

Dispersive Liquid-Liquid Microextraction for Arsenic Speciation in Complex Food Matrices

Aliasghar Moharrami

Ardabil University of Medical Sciences

Eslam Pourbasheer

University of Mohaghegh Ardabili

Leila Farhoudi

Ardabil University of Medical Sciences

Farzaneh Fathi

f.fathi@arums.ac.ir

Ardabil University of Medical Sciences

Research Article

Keywords: Arsenic, Detection, DLLME, Food matrix, Microextraction

Posted Date: October 21st, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11124132/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Arsenic is a highly toxic metalloid that poses serious health risks through contaminated food and water. The World Health Organization (WHO) has established ultra-low permissible limits for arsenic, demanding analytical methods with exceptional sensitivity and accuracy. Dispersive liquid-liquid microextraction (DLLME) has emerged as an effective sample preparation technique for arsenic determination and speciation, offering high enrichment factors, rapid extraction, minimal solvent consumption, and operational simplicity. This review presents an overview of recent DLLME-based strategies for arsenic monitoring across food, aqueous, and biological matrices, with particular emphasis on food applications and related analytical challenges. Special emphasis is placed on advanced extraction media including deep eutectic solvents (DESs), ionic liquids (ILs), and magnetic ionic liquids (MILs), often integrated with magnetic solid-phase extraction or automated lab-in-syringe systems. Key performance metrics are compared for total arsenic, inorganic As(III)/As(V), and selected organic arsenic species across food, water, and biological matrices. By critically identifying matrix-specific challenges, speciation-related limitations, and gaps in method standardization, this review provides practical perspectives for developing more reliable DLLME-based strategies for arsenic monitoring through improved analytical approaches for food and water safety.

1. Introduction

Arsenic is a metalloid with multiple oxidation states and organic and inorganic species of analytical importance. The most common forms include As(III), As(V), monomethylarsonic acid (MMA), and dimethylarsinic acid (DMA) [1]. Their occurrence and distribution depend on environmental conditions such as pH and redox potential [2]. Arsenic enters food and water systems through both natural and anthropogenic sources. Natural inputs include weathering of arsenic-bearing minerals, volcanic activity, and geothermal processes, while anthropogenic sources mainly involve mining, pesticide use, fossil-fuel combustion, and industrial activities. Inorganic arsenic species are generally more toxic than most organic arsenic compounds [1]. The toxicity of arsenic can be acute or chronic, and its carcinogenic potential has been well established [3]. The WHO recommends a maximum arsenic concentration of $10 \mu\text{g L}^{-1}$ in drinking water [4]. Variations in arsenic species and matrix composition among different media directly influence the selection of complexing agents, extraction solvents, pH, digestion procedures, and DLLME conditions [5]. Therefore, the determination of total arsenic and individual arsenic species at trace and ultra-trace levels is essential for assessing food and water safety. However, accurate analysis in complex matrices remains challenging because of matrix interferences and the need to preserve arsenic speciation during sample preparation.

Conventional analytical techniques, including inductively coupled plasma mass spectrometry (ICP-MS), atomic absorption spectrometry (AAS), and high-performance liquid chromatography (HPLC), coupled with element-specific detection offer excellent sensitivity and selectivity [6, 7]. Nevertheless, these techniques generally require effective sample preparation to reduce matrix effects, improve analyte enrichment, and, in speciation analysis, prevent changes in arsenic species [8]. In response to the growing demand for rapid, cost-effective, and environmentally friendly analytical methods, dispersive liquid-liquid microextraction (DLLME) has emerged as a powerful sample pretreatment technique since its introduction in 2006 [9]. DLLME is based on a ternary solvent system comprising a disperser solvent and an extraction solvent, which rapidly forms a cloudy solution, resulting in a high surface area for efficient mass transfer of analytes [10, 11]. Its low solvent consumption, short extraction time, and high enrichment potential have made DLLME attractive for trace-element analysis, including arsenic determination.

In recent years, DLLME-based arsenic analysis has evolved beyond conventional organic extraction solvents toward more advanced extraction media and configurations [12, 13]. These developments include DESs, ILs, MILs, task-specific ionic liquids (TSILs), and automated DLLME systems [14, 15]. Such approaches can improve selectivity, facilitate phase separation, reduce the use of conventional volatile solvents, or enable automated and high-throughput sample

preparation. However, these advantages are accompanied by unresolved challenges, including matrix effects in food and biological samples, high viscosity of some alternative solvents, solvent toxicity and biodegradability, species interconversion during digestion or extraction, and limited standardization among reported procedures [16, 17]. These challenges are particularly relevant when DLLME is applied to food matrices, where proteins, lipids, carbohydrates, and high ionic strength can substantially influence extraction efficiency and method robustness.

Several reviews have addressed DLLME for arsenic determination. Viñas *et al.* reviewed DLLME applications in food analysis for a wide range of organic and inorganic compounds, without focusing specifically on arsenic determination and speciation [18]. Llorente-Mirandes *et al.* reviewed methods for inorganic arsenic determination in foods, with emphasis on evaluation methods, certified reference materials, and proficiency testing, while DLLME represented only one of several sample-preparation approaches considered [19]. Jagirani and Soylak reviewed arsenic speciation using emerging sample-preparation techniques, including solid- and liquid-phase microextraction, rather than providing a comparative assessment of different DLLME formats [20]. More recently, Notardonato and Avino reviewed advances in DLLME, but their orientation was not specifically centered on arsenic determination, food-matrix challenges, and arsenic speciation [21]. Accordingly, a focused synthesis is needed to integrate the recent development of DLLME strategies specifically for arsenic determination and speciation while considering the analytical consequences of solvent chemistry, matrix complexity, and extraction configuration. The present review therefore aims to provide an arsenic-focused comparative analysis of DLLME approaches within the broader context of miniaturized extraction techniques across food, water, and biological matrices. Particular attention is given to As(III)/As(V) and selected organic arsenic species, food-matrix effects, conventional versus green extraction media, magnetic and automated DLLME formats, and their coupling with spectrometric and chromatographic detection systems. Rather than merely summarizing individual studies, the review compares analytical performance, identifies methodological strengths and limitations, highlights unresolved challenges such as species interconversion and matrix-dependent extraction behavior, and discusses gaps in standardization and routine applicability. This framework is intended to clarify the current capabilities and limitations of DLLME for arsenic monitoring and to identify practical directions for the development of greener, more robust, and more automated sample-preparation strategies.

