Review Article

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Vahid Jalili, Rezvan Zendehehd, and Abdullah Barkhordari*

Supramolecular solvent-based microextraction techniques for sampling and preconcentration of heavy metals: A review

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Abstract: Even very low concentrations of heavy metal pollutants have adverse effects on the environment and on human health. Thus, determining even trace concentrations of heavy metals in various samples has attracted a lot of attention. The conventional analytical methods used for the sampling and analysis of heavy metals have some limitations, including the effects of the matrix and their high detection limits. Thus, various methods are used for the pretreatment and concentration of the target analytes, and these methods are time-consuming, expensive, and require the use of toxic solvents. In recent years, supramolecular solvent-based microextraction (SSME), a green analytical strategy, has been used to determine low concentrations of heavy metals in various matrices. This method has unique features such as high enrichment factor, short extraction time, and rapid analysis. In addition, it is cost effective because it consumes less chemical reagents than other methods. Also, it is ecofriendly, and it has good sensitivity and selectivity. Herein, we presented a comprehensive review of the application of the SSME technique for the analysis of heavy metals in water, food, and biological samples. Also, we have provided the distinctive properties of the SSME technique, discussed the challenges that lie ahead, and addressed the potential future trend.

Keywords: heavy metals, supramolecular solvent, microextraction techniques, review

Abbreviations

SSME	supramolecular solvent-based microextraction
ETAAS	electrothermal atomic absorption spectroscopy
ICP-MS	inductively coupled plasma mass spectrometry
SUPRASs	supramolecular solvents
LPME	liquid-phase microextraction
SPME	solid-phase microextraction
DLLME	dispersive liquid-liquid microextraction
SS-DLLME	SUPRAS based dispersive liquid-liquid microextraction
SS-LLME	SUPRAS based liquid-liquid microextraction
UV-Vis	ultraviolet-visible
LOD	limit of detection
LOQ	limit of quantification
RSD	relative standard deviation
SDME	single-drop microextraction
HF-LPME	hollow-fiber LPME
DI-SDME	direct-immersion SDME
HS-SDME	headspace SDME
SM-DLLM	supramolecular-DLLME
UA-SS-LLME	ultrasonic-assisted green supramolecular solvent liquid-liquid microextraction
SS-LSME	supramolecular solvent liquid-solid microextraction
HPLC	high-performance liquid chromatography
DS-LLME	dispersion solidification liquid-liquid microextraction
UA-DS-LLME	ultrasonic-assisted-DS-LLME
PF	preconcentration factor
EF	enrichment factor

* **Corresponding author: Abdullah Barkhordari**, Environmental and Occupational Health Research Center, Shahrood University of Medical Sciences, Shahrood, Iran,

E-mail: a.barkhordari2007@gmail.com; tel: +989104968497

Vahid Jalili: Student Research Committee, Department of Occupational Health Engineering, School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Rezvan Zendehehd: Environmental and Occupational Hazards Control Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

1 Introduction

Pollution from heavy metals has been found in many places around the globe. The contamination of the environment by these substances is one of the major challenges in modern human society, and it has various causes, such as the rapid pace of urbanization, land use changes, and industrialization, especially in developing countries [1,2]. Overall, there are two main sources of heavy metals, natural sources, and anthropogenic sources (Figure 1). Among the natural sources are the weathering of rocks that contain metals and the occurrence of volcanic eruptions. The anthropogenic sources include industrial emissions, mining and smelting wastes, and agricultural activities [3,4]. Some of these metals, such as zinc, copper, iron, manganese, and cobalt, are essential for plants, animals, and humans, but they can be toxic for humans and other life forms at high concentrations [5-7]. Other heavy metals, such as arsenic, cadmium, chromium, lead, and mercury, are nonessential for life and are considered systemic toxic chemicals even at low levels of exposure. Exposure to these metals in air, water, electronics, jewelry, and other products have been linked to cancer, developmental disorders, and other health problems. Among the parameters affecting their toxicity are the dosage, route of exposure, and type of metal, as well as the age, gender, genetic makeup, and nutritional status of individuals exposed to them [8-10]. Considering that these metals are harmful in different ways, they have been included in a list of dangerous substances and human carcinogens (known or probable) by

the Environmental Protection Agency and the Agency for Toxic Substances and Disease Registry [11]. The main routes by which humans are exposed to these metals are ingestion (e.g., drinking or eating) and inhalation. The metals can accumulate in body organs (e.g., liver, heart, kidney, and brain) and disturb vital activities [12].

