct-SPME) or by exposition of the fibre to the headspace of a sample placed into a closed vial (HS-SPME). Both high molecular weight polymeric 'liquids' and solid sorbent porous materials with a large surface area can be employed for microextraction.

After a predetermined microextraction time, the analytes are desorbed from the fibre into an analytical instrument for their determination. Desorption of analytes from the fibre can be thermal or by elution with organic solvents. Thermal desorption is generally carried out by insertion of the fibre into the injection port of a gas chromatograph, although the use of a volatilizator has also been reported [93]. The maximum volume of PDMS coated onto the fibre is relatively low (0.5 μL). Therefore, due to the large phase ratio for the PDMS extraction phase and the water sample, quantitative extraction cannot be obtained with SPME.

Drawbacks of SPME are mainly related to the polymeric extractant phase nature and the desorption process. The use of a polymer as extractant phase includes disadvantages such as batch-to-batch variation. Moreover, damaged areas on the fibre coating and contamination of new fibbers as well as a highly variable number of pores of Carboxen-PDMS fibbers were reported by Haberhauer-Troyer et al. [94], which indicates a lack of inertness of SPME fibres. Analysis of trace levels of organotin, organolead and organosulphur showed artefact formation and low repeatability.

As it was pointed out above, thermal or liquid desorption of analytes can be performed after extraction with SPME. Thermal desorption, typically at a temperature between 150 and 300 °C, is preferred because complete transfer of analytes into the analytical system is achieved. Moreover, the SPME fibres can be inserted perfectly into the heated injection port of a gas chromatograph for thermal desorption. Liquid desorption of analytes from the polymeric extractant phase can be done by using organic solvents. Although liquid desorption broadens the field of action of SPME, a loss of sensitivity occurs as a consequence of this step and moreover, its character as a solventless technique is lost.

5.2. Stir bar sorptive extraction (SBSE)

SBSE is a microextraction technique introduced in 1999 by Baltussen et al. [95]. Like SPME, SBSE uses a polymeric coating for the extraction of target analytes. In this case, a layer of a polymer (generally PDMS) coated on a magnetic stir bar of 1–4 cm is used. The coated stir bar can be added to the sample for stirring and extraction (Direct-SBSE) or exposed to the headspace of the sample (HS-SBSE). Once the extraction step is finished, the stir bar is removed from the sample and desorbed for the subsequent analysis. Although the basic principles of SPME and SBSE are identical and the extraction phase is generally the same, the amount of PDMS is 50–250 times larger than in SBSE, which increases the preconcentration efficiency [87]. When the equilibrium is achieved, calibration and quantitation are straightforward for SBSE, because most experimental conditions do not play such an important role and extraction is more or less quantitative [87]. Nevertheless, like SPME, working at equilibrium is not necessary when the extraction conditions are kept constant. These non-equilibrium conditions often result in sufficient sensitivity and good repeatability while the extraction time is not excessively long [96].

Since extraction of analytes by SPME and SBSE is based on the same principles, common advantages and drawbacks commented above for SPME can also be ascribed to SBSE. The larger amount of extractant phase used in SBSE in comparison with SPME fibres gives rise to higher extraction efficiency but longer desorption times are needed after SBSE.

SBSE has been employed in both Direct and Headspace modes for the extraction and preconcentration of several organic analytes, but its use in the inorganic field is scarce. In fact, up to date, there are only two articles where SBSE is employed for the determination of organotin [97] and methylmercury and butyltin species [98]. In both cases the derivatization of the organometallic species was carried out by ethylation with sodium tetraethylborate reagent.

Vercauteren et al. [97] employed a stir bar coated with 55 μL of PDMS to perform the combination between Direct-SBSE and GC-ICP-MS for the determination of tributyltin and triphenyltin in environmental samples. Extremely low detection limits (2–3 orders of magnitude lower than LODs obtained by using HS-SPME-GC-ICP-MS) were obtained after a 15 min extraction time. It should be pointed out here that signal suppression was observed when real samples were analysed owing to the sorption of organic material onto the stir bar, so both standard addition and internal standards were used to correct for the signal suppression and for variations in the derivatization and extraction efficiency, respectively.