2. Microextraction techniques for arsenic determination

At present, arsenic contamination is regarded as a global issue, necessitating analytical methods capable of measuring its concentration even at very low levels. A number of techniques, such as colorimetry, electrochemical methods and electrophoresis, have been employed; however, many of these methods suffer from limitations in sensitivity and selectivity for trace arsenic determination [22]. Consequently, more precise instrumental methods based on atomic absorption, atomic emission and mass spectrometry, such as ICP-MS, HG-AAS and GFAAS, have been used for arsenic determination and, when combined with an appropriate separation or selective sample-treatment step, for arsenic speciation in different types of samples [22]. Sample preparation also plays a crucial role in the accuracy of the obtained results; hence, combined extraction techniques (liquid–liquid, solid-phase, sonication, supercritical fluid, etc.), along with various sorbents and nanomaterials, are employed for the separation and preconcentration of arsenic species. Along this line, the use of miniaturized and efficient techniques such as microextraction, has gained increasing importance as a rapid, low-solvent, and cost-effective strategy for the preconcentration of arsenic and for improving the performance of instrumental methods in complex matrices. The main advantages of microextraction include reduced solvent consumption, rapid extraction, potential for automation, and integration with instrumental analysis [23–26]. However, these advantages do not necessarily translate into greater routine applicability, as method robustness, matrix tolerance, phase handling, and reproducibility vary substantially among microextraction formats[27].

The most well-known and widely used conventional extraction methods are liquid-liquid extraction (LLE) and solid-phase extraction (SPE). Although both techniques can provide effective separation and preconcentration, LLE

commonly requires relatively large volumes of organic solvents, whereas SPE may involve time-consuming and multistep operations [10, 18, 28]. DLLME functions as a sample-preparation and preconcentration technique that is commonly coupled with HPLC, AAS, ICP-MS and related detection systems. Compared with conventional approaches, DLLME provides a more favorable combination of rapid mass transfer, low extraction-solvent consumption, high enrichment potential, and simple integration with spectrometric detection. Its use of microliter-scale extraction phases and rapid dispersion can substantially reduce extraction time and solvent consumption compared with conventional LLE, while avoiding some of the sorbent conditioning, loading, washing, and elution steps associated with SPE [9, 28]. These characteristics make DLLME particularly attractive for trace arsenic determination, as the dispersion of microliter volumes of extraction solvent into fine droplets enhances mass transfer, enabling simultaneous extraction and preconcentration in a single step [29]. In a typical inter-laboratory comparison study, an automated DLLME technique for arsenic speciation in rice attained a limit of detection (LOD) of $0.005 \mu\text{g L}^{-1}$ and recoveries ranging between 94.2% and 108.9%, compared to LOD of $0.02 \mu\text{g L}^{-1}$ in the case of the referenced SPE-ETAAS method; it must be remembered that any difference in matrices and laboratory conditions influences the validity of such a comparison [8].

Although DLLME is the primary focus of this review, its recent development should be considered within the broader context of miniaturized extraction approaches. Accordingly, Solid-Phase Microextraction (SPME) and Liquid-Phase Microextraction (LPME) are briefly reviewed to highlight their recent analytical developments and to clarify the advantages and limitations that have driven the evolution of DLLME for arsenic determination. Conventional LLE and SPE are also considered as reference approaches because they provide the basis for evaluating the practical benefits of miniaturized extraction.

2.1. Solid-Phase Microextraction (SPME)

SPME is based on a fused-silica or metal support coated with a liquid polymer or solid sorbent phase [30]. Created by C.L. Arthur and J. Pawliszyn in the early 1990s, SPME integrates sampling, extraction, and preconcentration in a single step with little or no consumption of organic solvents [31, 32]. In recent years, various materials such as molecularly imprinted polymers (MIPs), restricted access materials (RAMs), metal-organic frameworks (MOFs), covalent organic frameworks (COFs), and other advanced sorbent materials have been used as sorbents in microextraction technologies [33, 34]. Some of the main disadvantages of this technique include fiber brittleness, limited mechanical stability [35], low fiber capacity for analyte extraction, and thermal degradation of the fiber coating [36]. DLLME typically involves microliters of an extraction solvent, usually in combination with a disperser solvent, but provides fast mass transport due to the formation of fine droplets of extractant [29]. Both SPME and DLLME can be used for arsenic speciation if selective sorbent or conditions of complexation are utilized. So, in case of an online sequential SPME-ICP-MS technique, the quantification of As(III) and As(V) in drinking water and environmental samples was performed with the signal enhancement factor of 60, limits of detection of $0.005 \mu\text{g L}^{-1}$, and relative standard deviations of 3.2–3.8% [37]. Also, an automated DLLME-GFAAS method for arsenic speciation in rice allowed to determine the limit of detection of $0.005 \mu\text{g L}^{-1}$ and relative standard deviation of 3.7% [8]. For arsenic analysis, SPME has been widely used for trace determination and speciation in environmental, biological, and food samples. Its solvent-free or near-solvent-free operation facilitates coupling with chromatographic and spectrometric techniques. However, its performance depends on fiber chemistry, analyte-coating interactions, and fiber stability, which affect extraction efficiency and reproducibility. Compared with SPME, DLLME generally provides faster extraction and easier automation, whereas SPME offers lower solvent consumption and reusable extraction phases. These studies demonstrate that both SPME and DLLME enable sensitive arsenic determination and are compatible with automated workflows. However, their strengths differ: SPME minimizes solvent consumption and provides selective extraction through tailored sorbents, whereas DLLME generally offers faster extraction, higher preconcentration, and greater flexibility in extraction-phase design. Direct comparisons

should be interpreted cautiously because reported performances depend on the sample matrix, extraction conditions, and detection system. Overall, SPME is preferable for selective, solvent-free extraction, while DLLME is more suitable for rapid extraction and coupling with atomic spectrometric techniques.

2.2. Liquid-Phase Microextraction (LPME)

LPME is a miniaturized version of the liquid-liquid extraction technique, used for sample preparation, separation, and pre-concentration before instrumental analysis [38]. In this method, very small volumes (μL) of immiscible solvents (usually organic solvents) are used, which make physical contact with the sample [39]. Alternatively, the solvent can reside within the pores of a hydrophobic membrane or be separated from the donor phase by a membrane interface [40].