Because heavy metals may be found in very low concentrations in the environment (which can nonetheless have effects on health), sensitive analytical methods are required to extract, separate, and quantify their trace amounts in various samples. The traditional methods used are electrothermal atomic absorption spectroscopy (ETAAS), flame atomic absorption spectroscopy (FAAS), and inductively coupled plasma mass spectrometry (ICP-MS). However, they face challenges such as effects of the matrix and difficulties in identifying metals at trace concentrations. Hence, preconcentration and isolation procedures are crucial steps in the extraction of heavy metals from different samples [13-15]. The main goal of sample preparation is the preparation of appropriate concentrations for precise and accurate determinations of small amounts of metals. Sample preparation can also reduce the interference and increased selectivity and sensitivity extraction of target analytes [16]. For these reasons, methods such as liquid-liquid extraction and solid-phase extraction are used in the analysis of various analytes. These methods also have shortcomings, however, such as the involvement of multiple steps and much time, high costs, and the requirement for complex instruments and dangerous solvents [17,18]. Because of these limitations, attempts have been made to design studies that are

Figure 1: Sources of heavy metals in environment.

simple, low cost, and rapid and use separation methods that incorporate the concepts of green chemistry. During recent decades, microextraction techniques that have the above benefits have received a great deal of attention from researchers who perform analyte extraction [19]. Some of these techniques are solvent-free, whereas some of the other techniques use organic solvents that can be toxic to the environment. Supramolecular solvents (SUPRASs) have been developed to reduce environmental pollution from organic solvents [20-22]. Recently, supramolecular solvent-based microextraction technique (SSME) have been developed as an alternative to other microextraction techniques. SSME have been successfully used for the extraction and identification of a wide range of organic and inorganic pollutants, such as heavy metals. These techniques have also shown a high enrichment factor and good sensitivity and selectivity [23-25]. A summary of applications of SSME for the analysis of heavy metals in different samples is presented in Figure 2. To the best

of our knowledge, no review article has summarized this subject. In the present paper, for the first time, we reviewed the use of SSME techniques for heavy metal analysis in different samples.

2 SUPRASs-based microextraction techniques

A SUPRAS is a water-immiscible solvent generated by the sequential self-assembly of amphiphiles at a nanoscale [26,27]. The production of SUPRASs takes place in two steps of self-aggregation of the amphiphiles: (1) self-aggregation of the amphiphiles at a concentration higher than the critical aggregation concentration in order to produce reverse micelles or vesicles and (2) additional aggregation of nanostructure aggregates to produce a water-immiscible phase by changes in external stimuli. The external

Figure 2: Schematic representation of the applications of SSME for sampling and analysis of heavy metals from different matrices.

stimulus used in this process can include pH modifications, temperature changes, and salt additions [28,29]. The solvents have outstanding features that allow them to be used for different types of microextraction techniques. These unique features include the use of available self-assembly-based methods, availability of amphiphiles in nature and as synthetic chemical compounds, ability to change solvent properties, excellent solvation for different compounds due to the existence of polarity regions, absence of volatility, and absence of flammability [30-32]. In addition, the solvents can perform extraction easily because of the special structure of their ordered aggregates. In the past, nonionic, micelle-based SUPRASs were used to extract pollutants from environmental samples in the cloud point technique [33-35]. In response to the problem of the coelution of nonionic surfactants in liquid chromatography systems and extractions compatible with mass spectrometry, SUPRASs made up of zwitterionic, cationic, or anionic micelles were developed [36]. In recent decades, studies on the use of SUPRASs based on vesicles and reverse micelles of biosurfactants have been reported [37,38]. The attributes of ionic form of hydrogen bonding of, π -cation interactions with, and hydrophobic interactions with target analytes by these solvents can play an important role in improving extraction efficiency [39-41]. SUPRASs solubilization in cations occurs using ether bonds between metal ions and polyoxyethylene groups of surfactant molecules that have formed aggregates in the SUPRASs. Overall, SUPRASs can extract metal ions without chelating agents. However, the formation of an insoluble complex between the metal ions and the organic ligands causes a remarkable improvement in the extraction efficiencies. Thus, extraction methods usually use organic ligands when metals are being extracted by SUPRAS. However, when chelating agents are used, the efficiency of the extraction of metals can be affected adversely by the equilibrium constants of the complexes that are formed, by the kinetics of the formation of the complexes, by the reaction conditions, and by the complex hydrophobicities. Over time, different types of chelating agents have been used to extract metal ions. Generally, Azo dyes and dithiocarbamates are used extensively due to their low solubility in water and their ability to form complexes with a wide range of metals [42-44]. The efficiency of the extraction of metals depends mainly on the concentration of the chelating agent, pH, and temperature. The concentration of the chelating agent affects both the nature and the amount of the complex that is formed. The highest extraction efficiencies are obtained when the chelating agent is at a concentration that allows the quantitative formation of neutral complexes. The pH

