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A Review on Application of Microextraction Techniques for Analysis of Chemical Compounds and Metal Ions in Foodstuffs

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$[C_4mim][PF_6]$, 1-butyl-3-methylimidazolium hexafluorophosphate; $[C_8MIM][BF_4]$, 1-octyl-3-methylimidazolium tetrafluoroborate; $[C_8MIM][PF_6]$, 1-octyl-3-methylimidazolium hexafluorophosphate; [Hmim][Tf2N], 1-hexyl-3-methylimmidazolium bis(trifluormethylsulfonyl)imid; AA, acetic anhydride; AALLME, air-assisted liquid-liquid microextraction; ANW, alumina nanowire; APDC, ammonium pyrrolidinedithiocarbamate; BP, bisphenol; BPA, bisphenol A; BPS bisphenol S; BSTFA, bis(trimethylsilyl) trifluoroacetamide; CAR/PDMS, CarboxenTM/polydimethylsiloxane; CE, capillary electrophoresis; CIAME, cold-induced aggregation microextraction; CW, carbowax; CW/DVB, carbowax/divinylbenzene; DA, N,N-dimethylaniline; DAD, diode array detection; DDSME, drop-to-drop solvent microextraction; SPE, solid phase extraction; SPME, solid phase microextraction; DI-SPME, Direct extraction SPME; DLLME, dispersive liquid-liquid microextraction; DSDME, directly suspended droplet microextraction; ECD, electron capture detector; EFs, enrichment factors; EnFs, enhancement factors; ETAAS, electrothermal atomic absorption spectrophotometry; FAAS, flame atomic absorption spectrophotometry; FID, flame ionization detector; FLD, fluorescence detection; FPD, flame photometric detection; GC, gas chromatography; HD, hydrodistillation; HF-LPME, hollow fiber protected liquid phase microextraction; HPLC, high-performance liquid chromatography; HS-SPME, Headspace-SPME; IL, ionic liquid; IL-CIA-DLLME, ionic liquid cold-induced aggregation dispersive liquid-liquid microextraction; IL-DLLME, ionic liquid-DLLME; LC, liquid chromatography; LC-ESI-QTOF-MS, LC-electrospray ionization-quadrupole time-of-flight mass spectrometry; LLE, liquid-liquid extraction; LODs, limit of detections; LOQs, limit of quantitations; LPME, liquid phase microextraction; LRs, linear ranges; M-CIAME, modified cold-induced aggregation microextraction; MS, mass spectrometry; *o*-NA, *o*-nitroaniline; OPPs, organophosphorus pesticides; PA, polyacrylate; *p*-AA, *p*-aminoacetylbenzene; PAHs, polycyclic aromatic hydrocarbons; PAN, 1-(2-pyridylazo)-2-naphthol; PCBs, polychlorinated biphenyls; PDMS/DVB, poly (dimethylsiloxane)/ divinylbenzene; PEG, poly(ethylene glycol); PEG/CNTs, PEG reinforced with multi-walled carbon nanotubes; PLS, partial least squares; *p*-NA, *p*-nitroaniline; PVA, poly(vinyl alcohol); RP-HPLC, reverse phase high performance liquid chromatography; RSDs, relative standard deviations; SBSE, stir bar sorptive extraction; SDME, single drop microextraction; SFODME, solidification of a floating organic droplet microextraction; USAE-SFODME, ultrasound-assisted emulsification solidified floating organic drop microextraction; UV, ultraviolet; VWD, variable wavelength detector.

Foodstuffs analysis is very important due to population growth and increasing consumer demand for safety and nutritional excellence. The direct analysis of different compounds in foodstuffs without any sample preparation method is generally very difficult. Traditional techniques require large amounts of toxic organic solvents. As a result, they are not only expensive but also environmentally unfriendly and they generate a considerable amount of waste. Nowadays efforts are being focused on development of microextraction techniques. Different microextraction techniques such as solid phase microextraction (SPME), stir bar sorptive extraction (SBSE), and liquid phase microextraction (LPME) have found an important place in sample preparation because of their inherent advantages over the conventional procedures. In particular, they have been applied with successfully for the analysis of food samples despite their complexity. The review

discusses different microextraction approaches used in analysis of chemical compounds and metal ions in foodstuffs. It summarizes the application of microextraction techniques in food analysis in details as possible.

Keywords: Food analysis, Sample preparation, Microextraction, Chromatography, Spectrometry

INTRODUCTION

Nowadays, food chemistry is one of the most important fields of science. The increase in food demand for the growing world population as well as consumer demand for safety and nutritional excellence emphasize the importance of food analysis. In general, food samples cannot be analyzed without some preliminary sample preparation, because contaminants (analytes) are too diluted and the matrix is rather complex [1,2]. Sample preparation, such as extraction, enrichment, and isolation of analytes, greatly influences the reliability and accuracy of the analysis [1]. Liquid-liquid extraction (LLE), based on the transfer of analyte from an aqueous sample to a water-immiscible solvent, is widely employed for sample preparation. Nevertheless, some shortcomings such as emulsion formation, use of large sample volumes and toxic organic solvents makes LLE time-consuming, expensive, and environmentally unfriendly. Another popular sample preparation approach is solid phase extraction (SPE). Although it uses less solvent than LLE, the amount of solvent used can still be considered significant, and normally an extra step of concentrating the extract down to a small volume is needed. SPE can be automated but this entails complexity and additional cost [3,4]. Nowadays efforts are being focused on development of new approaches to save time, labor and materials. In this sense, current trends are moving towards its simplification, miniaturization, and automation involving also the use of solvent-free or environmentally friendly procedures, and maintaining at the same time good/acceptable extraction efficiencies. Over the last years, some new miniaturized extraction procedures have been explored as alternatives to conventional sample preparation procedures such as solid phase microextraction, stir bar sorptive extraction, single drop microextraction, hollow fiber-liquid phase microextraction, dispersive liquid-liquid microextraction, air-assisted liquid-liquid microextraction, *etc.*

The aim of this review is to compile and discuss the applications of different kinds of microextraction techniques for analysis of chemical compounds and metal ions in food products. In this review, after brief explanations of the principles of the microextraction methods, their applications to the analysis of foodstuffs are explained in detail.

MICROEXTRACTION TECHNIQUES

Solid Phase Microextraction (SPME)

SPME was developed by Pawliszyn and co-workers in 1990 [5,6]. This technique uses a silica fiber that is coated with an appropriate adsorbent phase. The analyte in the sample is directly extracted and concentrated to the fiber coating. SPME integrates sampling, extraction, concentration, and sample introduction into a single solvent-free step. During the SPME operation, the fiber is first drawn into the syringe needle and then lowered into a vial (which is sealed with a septum type cap) by pressing the plunger. The type of fused silica coating is dependent upon the nature of the analyte. The fiber should be cleaned before analyzing any sample. Unconditioned fiber gives a high background in the chromatogram [7]. The most common procedure for desorbing analytes from the fiber in SPME is the thermal desorption into the injection port of a gas chromatograph because this desorption method completely eliminates the use of organic solvents [8]. The analytes adsorbed on the fibers can also be desorbed by using a polar organic solvent, such as methanol or acetonitrile. This approach is used to combine this extraction technique with liquid chromatography (LC). The main advantages of SPME are simplicity, high sensitivity, and the need for small sample volume. Other significant aspects of SPME technique are reproducibility, repeatability, and the possibility of quantitative determinations [9]. SPME can be successfully applied for polar and non-polar compounds in

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gas, liquid, and solid samples, and it can be easily coupled with various analytical instruments such as gas chromatography (GC), high-performance liquid chromatography (HPLC), *etc*. [9-11]. There are three basic modes of SPME based on the position of the extraction fiber: (1) direct extraction, (2) headspace extraction, and (3) in-tube SPME. These extraction modes are discussed in the following section.

