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Miguel Ángel Aguirre, Paola Baile, Lorena Vidal, Antonio Canals

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1 **Metal applications of liquid-phase microextraction**

2 Miguel Ángel Aguirre*, Paola Baile, Lorena Vidal*, Antonio Canals

3 *Department of Analytical Chemistry and Food Science and University Institute of Materials, Faculty of Science,*

4 *University of Alicante, P.O. Box 99, 03080 Alicante, Spain.*

5 *Corresponding authors:* aguirre.pastor@ua.es *(M.A. Aguirre) and* lorena.vidal@ua.es *(L. Vidal).*

6

## Abstract

8 This review focuses on the combination of elemental detection techniques with liquid-
9 phase microextraction (LPME), namely, single drop microextraction, hollow fiber based
10 liquid-phase microextraction, dispersive liquid-liquid microextraction, and related
11 techniques. General features of different microextraction procedures, historical
12 overview and automation of LPME are described and compared, along with examples
13 of new developments and applications presented to demonstrate its potential for trace
14 and ultra-trace metal analysis. Furthermore, potential applications and an outlook on the
15 combination of LPME and elemental detection techniques for inorganic analysis are
16 presented.

17

## Keywords

19 Sample preparation.

20 Preconcentration.

21 Liquid-phase microextraction.

22 Single drop microextraction.

23 Hollow fiber liquid-phase microextraction.

24 Dispersive liquid-liquid microextraction.

25 Trace element analysis.

26 Elemental detectors.

27

28 **Abbreviations**

| | |
|---|---|
| [Hmim][PF6] | 1-hexyl-3-methylimidazolium hexafluorophosphate |
| AA-LLME | Air-assisted liquid-liquid microextraction |
| APDC | Ammonium pyrrolidine dithiocarbamate |
| CFME | Continuous flow microextraction |
| CVAFS | Cold vapour atomic fluorescence spectrometry |
| DES | Deep eutectic solvent |
| DI-SDME | Direct immersion single drop microextraction |
| DLLME | Dispersive liquid-liquid microextraction |
| DSD | Directly suspended drop |
| EME | Electromembrane extraction |
| ETAAS | Electrothermal atomic absorption spectrometry |
| ETV-ICP-MS | Electrothermal vaporization inductively coupled plasma mass spectroscopy |
| FAAS | Flame atomic absorption spectrophotometry |
| HF | Hollow fiber |
| HF-LLLME | Hollow fiber liquid-liquid-liquid microextraction |
| HF-LPME | Hollow fiber liquid-phase microextraction |
| HS-SDME | Headspace single drop microextraction |
| ICP-MS | Inductively coupled plasma mass spectrometry |
| ICP-OES | Inductively coupled plasma optical emission spectrometry |
| IL | Ionic liquid |
| LIBS | Laser induced breakdown spectrometry |
| LLE | Liquid-liquid extraction |
| LOD | Limit of detection |
| LPME | Liquid-phase microextraction |
| ME | Microextraction |
| MEA-IL-DLLME | Magnetic effervescent tablet-assisted ionic liquid dispersive liquid-liquid microextraction |
| MIL | Magnetic ionic liquid |
| PAN | 1-(2-Pyridylazo)-2-naphthol |
| P-TEA-C | Protonated triethylamine carbonate |
| SBME | Solvent bar microextraction |
| SDME | Single drop microextraction |
| SFOD | Solidified floating organic drop |
| SM-DLLME | Supramolecular-based dispersive liquid-liquid microextraction |
| SS | Switchable solvent |
| SS-LPME | Switchable solvent-based liquid-phase microextraction |
| SUPRA | Supramolecular solvent |
| TEA | Triethylamine |
| THF | Tetrahydrofuran |
| TSIL | Task-specific ionic liquid |
| US | Ultrasound |
| VALLME | Vortex assisted liquid liquid microextraction |

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## 1. Introduction

LPME can be defined as a miniaturization of LLE technique where the volume of the extractant phase is equal or below 100 μL [1]. The main advantages of LPME techniques are low cost, easiness, low sample volume, rapidity, extremely low solvent consumption, high enrichment factor, reduced generation of wastes, and its affordability to any laboratory. Many of these features convert LPME into an environmentally friendly sample preparation technique that fits perfectly with the principles of green analytical chemistry [2].