is a critical parameter in pH-dependent, complex formation reactions. Due to the characteristics of the organic ligands that are used to extract metals, complexes can be formed at various conditions, e.g., alkaline, neutral, and slightly acid conditions. Another important factor is temperature because it can affect both the equilibrium and the kinetics associated with the formation of complexes. Thus, high temperatures are required for the efficient extraction of inert inorganic species. However, high temperatures reduce the stability of the chelating agents, which can result in reduced recoveries [45,46]. It is worth mentioning that SUPRASs have good compatibility with microextraction techniques such as various types of liquid-phase microextraction (LPME) configurations, as well as analytical instruments [47-49]. Compared with conventional methods, SSME has advantages such as a high extraction capability, short extraction time, rapid completion of analysis, low cost, easy sample preparation, less consumption of toxic substances, decreased secondary environmental pollution, and better ecofriendliness [50-52]. A schematic presentation of SSME technique is shown in Figure 3. To date, different microextraction techniques, such as LPME and solid-phase microextraction (SPME), have been used for sampling and analysis of heavy metals [53-56]. A schematic presentation of different LPME techniques is shown in Figure 4. During recent years, SSME techniques such as SUPRAS based dispersive liquid-liquid microextraction (SS-DLLME) and SUPRAS based liquid-liquid microextraction (SS-LLME) have been widely used for the identification of heavy metals in water, biological samples, and food samples [57-59]. Table 1 summarizes the advantages and limitations of SSMEs and other microextraction techniques. Application of SSME in determination of heavy metals in various matrices and their analytical figures of merit are summarized in Table 2.

3 Analysis of heavy metals in water samples

There are concerns about pollution of the environment by heavy metals as certain human activities have increased [60]. Heavy metals are some of the pollutants that have most severely damaged aquatic ecosystems [61,62]. This is due to their toxic effects and ability to bioaccumulate in sediments in these ecosystems and form a direct risk to detrital and deposit-feeding organisms [63,64]. These metals can be transported as either dissolved species in water or as suspended sediments in rivers and streams.

Figure 3: Schematic presentation of SSME technique.

They may then enter the underground water system and contaminate underground water sources and wells [65]. With the development of industries and increased release of wastewater containing hazardous heavy metals into rivers, the health of humans and other living beings, as well as the environment, are endangered [66]. Therefore, the extraction and quantification of heavy metals in water samples is of significant importance in the context of environmental and human health protections [67]. The concentration of heavy metals is commonly below the detection limit of instruments. Thus, the application of methods that can determine the presence of trace levels of these metals is very important [68].

Ozkantar et al. used the ultrasonic-assisted green SUPRAS-LPME technique (UA-SS-LLME), followed by ultraviolet-visible (UV-Vis) spectrophotometric analysis, at 540 nm for the identification of the inorganic chromium compounds Cr (VI) and Cr (III) in water samples. Tetrahydrofuran (THF) and decanoic acids were used for the microextraction of chromium speciation. In this study, Cr (III) was oxidized to Cr (VI) through H_2SO_4 for the calculation of the total chromium. Then, for the calculation of the

Cr (III) concentration, the Cr (VI) concentration was subtracted from the total chromium. The interference effects of the matrix components, which can be important parameters of extraction efficiency, were also investigated. Under optimal conditions, the limit of detections (LODs) and limit of quantifications (LOQs) were obtained at $0.79 \mu\text{g L}^{-1}$ and $2.64 \mu\text{g L}^{-1}$, respectively. The linearity was in the range of $4.5\text{--}135 \mu\text{g L}^{-1}$, with good linearity ($R^2 > 0.999$). The recovery percentages of the target analytes were in the range of 92–102%, and the relative standard deviation (RSD) value was 2.4%. The results showed that the use of UA-SS-LLME can be appropriate for identifying Cr (VI) and Cr (III) ions [69].