Direct extraction (DI-SPME). In direct extraction, the coated fiber is inserted directly into the sample [12]. Agitation is required to facilitate rapid extraction in the case of liquid sample matrices. However, for gaseous samples, natural flow of air is sufficient to achieve equilibrium for volatile compounds. In 2013, Zhang *et al*. [13] prepared a novel alumina nanowire (ANW) SPME fiber coating by a simple and rapid anodization-chemical etching method for the ultra-selective determination of trace volatile esters and alcohols from complicated banana and fermented glutinous rice samples coupled with GC-mass spectrometry (MS). Compared with most of commercial SPME fiber coatings, ANW-SPME fiber coatings achieved higher extraction capacity and special selectivity for volatile esters and alcohols. Recoveries for the volatile esters and alcohols from banana and fermented glutinous rice samples were 108-115% with relative standard deviations (RSDs) of 2.6-6.7% and 80.0-91.8% with RSDs of 0.3-1.3% (n = 3), respectively. Viñas *et al*. [14] used SPME combined with GC-MS for the sensitive determination of bisphenol A (BPA), bisphenol S (BPS) and biphenol (BP) in peas, carrots, sweet corn, artichoke, mushroom, bean shoot, and vegetables. Derivatization was done using both acetic anhydride (AA) and bis-(trimethylsilyl)trifluoroacetamide (BSTFA) to convert the non-volatile compounds into volatile derivatives. Limit of detections (LODs) were better using BSTFA than AA, and also were ~100 times better than those obtained without derivatization. LODs ranged from 3 to 16 pg ml^{-1}, depending on the compound. Recoveries obtained for spiked samples were satisfactory for all the compounds. In addition, other application of direct extraction method have been reported, including: DI-SPME-GC-flame photometric detection (FPD) with sol-gel crown ether fiber for determination of some pesticides in honey, juice, and orange samples [15]; DI-SPME-capillary electrophoresis (CE)-ultraviolet (UV) with poly (dimethylsiloxane)/divinylbenzene (PDMS/DVB) fiber for determination of pesticide multi residues in water and fruit juice samples [16]; DI-SPME-GC-positive chemical ionization tandem mass spectrometry with carbowax/ divinylbenzene (CW/DVB) fiber for determination of acrylamide in French fries and potato crisps samples [17].

Headspace extraction. Headspace (HS) extraction involves two states of equilibrium; one between the sample matrix and the gaseous phase (headspace) above it and the other between the headspace and the coating on the extracting fiber [7]. The use of HS-SPME mitigates swelling of the SPME fiber as well as matrix effects, both of which can lead to irreproducible results and/or degrade the fiber (18). Due to the specificity of food matrices (presence of sugars, lipids, proteins, colorants and other non-volatiles), SPME is used almost exclusively as the headspace extraction method [19], because some complex matrices like milk adversely affect DI-SPME performance in such circumstances [20,21]. Fouling of the SPME fiber can be lessened by removing matrix components (*e.g.* saponifying milk fats) [22,23], diluting the sample [24], pH adjustment [25], or increasing the salt content of the solution [7,26,27].

Dong *et al*. [28] used HS-SPME procedure using 85 µm polyacrylate (PA) fiber for the simultaneous determination of preservatives (sorbic and benzoic acids) in food dressing by GC-flame ionization detector (FID). Under optimized conditions, linear ranges (LRs) were 0.02 to 40 mg l^{-1} and LODs of the method were 2.00 and 1.22 µg l^{-1} for sorbic acid and benzoic acid, respectively. Recoveries for the two analytes in all tested samples ranged from 83.44 to 113.2%. Kataoka *et al*. [29] developed HS-SPME coupled with GC-MS for the determination of isophorone in food samples such as tea, tomato juice, milk, honey, sugar, chicken, fresh fish and rice. The HS-SPME using a PDMS/DVB fiber provided effective analyte enrichment and was carried out by fiber exposure to samples at 60 ^{o}C for 45 min. The extracted isophorone was easily desorbed by fiber insertion into the injection port of a capillary GC-MS system, and carry over was not observed. Using this method, LR and LOD were obtained to be 20-1000 pg ml^{-1} and 0.5 pg ml^{-1}, respectively. The proposed method showed 25,000-fold higher sensitivity than the direct injection method (1 µl injection). Also, HS-SPME-GC-FID with

Carboxen^{TM}/polydimethylsiloxane (CAR/PDMS) fiber was applied for analysis of hexanal and pentane in infant formulas [30]. The fibers of poly(ethylene glycol) (PEG) and PEG reinforced with multi-walled carbon nanotubes (PEG/CNTs) were used for furan determination in baby food and fruit juice samples [31].

In-tube SPME. In-tube SPME is an effective sample preparation technique based on using a fused silica capillary column as the extraction device. Target analytes in aqueous matrices are directly extracted and concentrated by the coating in the capillary column by repeated withdrawal and expulsion of the sample solution. Then the enriched analytes can be directly transferred to a LC or GC for analysis. The procedure of in-tube SPME including extraction, concentration, desorption, and injection can be easily automated by use of a conventional autosampler [32,33]. In-tube SPME allows convenient automation of the extraction process, which not only reduces the analysis time, but also provides better accuracy, precision and sensitivity compared to manual off-line techniques [34]. On-line in-tube SPME is usually used in combination with HPLC and LC-MS [35]. The technique which uses a portion of a GC capillary column is also known as open-tubular trapping, and can be coupled on-line with GC [36,37]. Zheng *et al*. [38] determined seven trace quinolone antibacterial simultaneously in four different animal products including milk, egg, chicken, and fish by combination of polymer monolith in-tube SPME with LC and electrospray ionization-quadrupole time-of-flight mass spectrometry (LC-ESI-QTOF-MS). The extraction was performed with a poly (methacrylic acid-ethylene glycol dimethacrylate) monolithic column. The sensitivity together with mass accuracy of the ESI-QTOF-MS allowed the unambiguous identification of quinolone residues in the animal products. LODs for seven quinolones were found to be 0.3-1.2 ng g^{-1} in egg, 0.2-3.0 ng ml^{-1} in milk, 0.2-0.7 ng g^{-1} in chicken, and 0.2-1.0 ng g^{-1} in fish. The recoveries of quinolones spiked in four different matrices ranged from 80.2 to 115.0%, with RSDs less than 14.5%. Nonaka *et al*. [34] developed on-line in-tube SPME coupled with LC-MS for determination of aflatoxins (B1, B2, G1, and G2) in nuts, cereals, dried fruits, and spices. The in-tube SPME optimum conditions were 25 draw/eject cycles of 40 µl of sample using a Supel-Q PLOT capillary column as an extraction device. LRs were obtained in the range of 0.05-2.0 ng ml^{-1} using aflatoxin M1 as an internal standard, and LODs were 2.1-2.8 pg ml^{-1}. The in-tube SPME method showed >23-fold higher sensitivity than the direct injection method (10 µl injection volume). In addition, the application of in-tube-SPME-HPLC-diode array detection (DAD) with a Supel-Q porous layer open tubular capillary column for determination of daidzein and genistein in soybean foods [39], in-tube-SPME-HPLC-LC/MS with Supel-Q PLOT capillary column for determination of abietic acid and dehydroabietic acid in liquid samples (tea and soft drinks) as well as semi-solid and solid samples (sugar, mushroom, and wheat flour) [40], in tube-SPME-HPLC-fluorescence detection (FLD) with CP-Sil 19CB capillary column for determination of 15 polycyclic aromatic hydrocarbons (PAHs) in tea products and dried food (shiitake, radish, *etc*.) [41] has been reported. Table 1 summarizes different SPME techniques used for the analysis of various analytes in food samples.