LPME provides a general framework for miniaturized liquid-phase extraction, with the main advantages being low solvent consumption, reduced sample requirements, preconcentration, and potential automation [41, 42]. However, its practical performance depends strongly on the extraction configuration, membrane or solvent characteristics, phase stability, and matrix composition [43]. LPME can be classified into different modes, with the most commonly used methods including the Dispersive Liquid-Liquid Micro extraction (DLLME) [41]. In DLLME method, the accepting phase (high-density, water-immiscible organic extraction solvent) and an amphiphilic disperser solvent, which is soluble in both the organic and aqueous phases, are rapidly added to the sample. As a result, fine droplets of the organic solvent disperse in the aqueous sample, forming a turbid solution. It was first introduced by Rezaee and colleagues in 2006 [44]. This method allows for the simultaneous extraction and pre-concentration of analytes from samples, using micro-volumes of extraction solvent [45]. Conventional DLLME generally involves an aqueous donor phase, a water-immiscible extraction solvent, and a disperser solvent that facilitates rapid formation of fine extraction droplets [44, 45]. The schematic diagram of the DLLME method is shown in Fig. 1.

The disperser and extraction solvents are brought into contact with the aqueous phase, creating an emulsion that markedly increases the interfacial contact area, resulting in the rapid establishment of extraction equilibrium and, consequently, a very short extraction time [45]. Although the distribution coefficient influences extraction, the high efficiency of DLLME mainly results from the formation of fine droplets, which provide a large interfacial area and enhance mass transfer [47]. In addition, pH adjustment, complexation, or ion-pair formation can improve arsenic transfer into the extraction phase. However, the resulting stable dispersion may complicate phase separation, especially with microliter-scale solvent volumes, leading to analyte loss. Centrifugation is therefore commonly used to promote efficient phase separation [18]. After centrifugation, the organic phase settles, is recovered, and is used for instrumental analysis. DLLME offers rapid extraction, low solvent consumption, and high preconcentration capability [41, 48, 49]; however, its performance depends on solvent compatibility, phase separation efficiency, matrix effects, and reproducibility of dispersion conditions, particularly in complex food matrices where co-extracted components may affect analyte transfer and recovery.

3. Factors influencing DLLME

a) **Extraction solvent.** The physicochemical properties of the extraction solvent, particularly density, polarity, water immiscibility, and chemical compatibility with the arsenic–complex species, strongly influence phase formation, mass transfer, and phase separation. Therefore, solvent selection should be considered in relation to both extraction efficiency and practical factors such as toxicity, detector compatibility, viscosity, and ease of phase recovery [50]. In typical DLLME applications, chlorinated solvents, which have higher densities than water, are used. For example, chloroform is widely applied in biological sample determinations [50–55]. However, chlorinated solvents are considered one of the major drawbacks of DLLME due to their harmful effects on human health and the environment. These solvents are also incompatible with some detection techniques, such as ICP-MS or reverse-phase liquid

chromatography (RP-LC) [56]. In recent years, the development of DLLME has moved toward green chemistry, using safer, greener alternatives as extraction solvents to reduce environmental impacts and human health risks [57]. Some approaches adopted are mentioned below:

1. Low-density, organic solvents such as n-hexane, 1-octanol, heptane, or isooctane are used as extraction solvents [58–60]. Although they make it easier to separate the phases and will reduce dependence on heavy chlorinated solvents, the effect that they have on the environment and health cannot be generalized because each of these solvents is different [61, 62]. Low-density solvents facilitate phase recovery from the upper layer and can reduce dependence on dense chlorinated solvents; however, their environmental and toxicological profiles remain solvent-specific, and incomplete phase separation may increase the risk of aqueous-phase carryover. Thus, their practical advantage should be evaluated together with extraction efficiency and phase-purity requirements [63]. For arsenic analysis, an octanol-based low-density solvent DLLME method provided EFs of 6.2–70.8, detection limits of 0.001–0.039 $\mu\text{g L}^{-1}$, and recoveries of 81.8–111.7% for inorganic and phenyl arsenic species in water samples [64].
 2. The use of ionic liquids (ILs): ILs have attracted considerable attention because their physicochemical properties can be tailored to improve extraction selectivity and phase behavior. However, their low vapor pressure should not be equated with environmental safety, as toxicity, biodegradability, persistence, viscosity, and synthesis requirements vary substantially among IL structures. Consequently, IL-based DLLME should be assessed using a broader sustainability framework rather than vapor pressure alone [65–71].
 3. Deep eutectic solvents (DES): These are increasingly used as alternative extraction media in DLLME [72]. Generally, DESs are formed by combining two or more components (including hydrogen bond acceptors and donors). These components are mixed in specific ratios, resulting in a homogeneous mixture. The eutectic point of this mixture is lower than the melting points of its pure components. DESs are attractive because they can often be prepared by simple mixing of relatively accessible components and generally exhibit low volatility. Nevertheless, their viscosity, water sensitivity, component ratio, and batch-to-batch variability can influence mass transfer and extraction reproducibility. Thus, the designation of a solvent as “green” should not be based solely on its low volatility or ease of preparation, but should consider the composition and overall extraction procedure [72–74]. In DLLME studies, the solvent volume typically varies between 30 and 300 μL [49, 63].
- b) **Disperser solvent:** The disperser solvent must be miscible with both the aqueous and organic phases and should facilitate the formation of a cloudy solution. Recent arsenic DLLME studies increasingly evaluate disperser systems not only for efficient phase dispersion but also for their effects on matrix compatibility, solvent consumption, and extraction reproducibility. The choice of disperser can therefore influence both analytical recovery and the practical robustness of the method, particularly in viscous or lipid-rich food matrices [45]. These substances reduce the interfacial tension and increase the contact surface between the aqueous and organic phases [75].
- c) **Extraction time:** Because DLLME generates a large interfacial area, effective extraction is generally rapid, and recent arsenic applications commonly achieve effective extraction within a few minutes. Importantly, increasing extraction time does not necessarily improve recovery and may reduce the practical advantage of DLLME; therefore, recent developments have focused on ultrasound, vortexing, magnetic stirring, and automated dispersion to accelerate mass transfer without substantially increasing operational time. With the help of ultrasonication, solvent dispersion and analyte mass transfer can be increased. These developments are particularly relevant to routine analysis, where throughput and reproducibility are as important as extraction efficiency. In some DLLME techniques, ultrasonic energy is used to accelerate the extraction process. The ultrasound-assisted UA-DLLME method has been used in several studies [52, 66, 69, 76].