Abadi et al. used the SS-DLLME technique based on the solidification of floating organic drops (SS-DLLME-SFO), along with UV-Vis spectrophotometry, for the extraction of trace amounts of chromium in water samples. They used THF and decanoic acid as a dispersing solvent and also in the self-assembly of decanoic acid. Microextraction of chromium was performed by coacervates composed of reverse micelles that formed using decanoic acid and dispersion in the THF–water mixture. All the factors

Figure 4: Schematic of different types of LPME techniques: (A) SDME, (B) HF-LPME, and (C) DLLME.

affecting the analytical performance were investigated. The linear range of the calibration curve was from 1 to 40 $\mu\text{g L}^{-1}$ and the LOD was 0.23 $\mu\text{g L}^{-1}$. The enhancement factor and RSD were 50 and 3.8% ($n = 6$), respectively. The results suggest that SS-DLLME-SFO is a viable method with a good detection limit, high accuracy, and good reproducibility for the trace determination of chromium compounds in real samples [70].

Tafti *et al.* used SS-DLLME-SFO combined with ETAAS for the extraction of chromium compounds. Analytical parameters affecting the extraction were optimized. THF and decanoic acids were used to prepare a SUPRAS. Under optimum conditions, the linear calibration curve was from 0.008 to 0.4 $\mu\text{g L}^{-1}$ and the correlation coefficient was 0.9992. The LODs and LOQs were 0.0018 and 0.006 $\mu\text{g L}^{-1}$, respectively. The repeatability of the methods at the level of 0.1 $\mu\text{g L}^{-1}$ of Cr (VI) was 4.2% ($n = 6$). The recoveries of the samples were 97.0-103.6% and the enhancement factor was 127. The results demonstrated that the proposed method can be a powerful one for the identification of chromium compounds [71].

Khan *et al.* used SSME, along with UV-Vis spectrophotometry, for the separation and preconcentration of uranium at trace levels from water and soil samples. Undecanol-THF was used as the extraction solvent in all experiments. In this study, the analytical parameters such as solution pH, amount of ligand, type, and volume of SUPRAS, sample volume, and diverse ion effect were studied. The LODs

and LOQ were 0.31 $\mu\text{g L}^{-1}$ and 1.05 $\mu\text{g L}^{-1}$, respectively. The average RSD was calculated at 0.46 $\mu\text{g mL}^{-1}$ of U (VI) and was achieved at 0.2% ($n = 5$). The correlation coefficient, enhancement factor, and preconcentration factor were 0.982, 16, and 17, respectively. Based on the results, the method showed a good performance for uranium trace analysis in water and soil samples [72].

4 Heavy metals analysis in food sample

Heavy metals can contaminate agricultural lands, thereby adversely affecting the safety of food crops. This problem is particularly common in agricultural lands within city suburbs irrigated with wastewater and well water [73]. One of the major pathways of human exposure to heavy metals is the consumption of contaminated food. Heavy metal contamination in foods can occur due to contamination of the soil, residual muds, and from chemical fertilizers and pesticides [74,75]. Food products of both plant and animal origin can be contaminated. Among food animals, fish are most affected by heavy metal contamination and cause heavy metals to bioaccumulate in the food chain. Eventually, heavy metals consumed by the fish reach the consumer when that fish is eaten [76,77]. In plants, the uptake of heavy metals varies by plant species