Stir Bar Sorptive Extraction (SBSE)

SBSE is a microextraction method which was introduced in 1999 by Baltussen *et al.* [45]. This sorptive extraction technique is based on the same principles as SPME but with a greater extraction capacity. It helps to overcome the small volume of the coated SPME fiber for a better enrichment factor. In the SBSE technique, a magnetic stir bar with the length of 10-40 mm coated with 50-300 µl of PDMS is used as the extracting phase [46]. The analytes are adsorbed on a PDMS coated magnetic rod, by stirring the sample solution with the rod for a given time. The extraction time is kinetically controlled and determined by the sample volume, stirring rate, temperature, and stir bar dimensions and must be optimized for a given application [47]. Desorption of the solute from the bar may be done by either heating or back extraction with a small volume of a solvent. When SBSE is combined with GC, thermal desorption is the preferred way. The bar is inserted into the heated GC injection port and the analytes desorbed to the column for further analysis. Solvent desorption can be combined with both GC and LC. The stir bar is placed in a small vial, and desorption can be performed by adding either a few microliters of a proper solvent (for GC) or the mobile phase (for LC) [47]. In the SBSE method development, factors such as extraction time and

Table 1. Different SPME Techniques Used in Analysis of Food Samples

Food samples	Analyte	Type of fiber	Separation technique	LOD	Extraction time (min)	Recovery (RSD%)	Ref.
Banana	3-Methylbutyl 3-methylbutanoate, 1-butyl butyrate, 1-hexyl butyrate	ANW	GC-MS	0.04-0.07 μg l^{-1}	15	108-115 (2.6-6.7)	[13]
Fermented glutinous rice	1-Propanol, 2-methyl-1-propanol, 2-propanol, 2-furanmethanol			0.3-0.6 μg l^{-1}		80-91 (0.3-1.3)	
Orange juice	Furan	PEG	GC-FID	0.001 ng ml^{-1}	30	98.5 (6.2)	[31]
Apple juice						97 (7.2)	
Two type of baby food						92-95 (7.2- 10.7)	
Orange juice	Furan	PEG/CNTs	GC-FID	0.00025 ng ml^{-1}	10	103 (5.8)	[31]
Apple juice						98 (5.6)	
Tow type of Baby food						95-97.5 (6.1-5.9)	
Honey	Dichlorvos, phorate, dimethoate, diazinon, methyl parathion, ethion, fenitrothion, malathion, triazophos, fenthion,chlorpyrifos	Sol-gel crown ether	GC-FPD	0.004-0.7 ng g^{-1}	60	74-105 (2.1-15.0)	[15]
Fruit juice				0.003-0.2 ng g^{-1}		80-96 (2.0-9.2)	
Pakchoi				0.063-1.0 ng g^{-1}		76-101 (2.3-9.1)	
Milli-Q water	Pyrimethanil, pirimicarb, pyrifenox, cyprodinil	PDMS/DVB	CE-UV	2.5-6.0 μg ml^{-1}	150	38-46 (6-9)	[16]
Apple juice				3.1-12.4 μg ml^{-1}		14-36 (7-11)	
Orange juice				8.1-34.6 μg ml^{-1}		5-14 (6-13)	
Thousand island dressing	Benzoic acid, sorbic acid	PA	GC-FID	1.22-2.0 μg l^{-1}	40	83-86 (3.1-12.0)	[28]
HellMANN's salad dressing						110-113 (5-2.7)	
Tomato ketchup						94-103 (1.7-8.6)	
Potato crisps	Acrylamide	CW/DVB	GC-MS-MS	0.1 μg l^{-1}	20	-	[17]
Peas	Bisphenol A, bis(3-chloro-2-hydroxypropyl)ether, bisphenol F diglycidyl ether, 2,2-bis[4(glycidyloxy)phenyl] propane, 2,2-bis(4-hydroxyphenyl)propane	CW	HPLC-FLD	0.7-2.4 μg l^{-1}	20	7-65 (14-32)	[42]
Tuna							
Olives							
Maize							
Artichokes							

Table 1. Continued

Samples contacted with paper such as green tea	Abietic acid, dehydroabietic acid	Supel Q PLOT capillary column	LC-MS	2.1-2.9 ng l^{-1}	25	>79 (<6.6)	[40]
Water	Tetramethylene disulfotetramine	CW/DVB	GC-MS	2.7 ng g^{-1}	90	100 (7.0)	[43]
Fruit juice				3.6 ng g^{-1}		50 (12)	
Apple sauce				2.7 ng g^{-1}		130 (1)	
Potato chips				2.6 ng g^{-1}		200 (-)	
Peas				4.3 ng g^{-1}		90 (11)	
Peanut butter				1.3 ng g^{-1}		140 (-)	
Tuna				4.2 ng g^{-1}		130 (-)	
Yoghurt				0.9 ng g^{-1}		140 (7.8)	
Rice	Aflatoxin B2, aflatoxin B2, aflatoxin G1, aflatoxin G2	Supel-Q PLOT capillary column	LC-MS	2.1-2.8 pg ml^{-1}	25	80.8-10.9.0	[34]
Almond						94.5-109.1	
Baby food	Picoxystrobin, metominostrobin, kresoxim-methyl, trifloxystrobin, dimoxystrobin, pyraclostrobin, azoxystrobin	PDMS-DVB	GC-MS	1-30 pg ml^{-1}	40	96-109	[44]
Egg	Ofloxacin, flumequine, oxolinic acid, sarafloxacin, difloxacin, danofloxacinmethanesulphonate, ciprofloxacin, enrofloxacin	Poly(methacrylic acid-ethylene glycol dimethacrylate) monolithic column	LC-ESI-QTOF-MS	0.3-1.2 ng g^{-1}	6	31.9-96.4	[38]
Milk				0.2-3.0 ng g^{-1}		11.6-96.4	
Chicken				0.2-0.7 ng g^{-1}		11.4-69.1	
Fish				0.2-1.0 ng g^{-1}		15.0-83.1	
Liquid infantfoods and powdered infant formulas	Hexanal, pentane	CAR/PDMS	GC-FID	3.63-4.2 ng g^{-1}	60	95.39-106.6 (2.34-3.46)	[30]
Tea products	Naphthalene, phenanthrene, pyrene, acenaphthene, fluorine, fluoranthene, benz[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[a]pyrene, benzo[ghi]perylene, indeno[1,2,3- cd]pyrene, dibenz[a,h]anthracene, anthracene, benzo[ghi]perylene	CP-Sil 19CB capillary column	HPLC-FLD	0.21-3.08 ng g^{-1}	35	69.9-100.7	[41]
Dried food						-	
Soybean foods	Daidzein, genistein, daidzin, genistin, β-naphthol	A Supel-Q porous layer open tubular (PLOT) capillary column	HPLC-DAD	0.4-0.5 ng ml^{-1}	30	97.8-116.1	[39]

temperature, pH, ionic strength, sample volume, agitation speed and volume of the acceptor phase (in solvent desorption) are very important and need to be optimized for achieving higher extraction efficiency and lower detection limit [48,49]. The amount of coating (PDMS) in SBSE is usually 50-250 times larger than SPME, which increases the preconcentration efficiency. However, the large amount of coating increases the equilibrium time due to the diffusion into the large volume of the coating [50].

In SBSE technique, a coated stir bar can be added to the sample for both stirring and extraction (direct SBSE) or exposed to the headspace of the sample (HS-SBSE). In HS-SBSE, sampling is performed by suspending a polymer-coated stir bar in an HS vial and the polymer phase is in static contact with the vapor phase of a solid or liquid matrix. The sample is usually stirred by another magnetic stirrer (uncoated) in order to favor the presence of solute in the vapor phase. After HS sampling, it is also recommended that the polymer-coated stir bar be rinsed with distilled water and gently wiped with a clean tissue paper [51]. One of the disadvantages of SBSE is that it involves longer desorption time, due to the higher amount of stir bar coating [52]. De Jager *et al*. [53] developed an SBSE method combined with GC-MS for the determination of tetramethylene disulfotetraamine in water and foodstuffs such as potato chips, peas, yoghurt, and juice. Extraction has been performed using a 70 µm CW/DVB coating. Under the optimum condition, LODs ranged between 0.3 and 2.1 ng g^{-1}. HS-SBSE coupled with GC-MS-MS and GC-ECD (electron capture detector) with bulk PDMS fiber was applied for analysis of halogenated anisoles in wine [54]. Also, organophosphorus pesticides (OPPs) was determined by SBSE-GC-flame photometric detector (FPD) using PDMS-PVA (poly (vinyl alcohol)) coating [55].