A variety of LPME approaches have been suggested for the preconcentration of metals, metalloids and organometallics prior to their determination with elemental detectors. They can be classified into three main modalities (Figure 1):
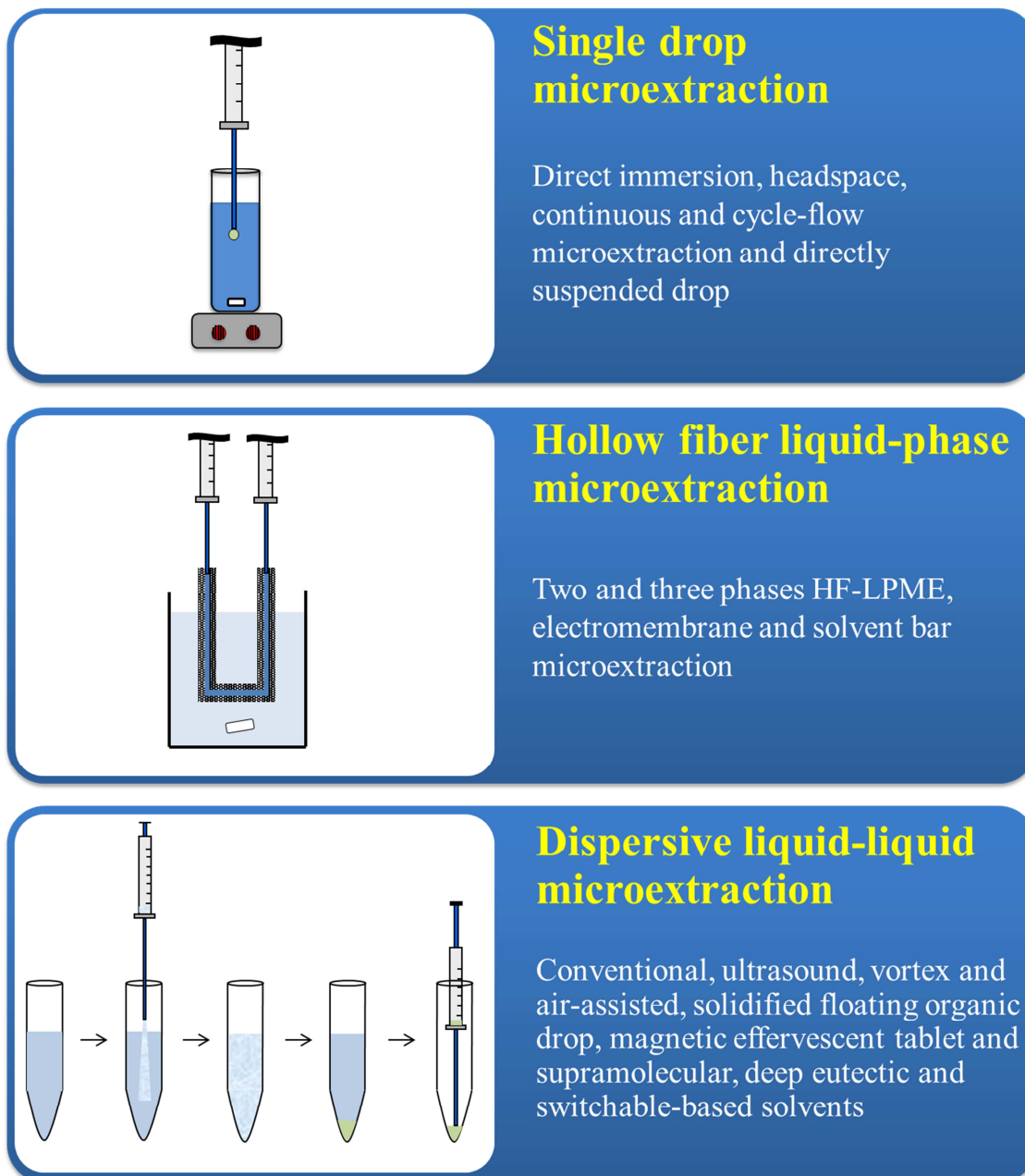
-Single drop microextraction (SDME).

-Hollow fiber liquid-phase microextraction (HF-LPME).

-Dispersive liquid-liquid microextraction (DLLME).

Moreover, several variations have also been introduced for each of these modalities, which clearly demonstrates its versatility.

LPME is usually combined with different spectrometric techniques, including FAAS, ETAAS, ICP-MS, ICP-OES, among others. The choice of the most convenient detection technique depends, among other things, on the properties and type of the analytes, the complexity of sample matrix and the volume of analyzed solution. It is also worth noting that improvement of LOD values is not only a result of the extraction type used for preconcentration of analytes, but depends heavily on the chosen measurement technique.

A brief overview of these LPME techniques is provided in the next section.

**Single drop microextraction**

Direct immersion, headspace, continuous and cycle-flow microextraction and directly suspended drop

**Hollow fiber liquid-phase microextraction**

Two and three phases HF-LPME, electromembrane and solvent bar microextraction

**Dispersive liquid-liquid microextraction**

Conventional, ultrasound, vortex and air-assisted, solidified floating organic drop, magnetic effervescent tablet and supramolecular, deep eutectic and switchable-based solvents

56

57    Figure 1. Classification of the LPME modalities.

## 2. Description of main LPME techniques

### 2.1. SDME and related techniques

SDME uses a few microliters of solvent held as a single drop on the tip of a syringe. The droplet can be either disposed to the headspace or directly immersed in the sample, distinguishing two SDME modalities: headspace SDME (HS-SDME) or direct immersion SDME (DI-SDME) [3]. In HS-SDME, a drop of extractant phase is exposed to the headspace above the sample solution for extraction of volatile and semivolatile analytes (or analyte derivatives). DI-SDME is based on the direct exposure of a microdroplet of extractant phase to the sample solution.

The SDME technique suffers from many drawbacks, such as the small surface area of the droplet, instability, ease of dislodgement from the tip of the syringe, droplet solubility, long times to reach equilibrium, and poor reproducibility.