Prieto et al. [98] developed a HS-SBSE-GC-MS to determine methylmercury, monobutyltin, dibutyltin and tributyltin. The extraction of the organometallic analytes from the aqueous sample was carried out for a long period of time (5 h) to guarantee equilibrium conditions, since simultaneous extractions could be made by a 15-position agitator. Addition of humic acid to water samples spiked with the organometallic analytes showed a decrease in recovery for all analytes, except for monobutyltin, up to a 10 mg L^{-1} humic acid content. Moreover, tributyltin showed null recovery in the presence of humic acids. This study suggests strong interactions between TBT and humic acids, which inhibits its extraction in the headspace.

6. Conclusions

An overview of three miniaturized methods based on LLE, i.e., SDME, HF-LPME and DLLME, which have been recently applied to extract and preconcentrate inorganic analytes from different matrices, is presented. The different requirements of each methodology (and its modes of implementation), especially the extraction phase, are discussed. Three kinds of extraction phases, i.e., organic solvents, ionic liquids and aqueous drops can be used, being compatible with many analytical techniques. Several features need to be addressed in the future so as to improve the performance of these methods, mainly concerning automation of operational procedures for microextraction, development of new materials for syringe fabrication thus limiting sample contamination from metallic components, and enhancing the mass transfer rate so that faster procedures can be achieved. While a significant number of applications have been reported so far, mainly concerning SDME in combination with ETAAS and ETV-ICP-MS, the potential of these microextraction techniques used along with hyphenated techniques for speciation is still to be established. Therefore, given the simplicity and feasibility of microextraction techniques, further research is expected to tackle current problems in the trace element analysis and speciation fields.

Acknowledgement

Financial support from the Spanish Education and Science Ministry (project CTQ2006-04111/BQU) is gratefully acknowledged.

Appendix A. Abbreviation

CFME continuous-flow microextraction
CIAME cold induced aggregation microextraction
Direct-SBSE direct-stir bar sorptive extraction
Direct-SDME direct single-drop microextraction
Direct-SPME direct-solid-phase microextraction
DLLME dispersive liquid–liquid microextraction
HF-LLLME hollow fibre liquid–liquid–liquid microextraction
HF-LPME hollow fibre liquid-phase microextraction
HS-SBSE headspace-stir bar sorptive extraction
HS-SDME headspace single-drop microextraction
HS-SPME headspace-solid-phase microextraction
LLE liquid–liquid extraction
LLLME liquid–liquid–liquid microextraction
LPME liquid-phase microextraction
SBSE stir bar sorptive extraction
SDME single-drop microextraction
SPME solid-phase microextraction
$[C_4MIM][PF_6]$ 1-butyl-3-methylimidazolium hexafluorophosphate
$[C_6MIM][PF_6]$ 1-hexyl-3-methylimidazolium hexafluorophosphate
$[C_6MIM][Tf_2N]$ 1-hexyl-3-methylimidazolium bis (trifluoromethyl-sulfonyl) imide
$[C_8MIM][PF_6]$ 1-octyl-3-methylimidazolium hexafluorophosphate
5-Br-PADAP 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol
8-HQ 8-hydroxyquinoline
AgDDC silver diethyldithiocarbamate
APDC ammonium pyrrolidine dithiocarbamate
BPHA N-benzoyl-N-phenylhydroxylamine
BZA benzoylacetone
CDTA 1,2-cyclohexanediamine-tetraacetic acid
CE capillary electrophoresis
$Cr(tfa)_3$ chromium trifluoroacetylacetonate
DBT dibutyltin
DDTC diethyldithiocarbamate
DES diethyl sulphide
DMDS dimethyl disulphide
DMS dimethyl sulphide
DPhT diphenyltin
DPrDS dipropyl disulphide
DPrTS dipropyl trisulphide
EDTA ethylenediaminetetraacetic acid
ETAAS electrothermal atomic absorption spectrometry
ETV-ICP-OES/MS electrothermal vaporization-inductively coupled plasma-optical emission spectrometry/mass spectrometry
FO-LADS fiber optic-linear array detection spectrophotometry
GC gas chromatography
GC-FID gas chromatography-flame ionization detector
GC-FPD gas chromatography-flame photometric detector
GC-MS gas chromatography-mass spectrometry
GC-ICP-MS gas chromatography-inductively coupled plasma-mass spectrometry
GC-MS-MS gas chromatography-tandem mass spectrometry
HPLC-UV high performance liquid chromatography with ultraviolet detection
Htfa 1,1,1-trifluoroacetylacetone
ILs ionic liquids
LOD limit of detection
LTETV-ICPMS low-temperature electrothermal vaporization-inductively coupled plasma-mass spectrometry
MAD microwave-assisted derivatization
MBT monobutyltin
MIBK 4-methyl-2-pentanone
MMT methylcyclopentadienylmanganese tricarbonyl
MPhT monophenyltin
MTK Michler thioketone
PAN 1-(2-pyridylazo)-2-naphtol
PDMS polydimethylsiloxane
PMBP 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone
PN-ICP-MS pneumatic nebulisation-inductively coupled plasma-mass spectrometry
RP-HPLC reverse phase high performance liquid chromatography
RSD relative standard deviation
RTILs room temperature ionic liquids
SDS sodium dodecyl sulphate
SIA sequential injection analysis
TBT tributyltin
TPhT triphenyltin
UV ultraviolet
VSCs volatile sulphur compounds
WAD cyanide weak acid dissociable cyanide