Liquid Phase Microextraction (LPME)

Extraction of analytes from aqueous matrices and headspace with a minimal amount of solvent started with the works introduced by Liu and Dasgupta [56], Jeannot and Cantwell [57], and He and Lee [58]. They noticed that a single droplet of solvent can be used for the effective extraction of analytes form samples. After initial use of polymer rod to which the solvent drop adhered, GC syringe became a tool which enabled withdrawal of the droplet into syringe needle and subsequent injection into GC. LPME term is an LLE with a minimized solvent volume (acceptor phase-water immiscible solvent) used to extract analytes from an aqueous solution (donor phase). So far, different approaches of LPME such as single drop microextraction (SDME), hollow fiber protected liquid phase microextraction (HF-LPME), dispersive liquid-liquid microextraction (DLLME) [59], air assisted liquid–liquid microextraction (ALLME), and *etc*. [60] have been developed for the analysis of different compounds in food samples, which are briefly discussed in the following paragraphs.

HF-LPME. In recent years, there was a growing interest in the use of porous hollow fiber based LPME [61-64]. This technique is simple and inexpensive, with the further advantage that the fiber is disposable after use due to its low cost, thus overcoming carry-over problems [65]. LPME has been applied successfully for the extraction and clean-up of complicated samples such as drug/pharmaceuticals [65,66], environmental samples [67,68], and foodstuff.

Saaid *et al*. [69] developed an HF-LPME with in situ derivatization using dansyl chloride for HPLC-UV determination of biogenic amines (tryptamine, putrescine, cadaverine, histamine, tyramine, spermidine) in shrimp sauce and tomato ketchup samples. Firstly, 4.0 ml of food sample was transferred into a centrifuge tube and 5 ml water was added. The mixture was vortexed until a homogeneous sample was obtained. The homogenate sample was centrifuged at 3000 rpm for 10 min. The supernatant was transferred into a volumetric flask (10 ml) and the final volume was adjusted to 10 ml with water. The sample was then subjected to the LPME procedure. Enrichment factors (EFs) and LODs obtained in the ranges of 47-456 and 0.0075-0.030 µg ml^{-1}, respectively. The determination of specific migration in three aqueous food stimulants (water, 3% acetic acid, and 10% ethanol) from experimental active packaging polypropylene-based films containing natural essential oils as active agents has been carried out by HF-LPME [70]. Bjorhovde *et al*. [71] evaluated the extraction of hydrophobic basic drugs from human breast milk. Direct LPME from breast milk samples provided low recoveries (18-38%) because the drugs were partially bound to the sample matrix (fat). Therefore, prior to extraction, the breast

milk was acidified and the majority of fat was removed by centrifugation. From the supernatant, where pH was adjusted into the alkaline region with NaOH to deionize the analytes, the drugs were extracted through a thin layer of polyphenyl-methylsiloxane present in the pores of a porous hollow fiber and into 15 µl of 10 mM HCl as acceptor solution present inside the lumen of the hollow fiber. Subsequently, the acceptor solution was directly subjected to CE. For four antidepressant drugs, the recoveries in the range of 42-69% were obtained. In another work, HF-LPME combined with HPLC-FLD was applied for determination of ochratoxin A in wine [72]. Pezo *et al.* [73] developed a two-phase based HF-LPME with a high automation degree capable of processing up to six samples simultaneously by means of a multiple channel syringe pump. The experimental set-up allows carrying out dynamic extractions with a considerable reduction of sample handling. The system has been applied for determination in aqueous food stimulant of migrants from prototypes of active packaging to assess their safety before marketing. The method showed LODs in the ng g^{-1} range, RSDs below 13%, and concentration factors ranging from 83 to 338. Also, dynamic HF-LPME combined with GC-ECD was applied for analysis of organochlorine pesticides in green tea leaves and ready-to-drink tea samples [74].

SDME. Both SPME and HF-LPME techniques require fibers for the extraction of analytes but in SDME only a single microdrop of solvent is used as an acceptor phase, which is hanging at angle cut tip of a microsyringe and immersed into the aqueous solution for the extraction of analytes. This method is very simple, convenient, and almost cost free compared with SPME and HF-LPME.

Wen *et al*. [75] used 1-butyl-3-methylimidazolium hexafluorophosphate ($[C_4mim][PF_6]$) as an extractant in SDME combined with UV-Vis spectrophotometer for analysis of ultra-trace copper in tea, defatted milk powder, and lake and tap waters. Under the optimal conditions, LOD was 0.15 µg l^{-1} with an enhancement factor of 33. The proposed method was green, simple, rapid, sensitive, and cost-efficient. Manzoori *et al.* [76] also developed this method combined with electrothermal atomic absorption spectrophotometry (ETAAS) for determination of lead in food and water samples. Habibi *et al*. [77] employed the same method coupled with GC-MS to extract and measure furan, 2-methylfuran, and 2,5-dimethylfuran in baby foods. Optimization of effective variables was carried out with the aid of response surface methodology based on central composite design.

The SDME typically uses several to 20 ml of an aqueous solution to extract analytes into the organic phase. From commercial and economic point of view, sample volume should be reduced to a small amount. Thus, static drop-to-drop solvent microextraction (DDSME) introduced by Wu *et al.* [78] is a good technique to satisfy this purpose, since only one drop (7 µl) of sample solution was used for the extraction of analyte. In 2007, Shrivas *et al*. [79] developed a DDSME-GC-MS method for analysis of caffeine in six beverages including coca cola, spirit, coke light, pepsi, colombia coffee, tea and six foods including black, green and oolong tea, Nescafe coffee, Kaiser's milk chocolate, and raisin choco ball branded samples. A sketch of DDSME apparatus for the extraction of caffeine from one drop of sample solution is illustrated in Fig. 1. One drop (7 µl) of the spiked pure water containing 10 µg ml^{-1} of caffeine was taken in a 100 µl sample vial. Then, 1 µl of acceptor organic solvent was taken in a 10-µl microsyringe for DDSME extraction and injection into GC-MS. The optimum experimental conditions for DDSME were: chloroform as the extraction solvent, 5 min extraction time, 0.5 µl exposure volume of the extraction phase, and no salt addition at room temperature. RSD and LOD were 4.4% and 4.0 ng ml^{-1}, respectively.

DLLME. DLLME is a sample preparation technique introduced by Assadi and co-workers [80]. It is performed in three steps: (i) rapid injection of an appropriate mixture of two solvents- one acts as an extraction solvent and the other as a disperser solvent-into an aqueous sample solution with a syringe; (ii) formation of a cloudy solution containing fine droplets of extraction solvent fully dispersed in the aqueous phase; (iii) centrifugation, which leads to accumulation of the extraction solvent containing the extracted analyte(s) in the bottom or at the top of the extraction vessel depending on the extraction solvent density. DLLME is a simple and fast microextraction technique in which small amounts of organic solvents are used. Also, high enrichment factors are usually obtained using this method. These advantages make DLLME a suitable method for analysis of different compounds in

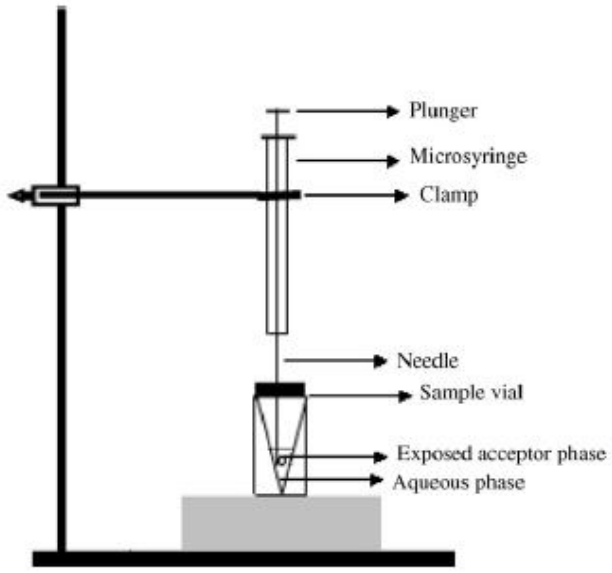

Fig. 1. Sketch of DDSME apparatus for the extraction of caffeine from one drop of sample solution.