d) Matrix effect: One limitation of DLLME is matrix interference. This method performs well in simple aqueous samples but shows reduced efficiency in more complex matrices, especially foods and biological samples. Proteins and lipids can interact with arsenic species or complexing agents and may stabilize emulsions, reduce analyte transfer, or alter phase separation. Carbohydrates can increase sample viscosity and hinder mass transfer, while high concentrations of inorganic salts may modify ionic strength, complexation equilibria, and solvent dispersion. Matrix components may therefore affect both extraction efficiency and species selectivity. Common strategies to minimize these effects include sample digestion or dilution, filtration, pH adjustment, optimization of the complexing-agent concentration, matrix matching, and standard addition. Importantly, the extent of matrix interference is matrix-specific; for example, standard addition was required for accurate quantification in sugar samples [77], whereas a preliminary cleanup step was necessary for honey because direct extraction produced low efficiency[45, 78–82]

e) Automation: Given the growing need for fast and online pre-concentration methods, automating DLLME is considered an important development. Automation can reduce operator-dependent variability and improve precision, reproducibility, and sample throughput. Recent developments have moved from manual DLLME toward formats that reduce centrifugation, phase-transfer, and operator-dependent steps, including ionic-liquid syringe extraction and cold-column trapping approaches [83, 84]. These configurations illustrate a broader trend toward integrating DLLME into automated or semi-automated workflows, although their wider adoption depends on method standardization, instrumental compatibility, and validation of long-term reproducibility. More recently, fully automated DLLME has also been applied to arsenic speciation in rice samples, demonstrating its potential for complex food-matrix analysis [8]. Nevertheless, further standardization and integration with routine analytical platforms are still required. Figure 2 presents a step-by-step overview of the DLLME method development process.

Recent research has increasingly addressed these limitations through methodological modifications rather than simply optimizing individual extraction parameters. High-viscosity extraction phases have been combined with ultrasound- or vortex-assisted dispersion to improve mass transfer, while magnetic extraction phases and modified phase-separation strategies have been developed to simplify phase recovery [28, 85, 86]. The use of DES/natural deep eutectic solvent (NADES) and ILs has also aimed to reduce reliance on conventional volatile solvents and improve extraction selectivity. In addition, automated and lab-in-syringe configurations have been introduced to reduce operator-dependent variability and improve throughput [8, 87]. For complex matrices, researchers have employed matrix-specific digestion, dilution, standard addition, and selective cleanup procedures to minimize matrix effects [64]. These developments indicate that current DLLME research is increasingly focused on improving robustness, reproducibility, and practical applicability rather than solely maximizing extraction efficiency.

4. Application of DLLME in arsenic determination and speciation

In this section, reports of DLLME applications for the determination of environmental arsenic species and operational formats are reviewed, as well as their analytical performance, potential for other applications in food and complex matrices, and their advantages and disadvantages. DLLME has evolved into a versatile sample-preparation technique applied in environmental, food, biological, and industrial analyses. For arsenic determination, it enables preconcentration, speciation, matrix cleanup, and integration with advanced detection systems. Recent developments have focused on assisted dispersion, magnetic phases, and automation to enhance extraction efficiency and analytical throughput. This review specifically addresses arsenic analysis due to the unique challenges of speciation, matrix effects, and trace-level detection.

4.1. Green Solvent-Based DLLME

Recently, the ultrasound- and vortex-assisted DLLME technique was used for the simultaneous preconcentration and extraction of heavy metal ions by Mafakheri *et al.* [79]. This method was used using a hydrophobic NADES called 1-menthol: salicylic acid (M:SA) with a molar ratio of 4:1 for the extraction of heavy metal ions Arsenic, (Cd(II), Hg(II), Pb(II) (Fig. 3a). The method combined ultrasound- and vortex-assisted DLLME with a hydrophobic NADES composed of 1-menthol and salicylic acid (M) for simultaneous extraction of As, Cd, Hg, and Pb from water and food matrices. The approach achieved high enrichment and satisfactory recovery, demonstrating the feasibility of NADES-based DLLME for multielement analysis in complex samples [79]. However, the use of ultrasound and vortexing indicates that the relatively high viscosity of the NADES may require additional dispersion energy to achieve efficient mass transfer. Fathi *et al.* [80] applied DES-based DLLME-GFAAS to As(III)/As(V) speciation and total arsenic determination in rice using an L-menthol/octanoic acid DES and DDTP as the complexing agent. Importantly, the authors used different digestion conditions for speciation and total arsenic determination to minimize species interconversion. The method achieved an LOD of 0.1 $\mu\text{g kg}^{-1}$, an EF of 200, and recoveries of 90.0–108.5% [80]. These results support the applicability of DES-DLLME to rice analysis, although the relatively high EF should be considered together with the need for controlled digestion conditions to preserve arsenic species. Ji *et al.* [81] developed an UA-DLLME method based on hydrophobic DES composed of tri octylmethyl ammonium chloride and DL-lactic acid (TAC–LA) for the preconcentration and determination of Cd and As in wine samples. Under the optimized conditions, the sample pH was adjusted to 7 and NaCl was added, and then a mixture of DES and methanol was added; after centrifugation, the DES-enriched phase was collected for measurement by FAAS. As shown in Fig. 3b, a vortex times of 1.0 min and sonication times of 4 min were determined to be optimal for maximum extraction recovery. Vortexing disperses the extraction solvent into fine droplets to increase the contact area, while ultrasonication disperses self-aggregated DES droplets and accelerates mass transfer between the DES and aqueous phases [81]. The combination of vortexing and ultrasonication improved dispersion and mass transfer and resulted in satisfactory recoveries for As. This study highlights the importance of assisted dispersion when relatively viscous DES phases are used, although the additional energy input and dependence on sonication conditions should be considered when assessing reproducibility and scalability [81].

Collectively, DES/NADES-based DLLME studies demonstrate a transition toward low-volatility extraction media while maintaining the rapid mass-transfer characteristics of DLLME. These approaches have successfully enabled arsenic extraction from food and aqueous matrices, highlighting the importance of solvent composition, hydrogen-bond donor/acceptor selection, and dispersion strategies (e.g., ultrasound or vortex-assisted agitation) in controlling extraction performance. However, the relatively high viscosity of some DES/NADES systems may affect mass transfer and phase separation, while solvent stability, preparation reproducibility, scalability, and compatibility with advanced detection platforms remain insufficiently investigated. Therefore, although DES/NADES solvents provide advantages such as low volatility, simple preparation, and reduced use of hazardous chlorinated solvents, further systematic evaluations are required before their routine adoption as universal alternatives to conventional DLLME extractants.