### 2.2. HF-LPME and related techniques

SDME has gained a widespread interest since its appearance and has obtained an undoubted relevance as a start point of miniaturized LPME techniques. However, some problems commented above, needed to be solved. HF-LPME offers an interesting solution for droplet instability by using a porous membrane. In this technique, analytes are transferred from the sample to the extractant solvent present inside the lumen of the porous HF through its pores, which are also filled with a solvent immiscible with the sample. The extractant phase that impregnates the pores of the HF can be the same as the one present inside the lumen of the HF (two phase mode, HF-LPME), or different (three phase mode, HF-LLLME) [4].

One major disadvantage of the procedure is that HF-LPME is a relatively slow process, and the transfer from the sample to the extractant solvent is normally the limiting step. A solution to improve the transport mechanisms and enhance extraction efficiency was proposed by introduction of electromembrane extraction (EME) [5]. Another modality to speed up extraction kinetics is the solvent-bar microextraction (SBME) [6]. In this SBME, the extractant solvent is confined within a short length of a HF (sealed at both ends) and it is placed in a stirred sample solution

The automation of HF-LPME is still the main drawback and it has limited its implementation in routine laboratories and applications [7].

### 2.3. DLLME and related techniques

92    In conventional DLLME, the extraction process is carried out by injecting a mixture

93    of solvents into a sample placed in a conical tube. Then a cloudy solution is formed and

94    afterwards, phases are separated by centrifugation. An aliquot of the enriched extractant

95    is finally taken from the bottom of the conical tube for analysis. Two solvents are used

96    in conventional DLLME to extract target analytes from the sample solution; extractant

97    and disperser solvents. The extractant phase must be immiscible and denser than water,

98    whereas the disperser solvent should be miscible with both the extractant phase and the

99    sample [8].

100    DLLME has gained rapid and widespread recognition, attracting the interest of the

101    scientific community and even coming to dominate LPME research publications in

102    recent years [1]. However, the conventional DLLME suffers from some limitations that

103    are in continuous revision [9]: (1) harmful organic solvents are used as extractants (i.e.,

104    chlorinated solvents); (2) emulsification requires a dispersant solvent that competes

105    with the extractant solvent for the analyte, thereby reducing extraction efficiency; and,

106    (3) centrifugation is necessary to separate phases after extraction. Numerous

107    modifications of conventional DLLME have been proposed to overcome the above-

108    mentioned drawbacks of the technique and develop efficient and easier approaches. One

109    of the most representative modifications is the employment of alternative extractant

110    solvents such as those less dense than water, ILs, or green solvents. Nowadays, the

111    combined use of green solvents and DLLME has become a novel area and a hot topic of

112    research in LPME and analytical chemists have focused on these solvents to developed

113    green preconcentration methods. LPME procedures have taken on a new perspective

114    with the use of supramolecular (SUPRA) solvent, deep eutectic solvent (DES), and

115    switchable solvent (SS) [10].

116

## 3. LPME in trace element determination: historical overview

118    The combination of LPME procedures with elemental detection techniques took

119    place for the first time in 2003, and as can be seen from Figure 2A, the use of LPME

120    procedures with elemental detection techniques has experienced a noteworthy growth,

121    especially from 2007 to 2013, mainly due to the introduction of DLLME. Then, a

122    certain stabilization is observed from 2013 up to 2015 and finally, it can be noticed an

123    important decreasing from 2015 to 2017.

124    Figure 2B shows the trend in applications of LPME procedures in trace element

125    analysis. As can be noticed, the DLLME is the most popular LPME procedure reaching

126  nearly 200 publications since 2007. This is due to DLLME has numerous positive
127  features, including rapidity, high enrichment factor, easy coupling to elemental
128  detection techniques and relative large volume of acceptor phase in comparison with
129  other LPME procedures (i.e., SDME). Finally, SDME is the second one most used and
130  HF-LPME the third one.

131  Figure 2C illustrates the different elemental detection techniques employed with
132  LPME procedures. It can be seen that ETAAS is the most popular technique hyphenated
133  with LPME procedures [11], being used in 65% of the publications, followed by FAAS,
134  ICP-OES, and ICP-MS. Other techniques such as LIBS [12, 13] and electrochemical
135  [14, 15] techniques have also been used. The trend can be easily explained by the fact
136  that the volume of acceptor phase required for measurement in ETAAS technique
137  perfectly matches with the one provided by the LPME procedure. In this detection
138  technique, few microliters of acceptor phase are necessary to complete the analysis and
139  it is more likely to be successfully combined with LPME procedures than FAAS, ICP-
140  MS and ICP-OES, since dilution or higher volumes of the acceptor phase is avoided.

141  The timeline of the LPME procedures is shown in Figure 2D. LPME techniques have
142  undergone important modifications where different modalities (i.e., SDME, HF-LPME,
143  and DLLME), different solvents (i.e., IL, TSIL, MIL, SUPRA solvent, DES, SS, etc.),
144  dispersion modes (i.e., *in situ* IL, US energy, vortex, air, effervescence, etc.), sampling
145  mode (i.e., SFOD, DSD, continuous-flow and recycling-flow ME, etc.), analytical
146  detection systems or automated procedures have been employed.