various matrices. Wen *et al.* [81] employed DLLME-UV-Vis spectrophotometry for preconcentration and determination of Cd(II) and Cu(II) in lake, river, tap and mineral waters, rice sample, defatted milk powder, and tea. All the real water samples were filtered through a 0.25 µm micropore member and acidified to pH about 5.0 with acetate buffer solution prior to use. Closed-vessel microwave digestion was chosen for decomposing the food samples and the digestion procedure was based on a reference method for corn [82]. The resultant digested/diluted solutions were then subjected to DLLME and subsequently analyzed by a spectrophotometer. Dithizone and diethyldithiocarbamate were utilized as the chelating agents for extraction of cadmium and copper, respectively. Methanol was the best disperser solvent for the extraction of Cd(II) while ethanol was suitable for Cu(II). 100 µl CCl_4 was used as the extraction solvent. Under the optimal conditions, the LODs for cadmium and copper were 0.01 ng l^{-1} and 0.5 µg l^{-1}, with enhancement factors (EnFs) of 3458 and 10, respectively. The tremendous contrast of EnFs could come from the different maximum absorption wavelengths caused by the different extraction acidity and the enhancement effect of acetone used as dilution solvent during the spectrophotometric determination. Daneshfar *et al*. [83] used DLLME technique for extraction and preconcentration of cholesterol from milk, egg yolk and olive oil samples prior to their determination using isocratic reverse phase high performance liquid chromatography (RP-HPLC) and UV detection. Under optimized conditions, LR and LOD were 0.03-10 µg l^{-1}, and 0.01 µg l^{-1}, respectively. Intra-day and inter-day precisions for the analysis of cholesterol were in the range of 1.0-3.1%. In 2013, Wu *et al.* [84] developed a rapid shaking-based ionic liquid-DLLME (IL-DLLME) coupled with HPLC-UV for the simultaneous determination of six synthetic food colorants (tartrazine, amaranth, sunset yellow, allura red, ponceau 4R, and erythrosine) in food samples comprising soft drinks, and sugar- and gelatin-based sweets. Appropriate amounts (0.3-2.5 g) of the samples were dissolved in 25 ml of water. The carbonated drinks were degassed by ultrasonication for 5 min. A warming process (50 ^{o}C for 30 min) was used for the complete dissolution of the sugar- and gelatin-based confectioneries. Samples were diluted to 50 ml in a volumetric flask with an acetate buffer solution (0.2 M, pH 5.0). These solutions were filtered through a paper filter. Then 350 µl 1-octyl-3-methylimidazolium tetrafluoroborate ($[C_8MIM][BF_4]$) was dispersed in the aqueous sample solution as fine droplets by manual shaking, enabling the easier migration of analytes into the ionic liquid phase. This DLLME technique also does not require heating or ultrasonication, which are both time and energy consuming. Disperser solvent or additional chemical reagents, which may pollute the environment, are also not necessary. The LODs were within 0.015-0.32 ng ml^{-1}. Good recoveries from 95.8%–104.5% were obtained. Khani *et al.* [85] developed a combined method including IL-DLLME and partial least squares method (PLS) for the simultaneous preconcentration and determination of cobalt and nickel in water, lettuce and spinach samples. In this work, 65 mg of an IL [1-hexyl-3-methylimidazolium bis (trifluormethylsulfonyl)imid ([Hmim][Tf_2N]) (as an extraction solvent) was dissolved in 500 µl ethanol (as a disperser solvent) and then the binary solution was rapidly injected by a syringe into 10 ml of the sample solution containing Co^{2+} and Ni^{2+}, which were complexed by 1-(2-pyridylazo)-2-naphthol (PAN). After preconcentration, the absorbance of the extracted ions was measured at the wavelength range of 200-700 nm. The PLS method was

then applied for the simultaneous determination of each individual ion. The simultaneous determination of cobalt and nickel using PAN as a chelating agent is very difficult due to a high spectral overlap observed in the absorption spectra of these components. To overcome the drawback of spectral interferences, PLS-1 multivariate calibration approaches has been applied. In 2012, Peng *et al*. [86] proposed an IL-DLLME method combined with HPLC-UV for the analysis of four toxic anilines (*p*-aminoacetylbenzene (*p*-AA), *o*-nitroaniline (*o*-NA), *p*-nitroaniline (*p*-NA), and N,N-dimethylaniline (DA)) in flour and maize steamed breads. The ionic liquid 1-octyl-3-methylimidazolium hexafluorophosphate ($[C_8MIM][PF_6]$) was successfully used as an extraction solvent and methanol as a disperser solvent in this extraction process. Under the optimum condition, the method exhibits a good linearity ($r^2 > 0.99$) over the studied range (50-1000 ng g^{-1}) for anilines. The extraction recoveries for the anilines in two kinds of steamed breads ranged between 34.1%-73.3% and 44.3%-95.3%. LODs and limits of quantitation (LOQs) ranged between 10-15 ng g^{-1} and 30-45 ng g^{-1}, respectively.

Application of DLLME coupled with derivatization reaction provides a one-step derivatization and extraction technique, greatly simplifying the operation steps and shortening the analysis time. Zarei *et al*. [87] developed a DLLME method combined with UV-Vis spectrophotometry for the preconcentration and determination of trace amounts of aziridine in food stimulants (distilled water, 3% (w/v) aqueous acetic acid, 15% (v/v) aqueous ethanol solution, and olive oil). The method is based on derivatization of aziridine with Folin's reagent (1,2-naphthoquione-4-sulphonic acid) and extraction of the colored product using DLLME technique. 400 µl of methanol (as disperser solvent) and 100 µl of chloroform (as extraction solvent) have been used in DLLME. The coupling of DLLME with UV-Vis spectrophotometry provides a simple and low cost procedure for the determination of aziridine without requiring sophisticated instruments such as GC and HPLC. LOD was 1.0 ng ml^{-1}, and RSD for 50 ng ml^{-1} of aziridine was 2.49 (n = 7). For the strong polar and nonvolatile samples, which are unsuitable for analysis by GC, derivatization is necessary to increase the analytes volatility. In 2013, Jain *et al*. [88] proposed the quantitative determination of parabens (methyl-, ethyl-, propyl-, and butyl paraben) in pickle samples, tomato sauce, vinegar, fruit juices, and water samples based on isobutyl chloroformate (IBCF) derivatization and preconcentration using DLLME in a single step. Under optimum conditions, solid samples were extracted with ethanol (disperser solvent) and 200 µl of this extract along with 50 µl of chloroform (extraction solvent) and 10 µl of IBCF was rapidly injected into 2 ml of ultra-pure water containing 150 µl of pyridine to induce formation of a cloudy state. After centrifugation, 1 µl of the sedimented phase was analyzed using GC-FID. LODs and LOQs were 0.029-0.102 µg ml^{-1} and 0.095-0.336 µg ml^{-1}, respectively. Viñas *et al*. [89] employed DLLME combined with LC-FLD for the preconcentration and determination of thiamine (vitamin B_1) in foodstuffs such as beer, brewer's yeast, honey, and baby foods including infant formulas, fermented milk, cereals, and purees. Derivatization was carried out by the chemical oxidation of thiamine with ferricyanide at pH 13 to form fluorescent thiochrome. For DLLME, 0.5 ml of acetonitrile (dispersing solvent) containing 90 µl of tetrachloroethane (extraction solvent) was rapidly injected into 10 ml of sample solution containing the derivatized thiochrome and 24% (w/v) sodium chloride; thereby a cloudy solution was formed. Phase separation was carried out by centrifugation, and a volume of 20 µl of the sedimented phase was submitted to LC. Also, the possibility of determining thiamine esters (thiamine monophosphate and thiamine pyrophosphate) after a suitable enzymatic treatment has been reported by this method.