References

[1] D.M. Templeton, F. Ariese, R. Cornelis, L.-G. Danielsson, H. Muntau, H.P. Van Leeuwen, R. Lobinski, Guidelines for terms related to chemical speciation and fractionation of elements. Definitions, structural aspects, and methodological approaches, Pure Appl. Chem. 72 (2000) 1453–1470.
[2] S. Liu, P.K. Dasgupta, Liquid droplet. A renewable gas sampling interface, Anal. Chem. 67 (1995) 2042–2049.
[3] E.A. Pereira, P.K. Dasgupta, Measurement of atmospheric formaldehyde using a drop collector and in-situ colorimetry, Int. J. Environ. Anal. Chem. 66 (1997) 201–213.
[4] A.A. Cardoso, H. Liu, P.K. Dasgupta, Fluorometric fiber optic drop sensor for atmospheric hydrogen sulfide, Talanta 44 (1997) 1099–1106.
[5] M.R. Milani, J.A. Gomes Neto, A.A. Cardoso, Colorimetric determination of sulfur dioxide in air using a droplet collector of malachite green solution, Microchem. J. 62 (1999) 273–281.
[6] A. Pretto, M.R. Milani, A.A. Cardoso, Colorimetric determination of formaldehyde in air using a hanging drop of chromotropic acid J. Environ. Mon. 2 (2000) 566–570.
[7] C. Ugucione, A.A. Cardoso, Flow cell within an LED: a proposal for an optical absorption detector, Anal. Bioanal. Chem. 389 (2007) 1647–1650.
[8] A.A. Cardoso, P.K. Dasgupta, Analytical chemistry in a liquid film/droplet, Anal. Chem. 67 (1995) 2562–2566.
[9] H. Liu, P.K. Dasgupta, A renewable liquid droplet as a sampler and a windowless optical cell. Automated sensor for gaseous chlorine, Anal. Chem. 67 (1995) 4221–4228.
[10] S. da Silva Borges, B.F. Reis, An automatic falling drop system based on multicommutation process for photometric chlorine determination in bleach, Anal. Chim. Acta 600 (2007) 66–71.
[11] P.K. Dasgupta, Automated diffusion-based collection and measurement of atmospheric trace gases, in: J. Pawliszyn (Ed.), Sampling and Sample Preparation for Field and Laboratory, Elsevier, Amsterdam, 2002, pp. 97–160.
[12] H. Liu, P.K. Dasgupta, Analytical chemistry in a drop. Solvent extraction in a microdrop, Anal. Chem. 68 (1996) 1817–1821.
[13] M.A. Jeannot, F.F. Cantwell, Solvent microextraction into a single drop, Anal. Chem. 68 (1996) 2236–2240.
[14] M.A. Jeannot, F.F. Cantwell, Mass transfer characteristics of solvent extraction into a single drop at the tip of a syringe needle, Anal. Chem. 69 (1997) 235–239.
[15] M. Chamsaz, M.H. Arbab-Zavar, S. Nazari, Determination of arsenic by electrothermal atomic absorption spectrometry using headspace liquid phase microextraction after in situ hydride generation, J. Anal. At. Spectrom. 18 (2003) 1279–1282.
[16] F.F. Cantwell, M. Losier, Liquid–liquid extraction, in: J. Pawliszyn (Ed.), Sampling and Sample Preparation for Field and Laboratory, Elsevier, Amsterdam, 2002, pp. 97–160.
[17] E. Psillakis, N. Kalogerakis, Developments in single-drop microextraction, TrAC, Trends Anal. Chem. 21 (2002) 53–63.
[18] A.L. Theis, A.J. Waldack, S.M. Hansen, M.A. Jeannot, Headspace solvent microextraction, Anal. Chem. 73 (2001) 5651–5654.
[19] Y.C. Fiamegos, C.D. Stalikas, Theoretical analysis and experimental evaluation of headspace in-drop derivatisation single-drop microextraction using aldehydes as model analytes, Anal. Chim. Acta 599 (2007) 76–83.
[20] M. Ma, F.F. Cantwell, Solvent microextraction with simultaneous back-extraction for sample cleanup and preconcentration: preconcentration into a single drop, Anal. Chem. 71 (1999) 388–393.
[21] W. Liu, H.K. Lee, Continuous-flow microextraction exceeding 1000-fold concentration of dilute analytes, Anal. Chem. 72 (2000) 4462–4467.
[22] L. Xia, B. Hu, Z. Jiang, Y. Wu, Y. Liang, Single-drop microextraction combined with low-temperature electrothermal vaporization ICPMS for the determination of Trace Be, Co, Pd, and Cd in biological samples, Anal. Chem. 76 (2004) 2910–2915.