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B)

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C)
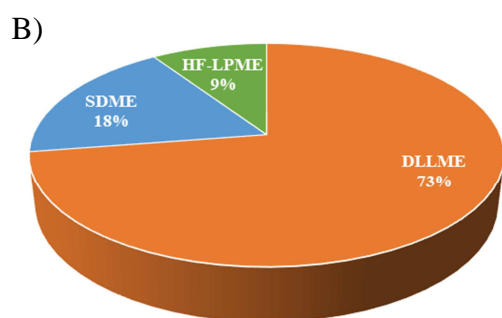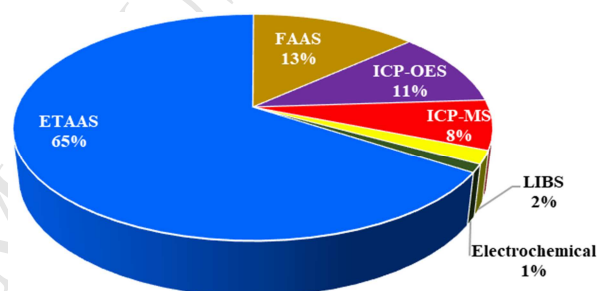


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D)

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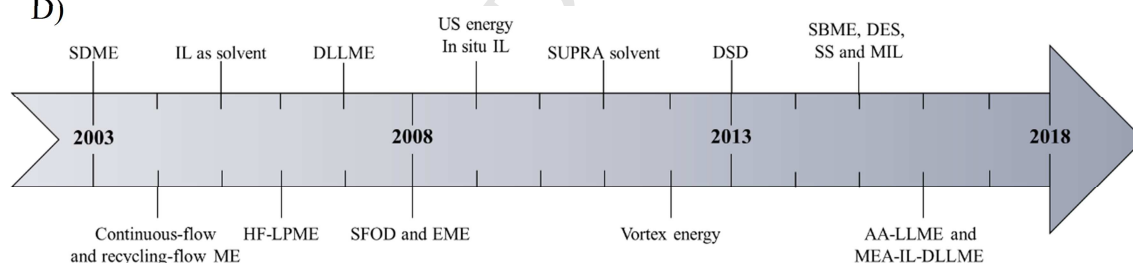