In 2010, a robust and practical sample preparation method termed ionic liquid cold-induced aggregation dispersive liquid-liquid microextraction (IL-CIA-DLLME) was developed by Zhang *et al*. [90] to reduce the extraction time and the required amount of IL. However, the performance of this microextraction method is significantly decreased by variations in the ionic strength of the sample solution. It is well established that the solubility of ILs increases as the salt content of aqueous solution goes up. Consequently, the volume of the settled phase depends strongly on the ionic strength of the samples. In 2011, Zeeb and Sadeghi [91] developed an efficient microextraction procedure based on modified IL-CIA-DLLME for trace determination of zinc(II) in water samples such as bottled mineral water, river water and tap water and food samples

such as wheat flour, corn flour, apple and potato by flame atomic absorption spectrophotometry (FAAS). In this study, by introducing a common ion of the ionic liquid into the sample solution, the solubility of IL was significantly decreased. Due to the common-ion effect, the volume of the settled phase was not affected by variations of the salt content of the sample. For IL-CIA-DLLME, 30 ml of the sample solution containing Zn^{2+} (in the range of 0.7-26 μg l^{-1}) and 8-hydroxyquinoline (6.62×10^{-5} M) was adjusted to pH 9.0 in a glass test tube with a conical bottom and 0.9 ml of $NaPF_6$ was added. Then, the resultant solution was kept in a thermostated bath at 50 °C for 5 min. A binary solution containing 650 μl of ethanol and 95 mg of [Hmim][PF_6] (extraction solvent) was rapidly injected into the sample solution with a 1.0-ml syringe. Then, the obtained solution was cooled in ice-water bath for 4 min and a cloudy condition was formed. The mixture was then centrifuged for 7 min at 4000 rpm. After this process, fine droplets of [Hmim][PF_6] were joined together and settled in the bottom of the test tube. After removal of the whole aqueous solution, the settled phase in the test tube was dissolved in 500 μl ethanol and introduced into the flame by conventional aspiration. At optimum conditions, the LOD is 0.18 μg l^{-1}, and RSD is 3.0% (n = 5). Also, the same method was reported for trace determination of chromium in water and food samples (non-fat long life cow's milk, black tea and green tea, and wheat flour) by FAAS and speciation of Cr(III) and Cr(VI) in water samples by using Na_2SO_3 as the reducing agent [92]. A mixture of water-immiscible [Hmim][PF_6] ionic liquid (extraction solvent) and ethanol (disperser solvent) were directly injected into a heated aqueous solution containing bis(2-methoxybenzaldehyde) ethylene diimine as a Schiff's base ligand (chelating agent), hexafluorophosphate ($NaPF_6$) as a common ion, together with Cr(III). Afterwards, the solution was placed in an ice-water bath and a cloudy solution was formed due to a considerable decrease of IL solubility. After centrifuging, the sedimented phase containing enriched analyte was subjected into the analytical instrument.

In addition, the application of DLLME-HPLC-VWD (variable wavelength detector) for determination of chloramphenicol and thiamphenicol in honey samples [93], DLLME-HPLC-FLD for determination of PAHs in water and fruit juice samples [94], DLLME-GC-ECD for determination of four polychlorinated biphenyls (PCBs) in fish samples [95], DLLME-GC-FPD for determination of OPPs in tea [96], DLLME-LC-VWD for determination of chloramphenicol in honey [97], DLLME-GC-FID for determination of phthalate esters in milk [98], DLLME-GC-FPD for determination of OPPs in cucumber and water melon samples [99], DLLME-GC-ECD for determination of chlorothalonil, captan, and folpet residues in grape samples [100], and DLLME-HPLC-FLD for determination of carbamate and OPPs in water and fruit juice samples [101] have been reported. Table 2 shows more details about these analyses along with the obtained results.

AALLME. The most significant drawback of DLLME is the use of relatively large volume of the disperser solvent (ml-level). The presence of the disperser in aqueous sample solution makes it relatively less polar. Therefore, the solubility of target lipophilic analytes increases in the aqueous sample solution, which in turn leads to relatively low extraction efficiency. To overcome this drawback, recently, a novel microextraction technique termed as air-assisted liquid-liquid microextraction (AALLME) has been developed [102] in which air was used as an assisting agent for agitation of the solution. This technique is similar to DLLME but it is performed in the absence of any disperser solvent and needs less amount of an organic extracting solvent. Fine organic droplets are formed by repeated aspiration and dispersion of the mixture of aqueous sample solution and extraction solvent in a test tube with a syringe. In 2013, an AALLME technique combined with GC-FID was proposed for the assessment of triazole pesticides residues in surface water, cucumber, tomato, and grape juices samples [60]. In the proposed method, a low density organic solvent (25 μl toluene) as the extraction solvent has been applied using a home-designed extraction vessel. Figure 2 shows a scheme of AALLME procedure using an extraction solvent with a density lower than that of water. The proposed method is rapid, precise, efficient, sensitive, and environment-friendly. Under the optimum extraction conditions, the method showed low LODs (0.53-1.13 ng ml^{-1}), high EFs (713-808) and high extraction recoveries (100 to 113%).

Other techniques of solvent microextraction. In 2007, Khalili Zanjani *et al.* [103] developed a new liquid-phase microextraction method based on solidification

Table 2. Applications of DLLME Combined with Different Instrumental Techniques in Foodstuffs Analysis

Analyte	Matrix	Extraction solvent kind and amount	Disperser solvent kind and volume	Instrument	LR	LOD	Ref.
Cr(III) and Cr(VI)	Milk, tea, wheat flour, and water	90 mg [Hmim][PF_6]	0.5 ml ethanol	FAAS	2-50 ng ml^{-1}	0. 7 ng ml^{-1}	[92]
Cd^{2+} and Cu^{2+}	Rice, defatted milk powder, tea, and water	100 µl CCl_4	0.5 ml ethanol or methanol	UV-Vis spectrophoto-meter	-	0.00001- 0.5 ng ml^{-1}	[81]
Co^{2+} and Ni^{2+}	Lettuce, spinach, and water	65 mg [Hmim][Tf_2N]	0.5 ml ethanol	UV-Vis spectrophoto-meter	2-20 ng ml^{-1}	0.32-0.65 ng ml^{-1}	[85]
Aziridine	Food stimulants	100 µl chloroform	0.4 ml methanol	UV-Vis spectrophoto-meter	2.0-350 ng ml^{-1}	1 ng ml^{-1}	[87]
Thiamine and its esters	Beer, brewer's yeast, honey, and baby foods	90 µl tetrachloroethane	0.5 ml acetonitrile	LC-FLD	1-10 ng ml^{-1}	0.09 ng ml^{-1}	[89]
Chloramphenicol	Honey	30 µl 1,1,2,2-tetrachloroethane	1 ml acetonitrile	HPLC-VWD	3-2000 ng g^{-1}	0.1-0.6 ng g^{-1}	[93]
Cholesterol	Milk, egg yolk, and olive oil	35 µl CCl_4	0.8 ml ethanol	HPLC-UV	0.03-10 ng ml^{-1}	0.01 ng ml^{-1}	[83]
Food colorants	Soft drinks, sugar, and sweets	350 µl [C_8MIM][BF_4]	-	HPLC-UV	0.05- 2000 ng ml^{-1}	0.015-0.32 ng ml^{-1}	[84]
Anilines	Steamed bread	0.15 ml [C_8MIM][PF_6]	0.3 ml methanol	HPLC-UV	50-1000 ng g^{-1}	10-15 ng g^{-1}	[86]
Carbamate and OPPs	Fruit juice and water	15 µl tetrachloroethane	1 ml acetonitrile	HPLC-FLD	0.1-1000 ng ml^{-1}	0.012- 0.016 ng ml^{-1}	[101]
PAHs	Fruit juice and water	16 µl $C_2H_2Cl_4$	1 ml acetonitrile	HPLC-FLD	0.01-100 ng ml^{-1}	0.001-0.01 ng ml^{-1}	[94]
Chloramphenicol and thiamphenicol	Honey	30 µl1,1,2,2-tetrachloroethane	1 ml acetonitrile	HPLC-VWD	3-2000 ng g^{-1}	0.1-0.6 ng g^{-1}	[97]
Parabens	Fruit juices, tomato sauce, pickle, vinegar, and water	50 µl of chloroform	0.2 ml ethanol	GC-FID	100-10000 ng ml^{-1}	29-102 ng ml^{-1}	[88]
Phthalate esters	Milk	40 µl CCl_4	0.8 ml methanol	GC-FID	0.8-51 ng g^{-1}	0.64-0.79 ng g^{-1}	[98]
OPPs	Tea	*n*-hexane	acetonitrile	GC-FPD	-	0.030-1 ng ml^{-1}	[96]
OPPs	Cucumber and water melon	27 µl chlorobenzene	1 ml acetonitrile	GC-FPD	-	0.010-0.190 ng ml^{-1}	[99]
PCBs	Fish	30 µl chlorobenzene	1 ml acetone	GC- ECD	5-2500 ng ml^{-1}	2.4-4.9 ng ml^{-1}	[95]
Chlorothalonil, captan and folpet residues	Grape	9 µL chlorobenzene	1 ml acetone	GC-ECD	10-150 ng g^{-1}	6-8 ng g^{-1}	[100]