[23] L. Xu, C. Basheer, H.K. Lee, Developments in single-drop microextraction, J. Chromatogr. A 1152 (2007) 184–192.
[24] S. Pedersen-Bjergaard, K.E. Rasmussen, Liquid–liquid–liquid microextraction for sample preparation of biological fluids prior to capillary electrophoresis, Anal. Chem. 71 (1999) 2650–2656.
[25] E. Psillakis, N. Kalogerakis, Developments in liquid-phase microextraction, TrAC, Trends Anal. Chem. 22 (2003) 565–574.
[26] J.Å. Jönsson, Liquid membrane techniques, in: J. Pawliszyn (Ed.), Sampling and Sample Preparation for Field and Laboratory, Elsevier, Amsterdam, 2002, pp. 503–530.
[27] K.E. Rasmussen, S. Pedersen-Bjergaard, Developments in hollow fibre-based, liquid-phase microextraction, TrAC, Trends Anal. Chem. 23 (2004) 1–10.
[28] M. Rezaee, Y. Assadi, M.R. Milani Hosseini, E. Aghaee, F. Ahmadi, S. Berijani, Determination of organic compounds in water using dispersive liquid–liquid microextraction, J. Chromatogr. A 1116 (2006) 1–9.
[29] L.L. Schramm, Emulsions, Foams, and Suspensions. Fundamentals and Applications, Willey-VCH, Weinheim, Germany, 2005.
[30] B. Takahiko, K. Fumio, N. Susumu, T. Katsuroku, Study of drop coalescence behavior for liquid–liquid extraction operation, Chem. Eng. Sci. 55 (2000) 5385–5391.
[31] M. Baghdadi, F. Shemirani, Cold-induced aggregation microextraction: a novel sample preparation technique based on ionic liquids, Anal. Chim. Acta 613 (2008) 56–63.
[32] E. Tserovsky, S. Arpadjan, I. Karadjova, Behavior of cadmium, cobalt and lead in chlorine-containing organic solvents in electrothermal atomic absorption spectrometry, J. Anal. At. Spectrom. 8 (1993) 85–88.
[33] E. Tserovsky, S. Arpadjan, Behavior of various organic solvents and analytes in electrothermal atomic absorption spectrometry, J. Anal. At. Spectrom. 6 (1991) 487–491.
[34] D. Tsalev, V.I. Slaveykova, L. Lampugnani, A. D'Ulivo, R. Georgieva, Permanent modification in electrothermal atomic absorption spectrometry-advances, anticipations and reality, Spectrochim. Acta, Part B 55 (2000) 473–490.
[35] J.F. Liu, J.A. Jonsson, G.B. Jiang, Application of ionic liquids in analytical chemistry, TrAC, Trends Anal. Chem. 24 (2005) 20–27.
[36] N. Sieffert, G. Wipff, Comparing an ionic liquid to a molecular solvent in the cesium cation extraction by a calixarene: a molecular dynamics study of the aqueous interface, J. Phys. Chem. B 110 (2006) 19497–19506.
[37] J.F. Liu, Y.G. Chi, G.B. Jiang, C. Tai, J.F. Peng, J.T. Hu, Ionic liquid-based liquid-phase microextraction, a new sample enrichment procedure for liquid chromatography, J. Chromatogr. A 1026 (2004) 143–147.
[38] J.F. Peng, J.F. Liu, G.B. Jiang, C. Tai, M.J. Huang, Ionic liquid for high temperature headspace liquid-phase microextraction of chlorinated anilines in environmental water samples, J. Chromatogr. A 1072 (2005) 3–6.
[39] J.F. Liu, Y.G. Chi, G.B. Jiang, Screening the extractability of some typical environmental pollutants by ionic liquids in liquid-phase microextraction, J. Sep. Sci. 28 (2005) 87–91.