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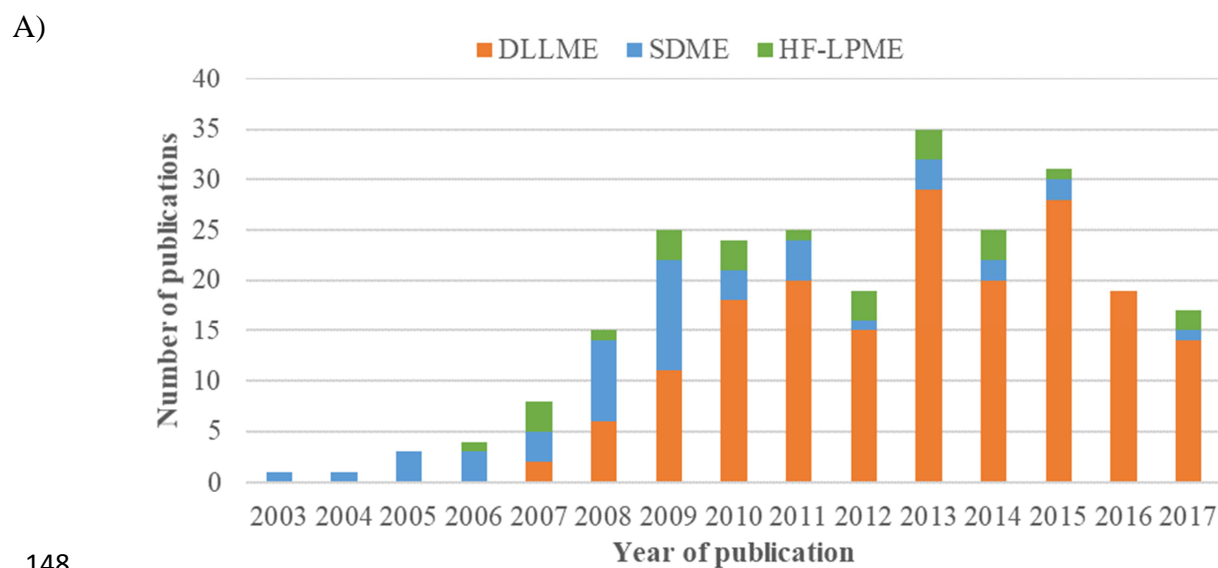
160 Figure 2. A: Number of publications regarding the combination of LPME procedures
161 with elemental detection techniques. B: Diagram showing the percentage of
162 publications using different LPME procedures in trace elemental analysis from 2003 to
163 2017. C: Diagram showing the percentage of publications using different elemental
164 detection systems from 2003 to 2017. Data generated from a search performed in
165 Scopus database (http://www.scopus.com). D: Timeline of LPME procedures firstly
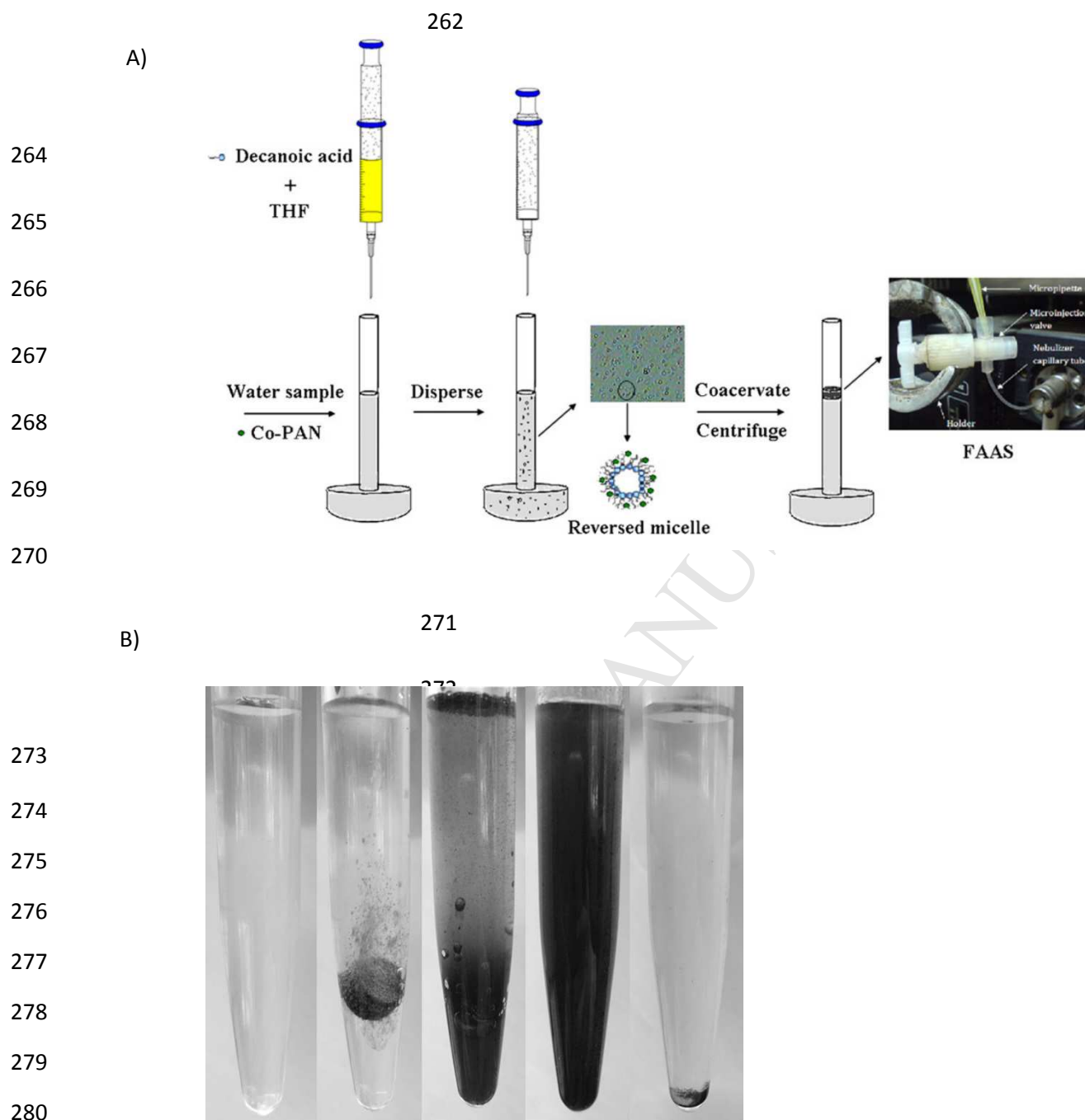166 applied to elemental analysis.

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169    Regarding different LPME and related procedures, in 2003, Chamsaz *et al.*
170    determined, for the first time, arsenic by ETAAS using HS-SDME after *in situ* hydride
171    generation [16]. Three years later, the HF-LPME was employed for the first time in
172    elemental analysis for the speciation of Se(IV) and Se(VI) in environmental water
173    samples using ETV-ICP-MS [17]. Next year, in 2007, the DLLME was successfully
174    combined to ETAAS for the determination of cadmium in water samples [18]. In 2008,
175    Basheer *et al.* [5] proposed to assist the extraction using an electric field (EME) for the
176    determination of lead from biological fluids and cosmetics for the first time. Finally, in
177    2015 another modification of HF-LPME termed solvent-bar microextraction (SBME)
178    was used by Pinto *et al.* [6] for determination of Ni in seawater samples.