Table 1: Strengths and weaknesses of different microextraction techniques

Technique	Advantages	Disadvantages
SUPRASs-based microextraction	<ul style="list-style-type: none"> • Ease of implementation • Rapid • Inexpensive • Miniaturization of solvent use • High enrichment factor • The low volatility of SUPRASs and in result reduce secondary pollution of the environment 	<ul style="list-style-type: none"> • Require dilute prior to chromatographic analysis due to high viscosity
Different types of LPME	<ul style="list-style-type: none"> • Ease of implementation • Rapid • Minimization of solvent use • Inexpensive • Good clean-up ability • Simplicity of automate • High repeatability • High extraction efficiency • High flexibility in the choice of analytical parameters • Reduces the analysis time 	<ul style="list-style-type: none"> • The problem of drop instability (SDME) • Possibility of fiber pores getting blocked (HF-LPME) • Limitation of solvent selection (DLLME) • Poor performance in samples with a complex matrix composition (DLLME) • Requires the use of three solvents (DLLME)
SPME	<ul style="list-style-type: none"> • Ease of implementation • Rapid • Solvent-free • Reusable • Simplicity of automate • Possibility of using different samples • Single-step extraction 	<ul style="list-style-type: none"> • Fiber fragility • Passive sampler • Non exhaustive • Costs related to fiber • Short lifetime • Limitation of desorption temperature • Limited extraction capacity

and bio-availability of the metal in the soils [78]. According to multiple studies, heavy-metal contaminated fruits, vegetables, and other crops may contain levels higher than the recommended maximum values proposed by international organizations [79]. Heavy metals entering the food chain and accumulating in the human body can cause serious health disorders [80]. Therefore, monitoring the levels of these metals in food is necessary. SUPRASs provide selective interactions with metal ions, so SSME methods are very efficient for the extraction of trace metal ions [81,82].

Altunay et al. used SS-LLME for the determination of manganese and zinc at trace levels in vegetables. In this study, 1-decanol reverse micelles dispersed THF were used to prepare a SUPRAS. In addition, analytical parameters such as pH, ligand mass, THF volume, 1-decanol concentration, matrix effect, and sonication time were investigated. The linear range concentration obtained for manganese was 0.1-200 $\mu\text{g L}^{-1}$, and the LODs were 0.035 $\mu\text{g L}^{-1}$. The RSD was between 1.3% and 2.2%, and the recoveries ranged from 96.1% to 102.5%. For zinc, the linear range concentration was 2-500 $\mu\text{g L}^{-1}$, and the LODs were 0.035 $\mu\text{g L}^{-1}$. The RSD was between 1.4% and 2.3%,

and the recoveries ranged from 95.8% to 102.3%. Results showed that the method was successfully applied for the extraction of Mn and Zn from vegetable samples [83].

Aydin et al. used the SSME technique alongside micro-sampling-FAAS (MS-FAAS) for cobalt traces in food samples, and a supramolecular solvent was prepared by 1-decanol- THF. Eventually, micelles formed in the nano and molecular size and transferred the diethyldithiocarbamate (DDTC)-cobalt (II) complex from the aqueous phase to the extraction phase. The analytical performance of the SSME technique was investigated. Under optimal conditions, the linear dynamic range (LDR) was obtained between 1 and 10 $\mu\text{g mL}^{-1}$ for cobalt, and the correlation coefficient was found to be 0.998. The LODs and LOQs were 1.89 and 6.32 $\mu\text{g L}^{-1}$, respectively. The RSD was 1.51%, and the pre-concentration factor (PF) was found to be 30. The results showed that the SSME technique was successfully applied to determine cobalt concentrations by MS-FAAS in food samples such as cereal, powdered beverages and fruit [84].

Rastegar et al. used the SS-DLLME method to monitor traces of lead extracted from various food samples using flow injection flame atomic absorption spectrometry

Table 2: Comparison the applications of SSME technique with common LPME techniques in determination of heavy metals in various matrices