[40] S. Fragueiro, I. Lavilla, C. Bendicho, Headspace sequestration of arsine onto a Pd(II)-containing aqueous drop as a preconcentration method for electrothermal atomic absorption spectrometry, Spectrochim. Acta Part B 59 (2004) 851–855.
[41] S. Gil, S. Fragueiro, I. Lavilla, C. Bendicho, Determination of methylmercury by electrothermal atomic absorption spectrometry using headspace single-drop microextraction with in situ hydride generation, Spectrochim. Acta Part B 60 (2005) 145–150.
[42] R. Figueroa, M. García, I. Lavilla, C. Bendicho, Photoassisted vapor generation in the presence of organic acids for ultrasensitive determination of Se by electrothermal-atomic absorption spectrometry following headspace single-drop microextraction, Spectrochim. Acta Part B 60 (2005) 1556–1563.
[43] S. Fragueiro, I. Lavilla, C. Bendicho, Hydride generation-headspace single-drop microextraction-electrothermal atomic absorption spectrometry method for determination of selenium in waters after photoassisted prereduction, Talanta 68 (2006) 1096–1101.
[44] X. Guo, R.E. Sturgeon, Z. Mester, G.J. Gardner, UV vapor generation for determination of selenium by heated quartz tube atomic absorption spectrometry, Anal. Chem. 75 (2003) 2092–2099.
[45] X. Guo, R.E. Sturgeon, Z. Mester, G.J. Gardner, UV light-mediated alkylation of inorganic selenium, Appl. Organomet. Chem. 17 (2003) 575–579.
[46] X. Guo, R.E. Sturgeon, Z. Mester, G.J. Gardner, Vapor Generation by UV Irradiation for Sample Introduction with Atomic Spectrometry, Anal. Chem. 76 (2004) 2401–2405.
[47] X. Guo, R.E. Sturgeon, Z. Mester, G.J. Gardner, UV photosynthesis of nickel carbonyl, Appl. Organomet. Chem. 18 (2004) 205–211.
[48] J. Zhang, T. Su, H.K. Lee, Headspace water-based liquid-phase microextraction, Anal. Chem. 77 (2005) 1988–1992.
[49] S. Jermak, B. Pranaityte, A. Padarauskas, Headspace single-drop microextraction with in-drop derivatization and capillary electrophoretic determination for free cyanide analysis, Electrophoresis 27 (2006) 4538–4544.
[50] S. Jermak, B. Pranaityte, A. Padarauskas, Ligand displacement, headspace single-drop microextraction, and capillary electrophoresis for the determination of weak acid dissociable cyanide, J. Chromatogr. A 1148 (2007) 123–127.
[51] B. Pranaityte, S. Jermak, E. Naujalis, A. Padarauskas, Capillary electrophoretic determination of ammonia using headspace single-drop microextraction, Microchem. J. 86 (2007) 48–52.
[52] H. Jiang, B. Hu, Determination of trace Cd and Pb in natural waters by direct single drop microextraction combined with electrothermal atomic absorption spectrometry, Microchim. Acta 161 (2008) 101–107.
[53] Z. Fan, W. Zhou, Dithizone–chloroform single drop microextraction system combined with electrothermal atomic absorption spectrometry using Ir as permanent modifier for the determination of Cd in water and biological samples, Spectrochim. Acta Part B 61 (2006) 870–874.