179    Relating to extractant solvents, in 2005, a microdrop of IL was used for the first time
180    to assess the preconcentration of organotin and organomercurial compounds before
181    ETAAS and CVAFS detection systems [19]. Modifications in cation and/or anion
182    composition in the IL offer a broad range of applications. Task-specific ILs (TSILs),
183    which obtained by tailoring either cationic or anionic of the IL structure with suitable
184    combination of specific metal-chelating functional groups, have great potential in the
185    field of metal preconcentration. TSILs are widely used for heavy metal extraction due to
186    a complexing agent is not needed [20]. Another interesting IL modification is to
187    incorporate a paramagnetic component in either the cation or anion of the IL structure.
188    MIL-based DLLME was first used for the extraction of Au and Ag (as thio-Michler's
189    ketone chelates) from well water and lime ore samples [21]. Jafarvand and Shemirani
190    [22, 23] developed an alternative DLLME procedure called SM-DLLME (Figure 3A).
191    In the first research work [22], the Co-PAN complex was extracted with coacervates
192    composed of reversed micelles made from decanoic acid and dispersed in THF-water
193    mixture. After the extraction, the coacervate phase was diluted with ethanol and injected
194    manually into the FAAS. In comparison with conventional DLLME, SM-DLLME uses
195    decanoic acid, which is a more environmentally friendly solvent. In the second research
196    work [23], reversed micelles were formed with the same reagents as in the previous
197    work (decanoic acid, THF-water mixture) in the separation and preconcentration of Cd-
198    APDC complex in combination with FAAS detection. In 2015, Karimi *et al.* [24] used a
199    DES in LPME for the first time. They applied this method to the ligandless extraction of
200    lead and cadmium in edible oils. DESs are composed of a mixture of safe, cheap,
201    renewable and biodegradable organic compounds that are capable of associating with
202    each other through hydrogen bonding and forming a compound that has a melting point

far below that of either component. A number of DESs are prepared by simply mixing and heating organic halide salts such as choline chloride (i.e., is a very cheap, biodegradable and non-toxic quaternary ammonium salt) with hydrogen bond donors such as urea, renewable carboxylic acids (e.g., oxalic, citric, succinic or amino acids) or renewable polyols (e.g., glycerol, carbohydrates). A well-known example is the mixture of choline chloride and urea in a 1:2 mole ratio. The melting point of the eutectic mixture is 12 °C, far below than the melting point of choline chloride, 302 °C and urea, 133 °C, allowing the mixture to be used as an ambient temperature solvent [25]. In this method [24], a DES consisting of choline chloride, urea and nitric acid was added to an oil sample. The mixture was vortexed and incubated in a water bath at 50 ºC and stirred. After the extraction was completed, the phases were separated by centrifugation, and the concentration of analytes in the DES phase were measured by ETAAS. In the same year, Yilmaz and Soylak [26] developed a SS-LPME method for the quantification of copper in an aqueous sample solution prior to microsampling FAAS determination. SSs consist of an amine dissolved in water. The nonionic form of a SS has very limited miscibility with water in the absence of $CO_2$, but complete miscibility with water in its ionic form. The change in miscibility is caused in the presence of $CO_2$ and water, which produces a water-soluble carbonate salt of the protonated amine. In this method, triethylamine (TEA) and protonated triethylamine carbonate (P-TEA-C) as green and cheap switchable solvents were used. Firstly, the P-TEA-C was added to the aqueous sample solution including the Cu-PAN complex. Then, a NaOH solution was injected into the centrifuge tube and a cloudy solution appeared. At this stage, P-TEA-C was turned into TEA and the Cu-PAN complex was transferred into fine droplets of the TEA phase. The TEA phase was collected on the surface of the aqueous phase by centrifugation and finally, the copper concentration in the TEA phase was measured with FAAS.

Regarding dispersion modes, in 2009, Baghdadi and Shemirani [27] proposed for the first time a novel IL-DLLME methodology based on the formation of the extractant phase for determination of inorganic species via a metathesis reaction between a water-miscible IL and an ion exchange reagent to form a water-immiscible IL. In this work, the water-miscible IL was dissolved into the sample containing the analytes. Then the ion exchange salt was added, forming immediately a cloudy solution. Finally, phases were separated by centrifugation and the enriched phase was analyzed by using spectrophotometric detection. In the same year, Ma *et al.* [28] firstly described the

10

237    application of US energy for the determination of trace cadmium in water samples. In

238    this study, FAAS was selected as a determination method and samples were diluted to a

239    certain volume before injecting into the detection system. About vortex agitation,

240    Chamsaz *et al.* [29] firstly employed VALLME for the determination of trace amounts

241    of cadmium by FAAS. In this research, the IL 1-hexyl-3-methylimidazolium

242    hexafluorophosphate ([Hmim][PF$_6$]), was used as an extractant solvent, Cd$^{2+}$ was

243    complexed with APDC, and then extracted into fine IL droplets by the assistance of

244    vortex agitator system. AA-LLME is one of the most recently developed DLLME

245    methodology, appearing in 2016 for simultaneous determination of ultra-trace of Cu, Pb

246    and Zn in water samples by ETAAS [30]. In this work, the extractant solvent and the

247    sample mixture was repeatedly sucked into a glass syringe and then injected into a tube

248    to achieve a cloudy solution resulting from dispersion of the extraction solvent into

249    aqueous solutions. After centrifuging the cloudy solution, the extractant enriched with

250    the heavy metals were settled down in the bottom of the centrifuge tube and used for