Analyte	Technique	Matrix	Extraction medium	LDR ($\mu\text{g L}^{-1}$)	R ² (entire LDR)	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	EF / PF	%RSD (number of replicates)	Ref.
Copper	SSME	Water	1-decanol Tetrahydrofuran (THF)	31.8-98.7	-	0.46	-	90	3.3 (3)	[96]
Chromium	SM-DLLME	Water	THF	1-40	-	0.23	-	50	3.8 (6)	[70]
Chromium	UA-SS-LLME	Water	Decanoic acid, THF	4.5-135	0.9997	0.79	2.64	50	2.4 (3)	[69]
Chromium	SM-DLLME	Water	Water-THF	0.008-0.4	0.9992	1.8	6	127	4.2 (6)	[71]
Copper, lead	SSME	Water	Nonanoic acid, THF, HCl	10-800, 10-500	0.999	0.29, 0.45	-	27, 22	2.3, 3.6 (6)	[97]
Cobalt	SSME	Water	THF, 1-decanol	-	-	1.29	3.88	38.5	3.2 (7)	[98]
Palladium	UA-SS-LLME	Water	THF, 1-dodecanol	1-400	0.9960	0.63	-	93	3.2 (10)	[99]
Uranium	SSME	Water, soil	1-decanol-THF, undecanol-THF, decanoic acid-THF	-	0.982	0.31	1.05	17	0.2 (5)	[72]
Copper	SDME	Water	Ionic liquid ([C4mim]PF ₆)	-	0.9970	0.15	-	33	3.4 (11)	[100]
Lead	DLLME	Water	1,2-dichloroethane	10-500	0.9972-0.9994	2.7	9	-	4.45-11.7 (3)	[101]
Cobalt	HF-LPME	Water	Toluene	1-300	0.9987	0.4	-	119	3.3 (3)	[102]
Lead	SS-LSME	Food	Cetyltrimethylammonium bromide and sodium dodecyl sulphate surfactant	0.1-2	0.996	0.047	-	77	5.2-6.5 (4)	[103]
Selenium	SSME	Food	Octanoic acid in THF	0.4-100	0.9990	0.1	-	58	4.3 (4)	[104]
Cobalt	SSME	Food	1-decanol in THF	1000-10000	0.9980	1.89	6.32	30	1.51 (8)	[105]
Lead ions	SM-DLLME	Food	1-decanol in THF	1-500	0.99	0.4	1	-	4.5 (6)	[51]

(continued)

Table 2: (continued)

Analyte	Technique	Matrix	Extraction medium	LDR ($\mu\text{g L}^{-1}$)	R ² (entire LDR)	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	EF / PF	%RSD (number of replicates)	Ref.
Lead	HF-LPME	Food	Titanium oxides	0.6-3000	0.9960	0.2	0.6	790	4.9 (5)	[106]
Cadmium	DLLME	Food	Tetrachloro-methane	-	0.9948	0.0001	-	3458	2.6 (11)	[107]
Manganese, zinc	UA-SS-LLME	Vegetables	1-decanol in THF-water	0.1-200, 2-500	-	0.035, 0.6	0.1, 2	62.5	1.4-2.2, 1.5-2.6 (5)	[83]
Cadmium	SDME	Vegetable oils	HNO ₃	0.01-1	0.9933	0.002 ng kg ⁻¹	0.7 ng kg ⁻¹	12	3.0 (10)	[108]
Bismuth	SS-LSME	Blood serum, human hair	Cetyltrimethylammonium bromide and sodiumdodecyl sulfate (SDS) surfactants	0.3-6	0.9960	0.158	-	47.5	5.1-6.2 (5)	[91]
Copper, cobalt	UA-DS-LLME	Blood serum, water	Decanoic acid-THF	5-700, 5-500	0.9973, 0.9981	2.9, 3.5	-	23.31, 22.38/20	4.1, 2.3 (5)	[93]
Cadmium	SS-LLME	Human hair	1-decanol in THF	0.75-200	0.998	0.23	-	25	4.5 (5)	[92]
Aluminum	SS-LLME	Human hair	Undecanol-THF	-	0.991	0.16	0.47	29.6/30	0.3 (3)	[109]
Copper	SS-DLLME	Human hair	1-decanol in THF	-	0.995	0.11	0.34	60.3	2.2 (10)	[19]
Mercury	SS-LLME	Environmental and biological	1-decanol in THF	1-100	0.9997	0.3	10	97/100	1.8 (6)	[110]
Aluminum	SS-LPME	Food, water, hair and urine	1-decanol in THF	2-150	0.9996	0.2	0.67	40	1 (3)	[59]
Lead	SDME	Biological sample	1-phenyl-3-methyl-4-benzoyl-5-pyrazolone	-	-	0.025	-	16	6.1 (7)	[111]
Cobalt	DLLME	Environmental and biological	[C6mim][PF6]	0.038-3.5	-	0.0038	-	120	3.4 (10)	[112]
Copper, lead	HF-LPME	Environmental and biological	CCl ₄	0.02-30	0.9972 - 0.999	0.033, 0.0045	-	305, 284	8.8, 6.1 (7)	[113]

LDR – linear dynamic range; LOD – limit of detection; LOQ – limit of quantification; EF – enrichment factor; PF – preconcentration factor; RSD – relative standard deviation.