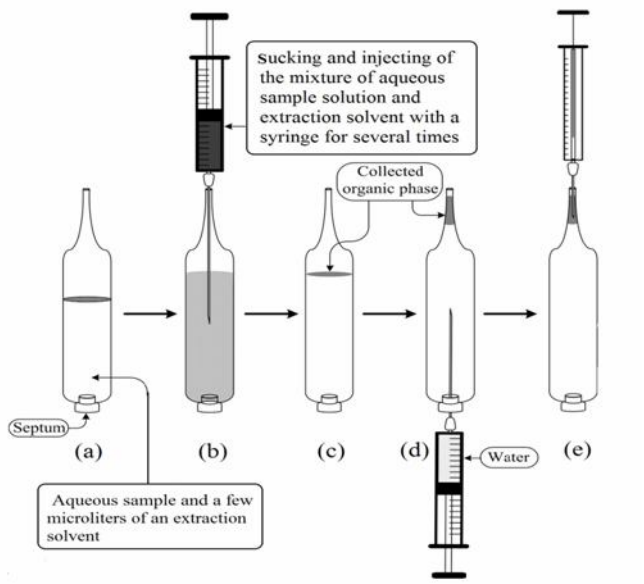

Fig. 2. Air-assisted liquid-liquid microextraction procedure using an extraction solvent lighter than water. (a) Extraction vessel having aqueous sample and an extraction solvent, (b) sucking and injecting of the mixture of aqueous sample solution and extraction solvent with a syringe for several times, (c) collection of organic phase at the top of aqueous phase after centrifuging, (d) elevating the organic phase by injecting about 1 ml de-ionized water through the septum in the bottom of vessel by using a syringe, and (e) removal of a portion of the collected organic phase in the narrow portion of the tube and injection into GC-FID system.

of a floating organic drop for determination of PAHs in tap water. In this method a drop of suitable organic solvent was floated on the surface of aqueous solution located in a glass vial. The aqueous phase was stirred for a selected time. Afterward, the sample vial is transferred into an ice-bath. The sudden decrease in temperature leads to solidification of the organic solvent in just a few minutes. The solidified extraction phase is then transferred into a suitable vial using a small spatula and immediately melted at room temperature. An aliquot of the solvent is subsequently retrieved and exposed to analysis using an appropriate instrumental method.

It is well known that ultrasound is a powerful energy for the acceleration of various steps in analytical procedures, such as homogenizing and emulsion forming [104]. This type of energy greatly helps in the processes of separation and extraction since it accelerates the mass-transfer process between two immiscible phases [105]. This leads to an increment in the extraction efficiency of the procedure in a minimum time [106]. As a result, the application of an ultrasound radiation to a miniaturized approach such as solidification of a floating organic droplet microextraction (SFODME) provides a new technique namely ultrasound-assisted emulsification solidified floating organic drop microextraction (USAE-SFODME). Figure 3 shows a scheme of the USAE-SFODME procedure. This method offers some advantages such as simplicity, low cost, rapidity, high EF, and low consumption of the extraction solvent. Khayatian *et al*. [107] proposed USAE-SFODME combined with FAAS for the extraction and determination of Fe(III) and Cu(II) in environmental waters and some food samples including cheese, rice, honey, and powdered milk. 2-Mercaptopyridinen-oxide was used as a chelating agent and 1-dodecanol was selected as an extraction solvent. Under optimum conditions, an enrichment factor of 13 was obtained for both iron and copper from only 6.7 ml aqueous phase. The linear ranges were 40-800 and 20-1,200 µg l^{-1} for iron and copper, respectively. Also determination of trace amounts of zinc and cadmium ions in water samples were successfully performed with this method [108,109].

In 2013, Amjadi *et al*. [110] developed a simple and rapid method based on ultrasound assisted temperature-controlled ionic liquid microextraction combined with FAAS for determination of tin in various canned products including peach, pineapple and aloe vera juice, canned pea, and canned cheese. In this method, 30 ml of tin solution (or sample) was placed into a conical bottom glass centrifuge tube and 1.2 ml ammonium pyrrolidinedithiocarbamate (APDC) was added as a chelating agent and then buffered at pH 4.4 with 500 µl acetate buffer. Then 250 µl 1-hexyl-3-methylimidazolium hexafluorophosphate as an extraction solvent was added into the solution. The sample solution was placed in an ultrasonic bath and sonicated for 10 min with temperature controlled at 80 °C. The IL is dissolved completely and mixed entirely with the aqueous phase in order to make the complex migrate into the IL phase. Then the tube cooled within the ice-water bath and the solution

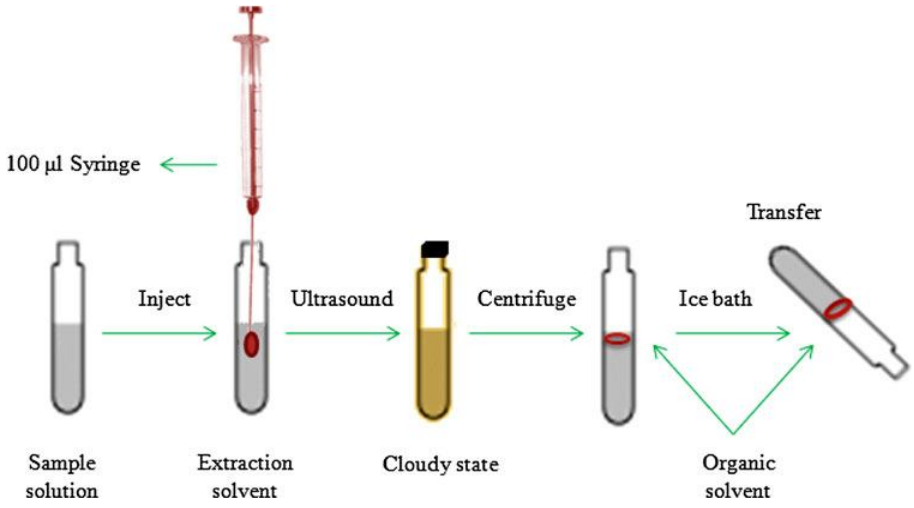

Fig. 3. Schematic diagram for the USAE-SFODME procedure.

became turbid. In this step the tin-APDC complex was extracted into the fine droplets of IL. Under the optimum conditions, LOD and EF were 42 µg l^{-1} and 52.7, respectively.