4.2. Ionic liquid-based DLLME

Jamshed Ali *et al.* [82] developed a pressure-induced IL-DLLME method coupled with HG-AAS for total arsenic determination in water and diverse food matrices. The method used a hydrophobic imidazolium-based IL and pressure-induced dispersion, achieving recoveries of 97.5–100% in food samples. The broad range of matrices demonstrates the versatility of the approach; however, the need to reduce the viscosity of the IL-rich phase before instrumental analysis adds an additional procedural step that may affect routine applicability. For the determination of arsenic(III) and arsenic(V), an *in situ* DLLME method based on a TSIL was used by Ashouri *et al.* [88]. They developed an *in situ* DLLME method based on an APDC-functionalized TSIL for As(III)/As(V) speciation in water, urine, and rice (Fig. 4a). The TSIL served simultaneously as the extraction medium and complexing agent, providing selective extraction of As(III). As(V) was determined after reduction to As(III), allowing speciation by difference. The method achieved high enrichment and

recoveries of 90.8–104.3% [89]. Its main advantage is the integration of complexation and extraction within a single functionalized solvent; however, the need for redox conversion introduces an additional potential source of uncertainty in speciation analysis.

Fiorentini *et al.* [78] applied magnetic-IL-DLLME with ETAAS for arsenic determination in honey using [P6,6,6,14]FeCl₄ as the extraction phase (Fig. 4b). A preliminary cleanup step was necessary because direct extraction from the honey matrix produced an extraction efficiency below 46.9%, demonstrating the strong influence of matrix components on DLLME performance. Magnetic collection of the extraction phase subsequently enabled direct transfer to the ETAAS system. The study therefore illustrates both the potential of magnetic ILs for simplified phase recovery and the continuing importance of matrix-specific cleanup in complex food samples. The application of IL-based DLLME to a complex biological matrix demonstrates the versatility of these extraction media beyond food samples. Nevertheless, biological matrices generally impose greater demands on matrix cleanup and method validation, making precision, matrix effects, and recovery from independently prepared samples important considerations in assessing routine applicability.

Wang *et al.* [8] developed a fully automated magnetically stirred assisted lab-in-syringe dispersive liquid–liquid microextraction (MAS-LIS-DLLME) method for the selective preconcentration and separation of As(V) from As(III) in rice samples (Fig. 4c). The automated configuration reduced manual phase manipulation and enabled selective preconcentration of As(V), with an LOD of 0.005 µg L⁻¹ and recoveries of 94.2–108.9%. The reported automated configuration is particularly relevant to routine analysis because it addresses one of the main limitations of conventional DLLME: operator-dependent phase manipulation. Automation can improve throughput and reproducibility, although the increased instrumental complexity may limit adoption in laboratories without compatible equipment.

Shirkhanloo *et al.* extended IL-DLLME to arsenic speciation in blood and urine using selective complexation and flow-injection atomic absorption detection. In the first study, the authors used a rapid and sensitive method for the speciation and ultra-trace determination of mercury and arsenic in blood samples by combining IL-DLLME and FI-HG-AAS / FI-CV-AAS. This method was validated using reference materials and spiked blood samples, with a recovery of over 97%. However, its application in food matrices was not evaluated [90]. Shirkhanloo *et al.*, in their second study [91] used this method to determine arsenic species in urine samples. APDC 1% was used as a complexing agent and selective extractability method for As(III). LOD 5 ng/L and EF ≈ 10 were obtained. The methods achieved low detection limits and satisfactory recoveries, and the blood method was validated using reference materials and spiked samples. However, the reported applications were primarily limited to biological matrices, and their transferability to complex food matrices remains uncertain. The comparison between the two studies also suggests that optimization of the complexing agent and extraction configuration can substantially influence sensitivity and enrichment.

Collectively, IL-based studies indicate that the main advantage of ionic-liquid DLLME lies in the tunability of the extraction phase rather than only improved extraction efficiency. Task-specific ILs enable selective complexation, while magnetic ILs and automated formats improve phase recovery and reproducibility, which is particularly beneficial for arsenic speciation in complex matrices. However, high viscosity, variable environmental profiles, cost, and procedural complexity remain important limitations. Moreover, the use of indirect approaches for As(V) determination in some studies may introduce additional uncertainty compared with direct speciation methods. Therefore, IL-DLLME offers high versatility, but further efforts are needed to improve its practicality for routine arsenic analysis.

4.3. Advanced DLLME Configurations Hyphenated with Chromatographic and Spectrometric Techniques

Beyond conventional batch extraction, recent DLLME research has increasingly incorporated engineering-oriented strategies to improve mass transfer, phase recovery, process control, and analytical throughput. These include ultrasound- and vortex-assisted dispersion, magnetic extraction phases, lab-in-syringe and flow-based configurations, automated phase manipulation, and integration with chromatographic or spectrometric platforms [29, 64, 77, 92–96]. Such developments demonstrate that DLLME is increasingly being treated as an intensified and potentially automatable sample-preparation process rather than solely as a laboratory-scale extraction procedure.