(FI-FAAS). A SUPRAS comprising reverse micelles of 1-decanol in THF was used for microextraction. The extraction parameters, such as solution pH, dithizone concentration, type and amount of supramolecular solvent, ultrasonic mixing, centrifugation time, and salt concentration, were optimized. After optimizing the conditions, the proposed method was applied to extraction and trace detection of lead ions in 10 mL samples (food and agricultural products). Analysis reveals that the lead target ions were maintained from 1 to 500 $\mu\text{g L}^{-1}$ with a correlation coefficient of 0.99 and LOD of 0.4 $\mu\text{g L}^{-1}$. Then, the RSDs for 3, 10, and 100 $\mu\text{g L}^{-1}$ lead samples were determined to be 4.8%, 4.5%, and 4.1%, respectively. These results indicate that the applied SS-DLLME method can be efficiently used for trace extraction of lead in food samples [51].

5 Heavy metals analysis in biological samples

Biological monitoring is used to identify the structural properties and measuring the concentration of analytes within samples. For instance, in human biological samples, different compounds and their metabolites are investigated by biological monitoring. Although it is a complicated process, biological monitoring can provide more information than environmental monitoring [85,86], especially for heavy metals that can cause chronic or acute toxicity even in trace levels. While heavy metals have no known function in the human body, their toxicity to organisms and humans is related to their concentration and distribution in the body [87]. Hence, investigation of the absorption, distribution, metabolism, and excretion of heavy metals in biological samples is critical to understand their environmental and health effects [88]. Sample preparation is also very important to attain high accuracy in biological monitoring, since biological samples are complex matrices and often contain proteins, salts, acids, bases, and other compounds that can interfere with the extraction of target analytes [89,90]. Therefore, the application of SSME in the analysis of heavy metals from biological matrices has increased substantially in recent years.

Kahe *et al.* used a supramolecular-based liquid solid microextraction method coupled to ETAAS for the extraction and determination of trace bismuth in human blood serum and hair samples. A SUPRAS comprising cetyltrimethylammonium bromide and sodiumdodecyl sulfate surfactants was used for microextraction. In this study, the different parameters that influence the extraction

efficiency of the bismuth ion, such as the salt concentration, pH, centrifugation time, amount of chelating agent and solvent amounts, were studied. After the conditions were optimized, the linear range of the calibration graphs was between 0.6 and 3 $\mu\text{g L}^{-1}$, and the LOD was determined to be 0.16 $\mu\text{g L}^{-1}$ ($S/N = 3$). The RSD values ranged between 5.1% and 6.2%, with the recoveries ranging from 91% to 105.3%. These results demonstrated the applicability of the proposed method for the determination of bismuth in human blood serum and hair samples [91].

In another study, Panhwar *et al.* used the SS-DLLME method along with FAAS for the extraction of cadmium in water and hair. In this study, 1-decanol in THF were used to prepare a SUPRAS. The parameters influencing the extraction of cadmium, including the pH, the volume of the sample, the mass of the ligand, and the type and volume of SUPRAS, were investigated. The results showed a wide linear range, from 0.75 to 200 $\mu\text{g L}^{-1}$, and the LOD for cadmium was 0.23 $\mu\text{g L}^{-1}$. The results showed this method could be used to isolate low concentrations of cadmium in biological samples along with a favorable LOD and enrichment factors [92].