251    ETAAS analysis. Among the most recent publications devoted to DLLME, a current

252    work of Wang *et al.* [31] seems to be very promising (Figure 3B). The authors applied

253    this solution to the quantification of Se(IV) and Se(VI). They proposed a novel, simple

254    and rapid method based on MEA-IL-DLLME followed by ETAAS determination, for

255    the analysis of the selenium levels in various food and beverage samples. In this

256    procedure, a special magnetic effervescent tablet containing CO$_2$ source (sodium

257    carbonate and sodium dihydrogenphosphate), ILs and Fe$_3$O$_4$ magnetic nanoparticles

258    was used to combine extractant dispersion and magnetic phase separation into a single

259    step. The proposed method was successfully applied to food and beverage samples

260    including black tea, milk powder, mushroom, soybean, bamboo shoots, energy drink,

261    bottled water, carbonated drink and mineral water.

262

A)

264 — Decanoic acid
+
265 THF

266

267 Water sample → Disperse → Coacervate
Centrifuge

268 • Co-PAN

269

Reversed micelle

FAAS

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Figure 3. A: Schematic representation of SM-DLLME. Reprinted with permission from the reference [22]. Copyright (2011) Springer Nature. B: Sequential steps during the MEA-IL-DLLME procedure. Reprinted with permission from the reference [32]. Copyright (2016) Elsevier.

286

287     Relating to sampling mode, in 2004, it was reported for the first time the continuous-

288 flow ME combined with ETV-ICP-MS for the determination of Be, Co, Pd and Cd in

289 human hair and human urine [33]. Moreover, Xia *et al.* made some modification to the

290 basic continuous-flow ME setup and developed a recycling-flow ME system, in which

291 the waste from the chamber was returned to the sample vial, allowing a reduction in

292 sample consumption [33]. On the other hand, after one year of presentation of SFOD

293 technique for separation of organic substances, the feasibility of performance of SFOD

294 in combinations with ETAAS for trace monitoring of metal ions was considered and a

295 SFOD method for ultra-trace monitoring of lead was evaluated [34]. Reddy *et al.* [35]

296 firstly reported the combination of DSD microextraction in conjunction with ETAAS for

297 platinum determination from geological and spent automobile converter samples.

298

299 **4. Critical comparison of LPME techniques**

300     The choice of the most suitable LMPE procedure will depend on the type of analyte

301 to be measured, the complexity of the matrix and the compatibility of the elemental

302 detector with the extractant phase employed. The main advantages of LPME procedures

303 are the extremely low consumption of solvents (e.g., IL, organic and SUPRA solvents,

304 etc.) and their relative simplicity. By far the simplest is SDME, either by direct

305 immersion or from the headspace, since only one step is needed to perform the

306 extraction. However, SDME suffers from some basic drawbacks such as instability,

307 solubility of the droplet, long extraction time and poor repeatability. Droplet instability,

308 due to the small contact surface between the droplet and needle tip, limits the agitation

309 rate and consequently, increases the equilibrium time. This limitation will directly

310 deteriorate sensitivity and precision of determinations. Extraction time can be shortened

311 using continuous-flow ME or cycle-flow ME procedures [33]. In HF-LPME, the

312 equilibration times are even longer than in SDME, because the analytes cross the HF

313 wall exclusively by diffusion, although more vigorous stirring of the sample can be

314 applied in this technique [17]. An interesting modification allowing high stirring rates is

315 a HF filled with solvent and sealed at both ends to perform SBME [6]. Another very

316 promising modification to shorten the extraction time is the application of electric

317 potential across the membrane in EME [5]. In DLLME, the extraction process is very

318 fast, requiring a much lower extraction time than SDME or HF-LPME and could be

319 performed simultaneous extractions providing an excellent sample throughput.

320     HF-LPME is more tedious compared to SDME because of the need to prepare

321 disposable hollow fibers. However, HF-LPME is quite adequate for complex samples

322 treatment because the membrane can act as a protective barrier. On the other hand,

323 conventional DLLME involves injection of the extractant phase (i.e., denser than water)

324 together with the disperser solvent in order to form the corresponding turbid solution.

325 Thus, a centrifugation step is mandatory to deposit the solvent on the bottom of a

326 conical tube, from where it is collected by a syringe. In case of extractant solvents less

327 dense than water, the organic solvent remains in the upper layer after phase separation,

328 being its collection problematic. One solution is the combination of DLLME and SFOD

329 procedures. In SFOD procedure the floating organic solvent is solidified in an ice-bath,

330 separated from the aqueous phase with a micro spatula and then melted at room

331 temperature [34]. Nevertheless, this limits the choice of solvents to those with melting

332 point near room temperature (between 10 and 30 ºC). Moreover, SFOD is perhaps the

333 procedure that needs more handling steps to be accomplished. In addition, the extract is

334 commonly diluted for analysis, decreasing to a large extent the enrichment factor

335 previously achieved. An interesting approach is the use of a magnet to separate a MIL

336 from the aqueous phase, avoiding the centrifugation step [21, 36].