In the study by Javier Domínguez-Álvarez [96], capillary electrophoresis (CE) coupled to electrospray mass spectrometry (ESI(–)-MS) was used to determine organic and inorganic arsenic compounds including DMA, MMA, i-As(III) and i-As(V) in aqueous samples (Fig. 5a). Sample preparation was carried out in two approaches: 1) by DLLME for the determination of total inorganic arsenic and 2) by preconcentration by partial evaporation (about 50 times) for the measurement of individual species. DLLME was used to determine total inorganic arsenic in which, i-As(V) was reduced to As(III) by thiosulfate with a reported conversion of $105 \pm 9\%$ and after complex formation with APDC, the analyte was extracted into the organic phase (CCl_4) and then back-extracted into the aqueous phase using an aqueous ammonia solution. The detection limit for total inorganic arsenic in this method was reported to be $0.07 \mu\text{g/L}$. The results obtained were compared with reference ICP-MS methods and no significant difference was observed. The agreement with the reference ICP-MS results supports the analytical validity of the approach; however, the use of reduction and back-extraction steps adds procedural complexity. More importantly, DLLME in this configuration was used primarily for total inorganic arsenic, whereas individual species required a different preconcentration strategy, illustrating that DLLME does not necessarily provide a universal solution for simultaneous arsenic speciation. [96] In the study by Yue Yang *et al* [64], the LDS-DLLME-HPLC-ICP-MS method was used to analyze As(V), As(III), p-APAA, 4-HPAA, ROX and PAA species in aqueous samples. Optimization of the samples was performed at $\text{pH} = 10$ and after adding the optimized solvents using the response surface methodology (RSM) and $([\text{MTOA}]^+[\text{Cl}]^-)$ was used as the ion-pairing reagent, the LDS-DLLME extraction process was performed. Octanol was used as the extractant and methanol as the dispersant solvent. After centrifugation, the organic phase was injected into the HPLC-ICP-MS system. Separation of arsenic species was performed by reversed phase chromatography with a ZORBAX Eclipse plus C18 column. However, As(III) showed low extraction efficiency, and its chromatographic peak overlapped with that of As(V). This limitation is important because it demonstrates that coupling DLLME with a highly sensitive chromatographic detector does not automatically ensure reliable speciation. In this case, incomplete extraction of As(III) and chromatographic overlap with As(V) remained analytical challenges despite the low reported detection limits. The linear range for As(V) and the four phenylarsenic compounds was from 0.05 to $10 \mu\text{g/L}$. LOD was 0.001 to $0.039 \mu\text{g/L}$. The results showed that the LDS-DLLME-HPLC-ICP-MS method reduces matrix interferences and is effective for the determination of arsenic species in aqueous media [64]. These studies illustrate two complementary roles of DLLME in arsenic speciation: selective extraction of individual species and preconcentration before highly sensitive instrumental detection. The first strategy can simplify speciation when selective complex formation is sufficiently strong, whereas coupling DLLME with chromatographic separation provides more direct discrimination among arsenic species. The appropriate configuration therefore depends on whether the analytical priority is rapid targeted determination or comprehensive species-specific characterization.

In the study by Seeger *et al* [77], the DLLME-ICP-MS method was developed for simultaneous extraction and preconcentration of As and Cd in sugar samples. After screening of solvents, acetone was selected as the dispersing phase and carbon tetrachloride as the extraction solvent. Sample optimization at $\text{pH} = 2.0$ and mixture composition of APDC 1% + DDTC 1% was selected as the chelating agent. After three minutes of centrifugation, the precipitated phase was washed to reduce matrix interference and then evaporated, redissolved in $0.7 \text{ mol L}^{-1} \text{ HNO}_3$, and introduced into the ICP-MS system. Due to the sugar matrix, only standard addition (CAL3) enabled accurate quantification of both analytes, achieving excellent linearity over 0.25 – $10 \mu\text{g/L}$ for As and 0.25 – $5 \mu\text{g/L}$ for Cd. The need for standard addition

highlights the strong influence of the sugar matrix on quantitative accuracy. Validation was performed by comparing the results with the MIC (microwave-induced combustion) method and no significant differences were observed [77]. This finding indicates that high extraction efficiency alone is insufficient to ensure reliable quantification in complex food matrices and supports the use of matrix-matched validation when DLLME is applied to food analysis.

Elçi *et al* [92] used the DLLME method with a microsample injection system (MIS) coupled to ICP-MS for the speciation and determination of inorganic arsenic in natural water samples. The injection limitation of ICP-MS was solved with MIS and 90 µL was selected as the optimal volume. In the DLLME process, methanol as the dispersing solvent containing APDC (complexing agent) and CCl₄ as the extraction solvent was injected into the sample, resulting in the formation of a cloudy solution. After 2 min of centrifugation at 5000 rpm, the sedimented organic phase was collected and evaporated at room temperature to remove the effect of chloride interference (formation of ⁴⁰Ar³⁵Cl⁺) at m/z 75, then, the residue was dissolved in 0.1 mol L⁻¹ HNO₃ and introduced into the ICP-MS using the MIS. As(V) was reduced to As(III) by sodium thiosulfate and the amount of As(V) was calculated from the resulting difference. The speciation was determined from the direct measurement of As(III). Under optimal conditions, EF = 48, LOD = 0.0031 µg L⁻¹, limit of quantification (LOQ) = 0.0084 µg L⁻¹ and high recovery results of 95–108% and linear range of 0.0084–0.0800 µg L⁻¹ were obtained. The use of MIS addressed the limited injection volume of ICP-MS, while the additional evaporation step reduced chloride interference. However, the use of CCl₄ introduces an environmental and safety disadvantage, and the dependence on ICP-MS increases instrumental cost. Thus, the method provides excellent sensitivity but may be less attractive for routine laboratories where simpler and less hazardous extraction systems are preferred [92].

Shamsipur *et al* [93] used SPE–DLLME–SFO method with GFAAS for speciation and preconcentration of inorganic arsenic in water samples. In the SPE step, the As(III) sample is complexed with diethyldithiophosphate (DDTP) and concentrated on a C18 adsorbent and eluted with acetone (Fig. 5b). Undecanol-1 as the extraction solvent and water are injected into the resulting solution to perform the DLLME-SFO process. After the formation of a cloudy state, the floating organic phase is solidified with an ice bath and after melting, injected into GFAAS. Pd(NO₃)₂ and Mg(NO₃)₂ were used as chemical modifiers in GFAAS. The As(V) species was reduced to As(III) by KI and sodium thiosulfate; the As(V) amount is obtained from the difference. The values of LOD = 2.5 ng/L was obtained. The very low LOD demonstrates the sensitivity achievable by combining SPE, DLLME-SFO, and GFAAS. However, the sequential use of SPE, DLLME, phase solidification, and redox conversion also increases procedural complexity, which may limit throughput and reduce the practical advantage of microextraction for routine analysis.

Wei-Xun Wang *et al* [29], used the UA-DLLME–LC–MS method to measure very low levels of organic arsenic species (MMA, DMA and Roxarsone) in edible oils. Hexane was used as the dispersing solvent and Ammonium Formate buffer at pH = 7 was used as the extraction solvent, and the resulting mixture was ultrasonicated. After centrifugation, sedimented buffer phase was collected at the bottom of the tube and injected into the LC-ESI-MS system. The results showed that, because homogeneous dispersion of the aqueous extraction phase is difficult in the oil matrix, ultrasound-assisted DLLME achieved 1.5 to 2.7 times higher extraction efficiency for arsenic species (DMA and MMA) compared to shake-assisted methods, due to improved emulsification and more homogeneous dispersion of the extraction solvent in the oil phase (Fig. 5c) [29]. The 1.5- to 2.7-fold improvement over shake-assisted extraction provides direct evidence that dispersion strategy can be particularly important in viscous or non-aqueous food matrices. This finding supports ultrasound-assisted DLLME as a useful approach for edible oils, although the greater emulsification may also increase phase-separation demands and should therefore be evaluated together with reproducibility and sample throughput.