In 2008, Baghdadi and Shemirani [111] reported a new method termed cold-induced aggregation microextraction (CIAME) based on using ILs for extraction of mercury from water samples. In this method, very small amounts of [Hmim][PF_6] and [Hmim][Tf_2N] (as extractant solvents) were dissolved in a sample solution containing triton X-114 (as an anti-sticking agent). Afterwards, the solution was cooled in an ice-bath and a cloudy solution was formed. After centrifuging, the fine droplets of extractant phase were settled in the bottom of the conical glass centrifuge tube. CIAME is a simple and rapid method for extraction and preconcentration of metal ions from different samples and can be applied for the sample solutions containing high concentration of salt and water miscible organic solvents. Furthermore, this technique is much safer in comparison with the organic solvent extraction. In modified cold-induced aggregation microextraction (M-CIAME), triton X-114 was eliminated, so extractant phase merely contains [Hmim][PF6], which has high density, so it can easily settle up to 40% salt. In 2010, M-CIAME combined with UV-Vis spectrometer was employed for determination of palladium in sea water, tea, and food additive such as nitrate salt [112]. In this work, Michler's thioketone as the complexing agent was used. Under the optimum conditions, LOD was 0.2 ng ml^{-1} and RSD was 1.7% for 40 ng ml^{-1}.

In 2011, Zeeb *et al*. [113] developed an efficient in situ solvent formation microextraction method combined with stopped-flow injection spectrofluorimetry for the determination of copper in water samples and food samples such as black tea, green tea, tomato and rice. In the proposed approach, thiamine was oxidized with Cu(II) to form hydrophobic and highly fluorescent thiochrome, which was subsequently extracted into IL as an extractant phase. A small amount of an ion-pairing agent ($NaPF_6$) was added to the sample solution containing a water-miscible ionic liquid ([Hmim][BF_4]) to obtain a hydrophobic ionic liquid ([Hmim][PF_6]), which acted as the extraction phase. After centrifuging, phase separation was performed and the enriched analyte was determined. By using a peristaltic sipper equipped with a micro-cell, consumption of the extractant phase was minimized, and preconcentration factor and speed of the analysis were improved. LOD and RSD were 0.024 µg l^{-1} and 2.1%, respectively.

Yangcheng *et al.* [114] described a new sampling method termed directly suspended droplet microextraction (DSDME). In this technique a free microdroplet of a solvent is delivered to the surface of an immiscible aqueous sample while being agitated by a stir bar placed in the bottom of the sample vessel (Fig. 4). After prescribed time, the microdroplet of the solvent is withdrawn by a syringe and

analyzed. In DSDME, the chosen organic solvent should have a very low solubility in water to avoid dissolution in the aqueous sample, and also low vapor pressure to prevent loss during extraction. Vinas *et al*. [115] applied DSDME combined with GC-MS for the determination of different classes of polyphenols in fruits (black grape, white grape, apple, and pear), tea, tea-based drinks, fruit juices (peach, peach and grapes, and apple). A derivatization reaction in injection port with bis(trimethylsilyl) trifluoroacetamide was carried out to convert the polar nonvolatile polyphenols into volatile derivatives. Undecanone was used as an extraction solvent. Compared with other LPME methods, DSDME does not require special equipment, the organic drop is more stable and the equilibrium is reached quickly. In comparison with SPME methods for polyphenols determination, the cost is lower, as the SPME fibers are expensive and have a limited lifetime. Other advantages are the higher sensitivity, the absence of memory effects, and the higher analysis rate.

A wide variety of methods can be used to extract volatile and semivolatile compounds from plant materials and foodstuffs; such as steam distillation [116], hydrodistillation (HD) [117], dynamic headspace [118], ultrasound-assisted extraction [119], and supercritical fluid extraction [120]. HD and steam extraction are classical methodologies which are traditionally used to extract essential oils from plant materials because of their multiple advantages regarding simplicity of the procedure and low cost. However, HD presents some disadvantages such as long extraction times, possible solubilization of volatile

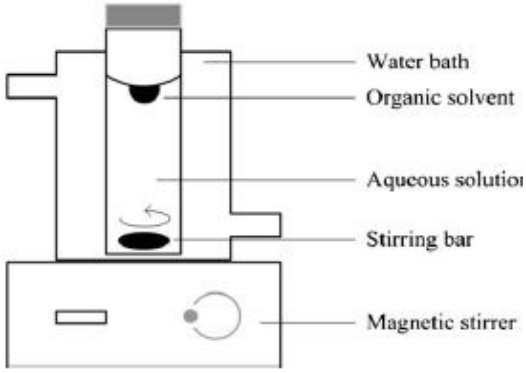

Fig. 4. Schematic diagram of directly suspended droplet microextraction.

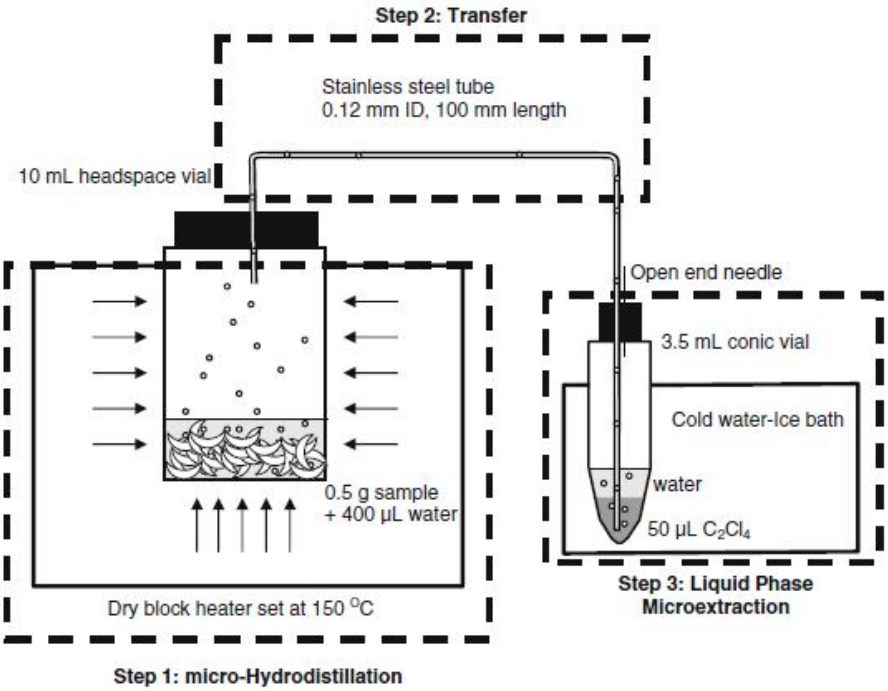

Fig. 5. Schematic diagram of the manifold developed for HD-LPME-ATR determination of semivolatile compounds in foodstuff.

compounds in water and the need for high amount of sample. In 2010, Gonzálvez *et al*. [121] developed a combination of HD and LPME to improve sensitivity and selectivity in attenuated total reflection infrared determination of semivolatile organic compounds from high water content plant and food matrices contributing to solve extraction efficiency drawback. In this methodology, the untreated sample is heated inside a 10-ml headspace vial with 400 µl water and the volatile and semivolatile organic compounds are transferred by using a 10-cm stainless steel line into a conic vial containing 50 µl of an acceptor solvent which extracts and preconcentrates those volatile and semivolatile compounds from the steam. Afterwards, analytes can be detected and determined by infrared spectroscopy using the attenuated total reflection sampling mode. Schematic diagram of the proposed method has been shown in Fig. 5.

CONCLUSIONS

Different microextraction techniques have found an important place in sample preparation because of their inherent advantages over the conventional procedures. In the forthcoming years, it is very probable that the microextraction techniques will be increasingly applied in food analysis, which is highly desirable. In this review article, initially the principles of most microextraction techniques have been described and then their applications in food analysis have been reviewed.

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