337

## 5. Automation of LPME techniques

339     Automation is one of the main challenges of LPME techniques. Several

340 developments have been reported towards the automation of LPME methods, although

341 their complete implementation in routine analysis is still far to be achieved. The

342 excellent benefits of this technique, such as simple sample preparation, fast analysis and

343 small sample and reagents consumption have stimulated scientists to apply this

344 technology to their research. However, automation of LPME methods surely involves

345 extra efforts in method optimization and evaluation as well as additional

346 instrumentation and analyst training. It is important to determine which advantages can

347 be gained to compensate these difficulties.

348     The merit of the first combination of the flow injection techniques with DLLME

349 belongs to Anthemidis and Ioannou [37], describing sequential injection DLLME

350 system for Cu and Pb preconcentration from water samples and determination using

351 FAAS. In this work, the stream of disperser and extractant solvents was merged on-line

352 with the stream of sample (aqueous phase), resulting a cloudy mixture, which consisted

353 of fine droplets of the extraction solvent dispersed entirely into the aqueous phase. By

14

354  this continuous process, metal chelating complexes were formed and extracted into the

355  fine droplets of the extraction solvent. Then, the hydrophobic droplets of organic phase

356  (i.e., xylene) were retained into a microcolumn packed with PTFE-turnings. Finally, a

357  portion of 300 µL of isobutylmethylketone was used for quantitative elution of the

358  analytes, which were transported directly to the nebulizer of FAAS system. Additional

359  four research works about the extraction of metal analytes (Cd, Ag, Pb, and Tl) using

360  similar assemblies coupled to either FAAS or ETAAS with differences in kind of

361  extraction solvent, chelating agent, extraction time, and flow rates have been published

362  [38-41].

363  Cerdà *et al.* introduced an automated in-syringe DLLME for Cu determination in

364  water samples using long path-length spectrophotometric detection [42]. Similar

365  methodology was later reported for fluorometric determination of Al in seawater [43].

366  In both works, selective analyte derivatization was performed within the syringe using

367  an automated syringe pump.

368  Regarding the automation of SDME and related techniques, Pena *et al.* [44] proposed

369  a semi-automated method combining both sequential injection analysis and ETAAS

370  technique for determination of Cr(VI) in waters using a home-made microextraction

371  vial. In this work, the furnace autosampler arm enabled the performance the SDME

372  procedure and its injection into the graphite furnace. A fully automatic SDME coupled

373  to ETAAS for Cd determination in water samples has been described by Anthemidis

374  and Adam [45]. The method involved the use of a home-made flow-through extraction

375  cell coupled on a sequential injection manifold. The automation of in-syringe SDME

376  hyphenated to ETAAS via a programmable platform for determination of Hg in

377  complex matrices has been also reported [46]. This method was based on the use of

378  palladium nitrate solution as sorbent in the drop, which also acts as matrix modifier for

379  the electrothermal atomization of mercury. The sequestration mechanism was based

380  either on the catalytic decomposition of the hydrides or on the amalgamation of $Hg^0$

381  with the finely dispersed $Pd^0$ formed on the drop surface.

382  Another way to achieve partial automation of the LPME is using a chip-based

383  device. Hu *et al.* [47] fabricated a chip-based LPME device and combined with ETV-

384  ICP-MS for the determination of trace Cu, Zn, Cd, Hg, Pb and Bi in cell and human

385  serum samples. Inside the chip, the aqueous and organic phase formed laminar flow and

386  in the interfacial contact between the aqueous and organic phase, the target metal

387  chelates enter into the organic phase. Then, the organic phase was collected and

15

388  introduced into the graphite furnace with a micropipette for subsequent ETV-ICP-MS

389  analysis.

390

391  **6. Conclusions and perspectives**

392  LPME is a powerful sample preparation technique, which offers a promising

393  substitute to LLE. LPME techniques including SDME, HF-LPME, and DLLME possess

394  many benefits such us low cost, simplicity, high enrichment efficiency and minimal

395  solvent consumption. It is fully demonstrated that the couple of LPME with elemental

396  detector techniques would provide excellent analytical performance in real world

397  sample analysis, for instance multi-element analysis ability, wide linear range, and high

398  sensitivity. Moreover, LPME procedures use a great variety of modalities,

399  configurations and solvent types, which have been deployed to counter their limitations

400  and expands their analytical scope.

401  In recent years, LPME procedures have made substantial progress in the field of

402  analytical chemistry, but its potential in metal applications has yet to be fully exploited.

403  The observed progress can be attributed to the development of new modalities and the

404  improvement of existing ones using advanced materials and configurations. In this

405  sense, the use of magnetic materials and new interfaces for LPME automation are key

406  milestones in this progress.

407  In the near future, the utility of LPME procedures are beyond question and their

408  complete acceptance in routine analytical laboratories [48] depends on their successful

409  automation and integration with conventional and non-conventional analytical

410  instruments.

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412  **Acknowledgements**

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**Highlights**

The combination of liquid-phase microextraction and elemental detectors are reviewed

A general description of main liquid-phase microextraction techniques is included

Historical overview of liquid-phase microextraction in trace element analysis is pointed out.

A critical comparison of different liquid-phase procedures is discussed.