CE coupled to electrospray mass spectrometry was used for the determination of organic and inorganic arsenic compounds in water samples. [96] Speciation of As(III) and As(V) in water samples by graphite furnace atomic absorption spectrometry (GFAAS) after solid phase extraction combined with dispersive liquid–liquid microextraction

based on the solidification of floating organic drop [93]. Comparison of ultrasound-assisted DLLME and shake-assisted-DLLME for extraction efficiency [29].

Liang *et al.* [94] used DLLME with GFAAS detection to determine inorganic arsenic species in aqueous samples. In this method, APDC was added to the sample as a chelating agent and at pH = 3, As(III) species complexed with APDC, and a cloudy solution was formed by rapid injection of a mixture of CCl₄ as the extractant solvent and methanol as the dispersant solvent. Phase separation was performed for 5 min in a centrifuge at 3000 rpm, and the sedimented phase was injected into the GFAAS system for measurement. As(V) was reduced to As(III) by sodium thiosulfate and KI. The amount of As(V) was calculated from the difference between total inorganic arsenic and As(III). In this method, LOD = 36 ng L⁻¹ values, EF of 45 were obtained for As(III) [94]. The method demonstrates that conventional DLLME coupled with GFAAS can provide adequate sensitivity without requiring highly sophisticated instrumentation. Its relative simplicity may favor routine application; however, the use of CCl₄ and the reliance on difference calculations for As(V) determination remain important limitations.

Chen *et al.* [95] used the MDMSPE method in combination with DLLME and GFAAS detection for the speciation of As(III) and As(V) in food matrices (dairy products). In the first step, at pH = 5, As(V) species was selectively adsorbed on ZnFe₂O₄ magnetic nanotubes (ZFONTs) and after separation with a magnet, it was desorbed with 0.5 mol L⁻¹ HNO₃ during 1.5 min of sonication and directly measured by GFAAS. The remaining As(III) in the supernatant aqueous phase was complexed with APDC at the same pH and introduced into DLLME with 0.4 mL of methanol as the dispersive solvent and 50 µL of CCl₄ as the extraction solvent. After 2 min of sonication and 4 min of centrifugation at 5000 rpm, the organic phase was collected and diluted with ethanol, and 20 µL of the extract was injected for measurement. In dairy samples, artificial gastric juice was used avoid interconversion between As(III) and As(V) [95]. The dairy-matrix application illustrates the need for selective and sequential sample preparation when arsenic species coexist with strongly interfering components. The combination of magnetic separation and DLLME improved species discrimination, while the use of artificial gastric juice to minimize interconversion emphasizes the importance of preserving arsenic speciation during sample preparation. However, the multi-step workflow may limit routine throughput compared with simpler DLLME formats. Table 1 summarizes representative examples of arsenic determination using different DLLME methods.

Table 1
Some examples of Arsenic determination by different DLLME methods.

Analyte	Matrix	Method	Extraction phase	Linear range, LOD	Enrichment Factor	Recovery Rate (%)	Ref.
As(III), Cd(II), Hg(II), Pb(II)	Water and food samples	DLLME-A-US-V-GFAAS	Hydrophobic NADES 1-Menthol–salicylic acid (M:SA)	0.005–14 µg/L, 0.0043–0.0088 µg/L	120 – 112	108 – 93 (ER90–96)	[79]
As(III), As(V) +totalAs	Rice samples	DLLME-A-US-V-GFAAS	L-menthol:OA DES (1:1.5, molar ratio)	0.3–100 µg kg ⁻¹ , 0.1 µg kg ⁻¹	200	90-108.5	[80]
Total As	Water and food samples	PI-IL-DLLME-HG-AAS	Ionic liquid of 1-hexyl-3-methylimidazolium bis(trifluoromethylsulfonfyl	.062–1.25 µg/L, 0.016 µg/L	87.5	97 <	[82]
As(III)+total As	Water, urine and rice samples	IL-DLLME-ETAAS	TSIL + Triton X-114	0.2–15 µg/L As(III) ,0.01 ng/mL	200	90.8–104.3	[88]
As, Cd	Wine samples	UA-DLLME	TAC/LA DES	Cd: 0.50–8.0 µg/L, 0.080 µg/L As: 2.0–50 µg/L, 0.30 µg/L	NR	90.6–103.6	[81]
i-As(V), i-As(III), MMA, DMA	Water samples	DLLME–CE–ESI-MS	Partial Evaporation	As(III): 1.3 µg·L ⁻¹ , As(V): 1.5 µg·L ⁻¹	100	9 ± 105	[96]
As(III)	Honey samples	MIL-DLLME-ETAAS	MIL [P6,6,6,14]FeCl4	0.02–5.0 µg/L, 12 ngL ⁻¹	110	95.2–102	[78]
As(V)⊗ As(III)⊗ p-APAA⊗	Water samples	LDS-DLLME + HPLC-ICP-MS	octanol	005–10 µg/L, 0.001–0.039 µg/L	6.2–70.8	81.8–111.7	[64]
As(V)	Rice samples	MAS-LIS-DLLME +GFAAS	(IL) [C ₆ MIM][PF ₆]	0.04–5.0 µg/L, 0.005 µg/L	NR	94.2–108.9	[8]
As,Cd	Sugar samples	DLLME-ICP-MS	Carbon tetrachloride	As: 0.25–10 µg L ⁻¹ Cd: 0.25–5 µg L ⁻¹	5–10	89–107	[77]

DES: Deep Eutectic Solvent, **NADES**: natural deep eutectic solvent, **M:SA**: 1-menthol : salicylic acid, **TAC–LA**: Trioctylmethylammonium chloride – DL-lactic acid, **TSIL**: Task-Specific Ionic Liquid, **MIL**: Magnetic Ionic Liquid, [BMIM][PF₆]: 1-Butyl-3-methylimidazolium hexafluorophosphate, [C₆MIM][PF₆]: 1-Hexyl-3-ethylimidazolium hexafluorophosphate, **GFAAS**: Graphite Furnace Atomic Absorption Spectrometry, **FAAS**: Flame Atomic Absorption Spectrometry, **HG-AAS**: Hydride Generation Atomic Absorption Spectrometry, **ETAAS**: Electrothermal Atomic Absorption Spectrometry, **ICP-MS**: Inductively Coupled Plasma Mass Spectrometry, **FI-HG-AAS**: Flow Injection Hydride Generation AAS, **LOD**: Limit of Detection