[54] S. Nazari, Determination of trace amounts of cadmium by modified graphite furnace atomic absorption spectrometry after liquid phase microextraction, Microchem. J. 90 (2008) 107–112.
[55] M.Y. Lin, C.W. Whang, Microwave-assisted derivatization and single-drop microextraction for gas chromatographic determination of chromium(III) in water, J. Chromatogr. A 1160 (2007) 336–339.
[56] F. Pena, I. Lavilla, C. Bendicho, Immersed single-drop microextraction interfaced with sequential injection analysis for determination of Cr(VI) in natural waters by electrothermal-atomic absorption spectrometry, Spectrochim. Acta Part B 63 (2008) 498–503.
[57] P. Liang, R. Liu, J. Cao, Single drop microextraction combined with graphite furnace atomic absorption spectrometry for determination of lead in biological samples, Microchim. Acta 160 (2008) 135–139.
[58] L. Xia, B. Hu, Z. Jiang, Y. Wu, L. Li, R. Chen, 8-Hydroxyquinoline-chloroform single drop microextraction and electrothermal vaporization ICP-MS for the fractionation of aluminium in natural waters and drinks, J. Anal. At. Spectrom. 20 (2005) 441–446.
[59] L. Li, B. Hu, L. Xia, Z. Jiang, Determination of trace Cd and Pb in environmental and biological samples by ETV-ICP-MS after single-drop microextraction, Talanta 70 (2006) 468–473.
[60] J. Cao, P. Liang, R. Liu, Determination of trace lead in water samples by continuous flow microextraction combined with graphite furnace atomic absorption spectrometry, J. Hazard. Mater. 152 (2008) 910–914.
[61] J.F. Peng, R. Liu, J.F. Liu, B. He, X.L. Hu, G.B. Jiang, Ultrasensitive determination of cadmium in seawater by hollow fiber supported liquid membrane extraction coupled with graphite furnace atomic absorption spectrometry, Spectrochim. Acta Part B 62 (2007) 499–503.
[62] L. Xia, Y. Wu, B. Hu, Hollow-fiber liquid-phase microextraction prior to low-temperature electrothermal vaporization ICP-MS for trace element analysis in environmental and biological samples, J. Mass Spectrom. 42 (2007) 803–810.
[63] L. Li, B. Hu, Hollow-fibre liquid phase microextraction for separation and preconcentration of vanadium species in natural waters and their determination by electrothermal vaporization-ICP-OES, Talanta 72 (2007) 472–479.
[64] M. Shamsipur, M. Ramezani, Selective determination of ultra trace amounts of gold by graphite furnace atomic absorption spectrometry after dispersive liquid–liquid microextraction, Talanta 75 (2008) 294–300.
[65] E.Z. Jahromi, A. Bidari, Y. Assadi, M.R. Milani Hosseini, M.R. Jamali, Dispersive liquid–liquid microextraction combined with graphite furnace atomic absorption spectrometry Ultra trace determination of cadmium in water samples, Anal. Chim. Acta 585 (2007) 305–311.
[66] H. Jiang, Y. Qin, B. Hu, Dispersive liquid phase microextraction (DLPME) combined with graphite furnace atomic absorption spectrometry (GFAAS) for determination of trace Co and Ni in environmental water and rice samples, Talanta 74 (2008) 1160–1165.