Moreover, Shokrollahi and Ebrahimi used SUPRAS-based ultrasonic-assisted dispersion solidification liquid-liquid microextraction (DSLLME) coupled with FAAS for the simultaneous extraction of copper and cobalt in water and blood serum samples. A SUPRAS comprising of decanoic acid-THF was used for microextraction. For the extraction of these metals, different variables, such as the pH, the concentration of the complexing agent, the volume of the extraction and dispersive solvents, the sonication time, and the ionic strength were studied. The linear concentration range was 5-700 $\mu\text{g L}^{-1}$ for copper and was 5-500 $\mu\text{g L}^{-1}$ for cobalt, with correlation coefficients of 0.9973 and 0.9981, respectively. In addition, the LODs for copper and cobalt were 2.90 and 3.50 $\mu\text{g L}^{-1}$, respectively. Enrichment factors were also obtained for copper and cobalt (23.31 and 22.38, respectively). This research demonstrated that SM-UA-DSLLME combined with FAAS served as a powerful method for the simultaneous extraction of trace copper and cobalt in water and blood serum samples [93].

6 Challenges and future trend

SUPRASs have unique features that make them appropriate for use in place of toxic organic solvents, including being environmentally friendly, non-volatile, and inflammable. There is a growing trend in the development of SUPRASs-based techniques for efficient extraction

of compounds [94]. In particular, as mentioned in the reviewed reports, SSME techniques can enable the efficient and reliable extraction of heavy metals from a variety of environmental, biological, and food samples [57,58]. Nonetheless, the use of SUPRASs in microextraction techniques faces key limitations, such as the use of tetrahydrofuran as a dispersion solvent and to cause the self-assembly of amphiphiles. Tetrahydrofuran is considered a class 2B carcinogen by the World Health Organization. In addition, the lack of practical information about the optimization and operability of these alternative solvents can limit implementation of these methods by laboratories. Finally, it is worth mentioning that the use of SUPRASs still poses some challenges to the environment [95]. Thus, there is value in continuing to search for greener alternative solvents with energy-free and spontaneous processes. Investigation of solvents with unique properties for the development of innovative microextraction techniques should be ongoing. Other interesting future trends are the design of SUPRASs with new functional properties such as magnetism, high stability, and volatility, and the coupling of SUPRAS-based methods with alternative detection systems. Furthermore, different amphiphiles can be explored for their applications in the pre-concentration of heavy metals in various matrices. The use of greener solvents for analysis of heavy metals in environmental, food and biological samples is expected to grow in future.

7 Conclusion

Heavy metals are characterized by their relatively high density and are released into the environment by both natural and anthropogenic sources. It is well known that long-term and continuous exposure to these metals has adverse effects on human health. In fact, heavy metals can be toxic even at trace levels; thus, efficient analytical methods are required to extract even trace levels of these metals from samples of interest. To date, the determination of heavy metals has been widely performed by conventional analysis methods (e.g., ETAAS, FAAS, ICP-MS). These methods usually face challenges stemming from effects of the matrix and problems in the extraction of trace levels of these metals. Accordingly, many efforts are underway to develop sample preparation methods that result in the extraction of target analytes in a highly sensitive and efficient procedure. In recent years, SSME has gained attention as a green and reliable techniques that can be used to separate heavy metals from different matrices. These techniques are characterized by

simplicity, rapidity, short analysis time, ease of implementation, environmental friendliness, high enrichment factors, and high extraction recoveries. As noted above, when using conventional methods, the matrix effect represents a major challenge in the determination of trace heavy metals, as interfering ions are typically found in the real matrices from which target heavy metals (like other ions or metals) are extracted. The studies reviewed here considered whether the matrix effect is an important factor in the extraction efficiency of heavy metals when using the SSME technique. Their results showed that matrix ions do not significantly interfere with the extraction of heavy metals and that the SSME technique is selective. To date, this technique has been used for the extraction of heavy metals from a variety of types of matrices, including environmental, food, and biological matrices. Due to the success of the SSME technique in the selective extraction of heavy metals, future studies are expected to broaden the application of this technique to the analysis of compounds in complex matrices such as those in biological samples. The choice of a suitable supramolecular solvent is another critical parameter in a successful analysis. The selection of best the supramolecular solvent has a significant effect on the quantity of heavy metals extracted. In the same vein, studies have examined different types of supramolecular solvents to ensure selection of the best solvent for targeted metal analysis. Here, we reviewed the studies that utilize SSME techniques for the extraction and quantification of heavy metals. Collectively, the studies reviewed in this paper support that SSME techniques presents significant opportunity for the analysis of trace amounts of heavy metals in different samples.

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