[67] M.T. Naseri, M.R. Milani Hosseini, Y. Assadi, A. Kiani, Rapid determination of lead in water samples by dispersive liquid–liquid microextraction coupled with electrothermal atomic absorption spectrometry, Talanta 75 (2008) 56–62.
[68] A.B. Volynskii, B.Y. Spivakov, Y.A. Zolotov, Solvent extraction-electrothermal atomic-absorption analysis, Talanta 31 (1984) 449–458.
[69] M.A. Farajzadeh, M. Bahram, B.G. Mehr, J.A. Jönsson, Optimization of dispersive liquid–liquid microextraction of copper (II) by atomic absorption spectrometry as its oxinate chelate: application to determination of copper in different water samples, Talanta 75 (2008) 832–840.
[70] M.T. Naseri, P. Hemmatkhah, M.R. Milani Hosseini, Y. Assadi, Combination of dispersive liquid–liquid microextraction with flame atomic absorption spectrometry using microsample introduction for determination of lead in water samples, Anal. Chim. Acta 610 (2008) 135–141.
[71] N. Shokoufi, F. Shemirani, Y. Assadi, Fiber optic-linear array detection spectrophotometry in combination with dispersive liquid–liquid microextraction for simultaneous preconcentration and determination of palladium and cobalt, Anal. Chim. Acta 597 (2007) 349–356.
[72] M. Gharehbaghi, F. Shemirani, M. Baghdadi, Dispersive liquid–liquid microextraction and spectrophotometric determination of cobalt in water samples, Int. J. Environ. Anal. Chem. 88 (2008) 513–523.
[73] A. Bidari, E. Zeini Jahromi, Y. Assadi, M.R. Milani Hosseini, Monitoring of selenium in water samples using dispersive liquid–liquid microextraction followed by iridium-modified tube graphite furnace atomic absorption spectrometry, Microchem. J. 87 (2007) 6–12.
[74] L. Xia, B. Hu, Z. Jiang, Y. Wu, R. Chen, L. Li, Hollow fiber liquid phase microextraction combined with electrothermal vaporization ICP-MS for the speciation of inorganic selenium in natural waters, J. Anal. At. Spectrom. 21 (2006) 362–365.
[75] M. Sharkouhi, Y. Yamini, M.R. Khalili Zanjani, A. Afsharnaderi, Liquid-phase microextraction and gas-chromatographic determination of selenium(IV) in aqueous samples, Int. J. Environ. Anal. Chem. 87 (2007) 603–614.
[76] Z. Fan, Determination of antimony(III) and total antimony by single-drop microextraction combined with electrothermal atomic absorption spectrometry, Anal. Chim. Acta 585 (2007) 300–304.
[77] H. Shioji, S. Tsunoi, H. Harino, M. Tanaka, Liquid-phase microextraction of tributyltin and triphenyltin coupled with gas chromatography-tandem mass spectrometry. Comparison between 4-fluorophenyl and ethyl derivatizations, J. Chromatogr. A 1048 (2004) 81–88.
[78] V. Colombini, C. Bancon-Montigny, L. Yang, P. Maxwell, R.E. Sturgeon, Z. Mester, Headspace single-drop microextration for the detection of organotin compounds, Talanta 63 (2004) 555–560.
[79] A.P. Birjandi, A. Bidari, F. Rezaei, M.R. Milani Hosseini, Y. Assadi, Speciation of butyl and phenyltin compounds using dispersive liquid–liquid microextraction and gas chromatography-flame photometric detection, J. Chromatogr. A 1193 (2008) 19–25.

[80] Z. Fan, X. Liu, Determination of methylmercury and phenylmercury in water samples by liquid–liquid–liquid microextraction coupled with capillary electrophoresis, J. Chromatogr. A 1180 (2008) 187–192.
[81] L. Xia, B. Hu, Y. Wu, Hollow fiber-based liquid–liquid–liquid microextraction combined with high-performance liquid chromatography for the speciation of organomercury, J. Chromatogr. A 1173 (2007) 44–51.
[82] H. Jiang, B. Hu, B. Chen, W. Zu, Hollow fiber liquid phase microextraction combined with graphite furnace atomic absorption spectrometry for the determination of methylmercury in human hair and sludge samples, Spectrochim. Acta Part B 63 (2008) 770–776.
[83] F.J. Pena Pereira, C. Bendicho, N. Kalogerakis, E. Psillakis, Headspace single drop microextraction of methylcyclopentadienyl-manganese tricarbonyl from water samples followed by gas chromatography-mass spectrometry, Talanta 74 (2007) 47–51.
[84] P. Das, M. Gupta, A. Jain, K.K. Verma, Single drop microextraction or solid phase microextraction-gas chromatography-mass spectrometry for the determination of iodine in pharmaceuticals, iodized salt, milk powder and vegetables involving conversion into 4-iodo-*N*,*N*-dimethylaniline, J. Chromatogr. A 1023 (2004) 33–39.
[85] Q. Xiao, C. Yu, J. Xing, B. Hu, Comparison of headspace and direct single-drop microextraction and headspace solid-phase microextraction for the measurement of volatile sulfur compounds in beer and beverage by gas chromatography with flame photometric detection, J. Chromatogr. A 1125 (2006) 133–137.
[86] K. Reddy-Noone, A. Jain, K.K. Verma, Liquid-phase microextraction-gas chromatography-mass spectrometry for the determination of bromate, iodate, bromide and iodide in high-chloride matrix, J. Chromatogr. A 1148 (2007) 145–151.
[87] E. Baltussen, C.A. Cramers, P.J.F. Sandra, Sorptive sample preparation — a review, Anal. Bioanal. Chem. 373 (2002) 3–22.
[88] Z. Mester, R. Sturgeon, J. Pawliszyn, Solid phase microextraction as a tool for trace element speciation, Spectrochim. Acta Part B 56 (2001) 233–260.
[89] Z. Mester, R. Sturgeon, Trace element speciation using solid phase microextraction, Spectrochim. Acta Part B 60 (2005) 1243–1269.
[90] A.K. Malik, V. Kaur, N. Verma, A review on solid phase microextraction—high performance liquid chromatography as a novel tool for the analysis of toxic metal ions, Talanta 68 (2006) 842–849.
[91] S. Díez, J.M. Bayona, Determination of Hg and organomercury species following SPME: a review, Talanta 77 (2008) 21–27.
[92] C.L. Arthur, J. Pawliszyn, Solid phase microextraction with thermal desorption using fused silica optical fibers, Anal. Chem. 62 (1990) 2145–2148.
[93] M.S. Fragueiro, F. Alava-Moreno, I. Lavilla, C. Bendicho, Determination of tetraethyllead by solid phase microextraction-thermal desorption-quartz furnace atomic absorption spectrometry, J. Anal. At. Spectrom. 15 (2000) 705–709.
[94] C. Haberhauer-Troyer, M. Crnoja, E. Rosenberg, M. Grasserbauer, Surface characterization of commercial fibers for solid-phase microextraction and related problems in their application, Fresenius J. Anal. Chem. 366 (2000) 329–331.
[95] E. Baltussen, P. Sandra, F. David, C. Cramers, Stir bar sorptive extraction (SBSE), a novel extraction technique for aqueous samples: theory and principles, J. Microcolumn Sep. 11 (1999) 737–747.
[96] F. David, P. Sandra, Stir bar sorptive extraction for trace analysis, J. Chromatogr. A 1152 (2007) 54–69.
[97] J. Vercauteren, C. Pèrés, C. Devos, P. Sandra, F. Vanhaecke, L. Moens, Stir bar sorptive extraction for the determination of ppq-level traces of organotin compounds in environmental samples with thermal desorption-capillary gas chromatography-ICP mass spectrometry, Anal. Chem. 73 (2001) 1509–1514.
[98] A. Prieto, O. Zuloaga, A. Usobiaga, N. Etxebarría, L.A. Fernández, C. Marcic, A. de Diego, Simultaneous speciation of methylmercury and butyltin species in environmental samples by headspace-stir bar sorptive extraction-thermal desorption-gas chromatography-mass spectrometry, J. Chromatogr. A 1185 (2008) 130–138.
[99] J.A. Riddick, W.B. Bunger, T.K. Sakano, 4th ed., Organic Solvents. Physical Properties and Methods of Purification, vol. II, Willey, New York, 1986.