Analyte	Matrix	Method	Extraction phase	Linear range, LOD	Enrichment Factor	Recovery Rate (%)	Ref.
As(III), As(V), Hg(II), R-Hg	blood samples	IL-DLLME-FI-HG/CV-AAS	hydrophobic + hydrophilic ILs [BMIM][PF ₆] ⁺ [BMIM][BF ₄]	As(III) 0.1 – 5.0 µg/L, As(III) 0.02 µg/L	~ 6.6	≥ 97	[90]
As(III), As(V)	Water samples	SPE-DLLME-SFO-GFAAS	1-Undecanol	10–100 ng/L, 2.5 ng/L	1520	95–103	[93]
As(III), As(V)	Water samples	DLLME-MIS-ICP-MS	Carbon tetrachloride	0.0031 µg/L	48	95–108	[92]
As(III), As(V)	Urine and whole blood samples	IL-DLLME-FI-HGAAS	APDC (as a chelating agent) (ILS)[BMIM][PF ₆]	0.02–10 µg/L, 5 ng/L	~ 10	96–107	[91]
As(III), As(V)	Natural water	DLLME-GFAAS	Carbon tetrachloride	0.1 – 10 µg/L, 36 ng/L	45	96–103	[94]
As(III), As(V)	Dairy products	MDMSPE-DLLME-GFAAS	Carbon tetrachloride	0.05-25 ng mL ⁻¹ , As(III): 1.3 pg/mL As(V): 2.0 pg/mL	As(III): 175 As(V): 163	90.8–105	[95]
DES: Deep Eutectic Solvent, NADES: natural deep eutectic solvent, M:SA: 1-menthol : salicylic acid, TAC-LA: Trioctylmethylammonium chloride – DL-lactic acid, TSIL: Task-Specific Ionic Liquid, MIL: Magnetic Ionic Liquid, [BMIM][PF₆]: 1-Butyl-3-methylimidazolium hexafluorophosphate, [C₆MIM][PF₆] 1-Hexyl-3-ethylimidazolium hexafluorophosphate, GFAAS: Graphite Furnace Atomic Absorption Spectrometry, FAAS: Flame Atomic Absorption Spectrometry, HG-AAS: Hydride Generation Atomic Absorption Spectrometry, ETAAS: Electrothermal Atomic Absorption Spectrometry, ICP-MS: Inductively Coupled Plasma Mass Spectrometry, FI-HG-AAS: Flow Injection Hydride Generation AAS, LOD: Limit of Detection							

A comparison of the studies summarized in Table 1 indicates that no single DLLME configuration consistently provides superior analytical performance across all arsenic applications. Instead, method efficiency is strongly dependent on the target species, sample matrix, and detection platform. The lowest detection limits are generally achieved using highly sensitive detectors such as ICP-MS or GFAAS, often combined with additional preconcentration or selective separation steps [8, 92, 93, 95]. In contrast, simpler DLLME-AAS approaches can provide sufficient sensitivity for routine food monitoring with lower instrumental requirements [79, 80, 82, 88]. The extraction medium also determines the balance between analytical performance and practicality: DES/NADES systems offer low volatility and simple preparation, whereas task-specific and magnetic ILs provide enhanced selectivity and improved phase manipulation. However, reported recoveries and enrichment factors should be interpreted alongside precision, matrix effects, calibration strategy, and validation procedures. For instance, the use of standard addition for sugar samples [88] demonstrates that high extraction efficiency alone may not fully overcome matrix-related quantification challenges. Therefore, the optimal DLLME strategy should be selected based on analytical requirements, matrix complexity, available instrumentation, and operational feasibility rather than recovery or EF values alone.

Beyond analytical sensitivity, the practical robustness of DLLME methods remains a critical consideration. Although many studies report excellent recoveries and low detection limits under optimized laboratory conditions, fewer

investigations systematically evaluate inter-day precision, inter-laboratory reproducibility, solvent stability, method ruggedness, or performance across different batches of complex matrices. These aspects are particularly important for routine arsenic monitoring because variations in solvent composition, pH, water content, extraction time, and phase separation can influence extraction efficiency. Separation-based approaches, including CE-ESI-MS, HPLC-ICP-MS, and LC-MS, provide direct identification and quantification of multiple arsenic species, whereas nonchromatographic methods commonly rely on selective complexation, redox conversion, sequential extraction, or difference calculations [29, 64, 77, 92–96]. Matrix-specific strategies, such as ultrasound-assisted dispersion for edible oils [29] and sequential magnetic separation for dairy samples [95], highlight the importance of tailored sample preparation. Automated and magnetically assisted DLLME formats may improve reproducibility and reduce operator-dependent variability, while conventional manual DLLME remains attractive because of its simplicity and low cost. Consequently, low LOD and high EF alone should not be considered sufficient indicators of routine applicability; comprehensive validation using matrix-matched calibration, certified reference materials, and ideally interlaboratory studies is required before emerging DLLME methods can be adopted for routine or surveillance arsenic analysis.

4.4. Comparative analysis of green solvent vs. ionic liquid-based DLLME for arsenic extraction

Both green solvent-based DLLME and ionic liquid-based DLLME focus on dispersive liquid-liquid microextraction for arsenic determination, yet they diverge significantly in their choice of extraction media, sample matrices, and analytical priorities. The primary distinction lies in the solvent systems: the first approach emphasizes NADES and DES, while the second centers on ILs and MILs. In terms of green chemistry, the DES-based approach offers potential sustainability advantages, particularly through low volatility and reduced use of conventional chlorinated extraction solvents. For instance, one study employs a natural DES composed of 1-menthol and salicylic acid, which acts as both complexing medium and an extractant, reducing the need for a separate complexing reagent [79]. Similarly, another work uses 1-menthol with different carboxylic acids. Conversely, the IL-based approach relies on task-specific ILs (e.g., [BMIM][PF₆]) and MILs like [P6,6,6,14]FeCl₄, which, despite their efficiency and tunability, raise concerns about toxicity and biodegradability [78]. Low volatility alone, however, does not establish the environmental safety of either solvent class. Some IL-based systems also offer unique advantages in selectivity and magnetic handling, as demonstrated by research using a magnet for phase separation, simplifying the process [78].

From a practical and environmental perspective, neither solvent class can be considered universally superior. DES/NADES systems are generally easier and less costly to prepare, offering potential advantages for scalability; however, variations in component purity, composition, water content, and viscosity may affect reproducibility. In contrast, ILs, especially task-specific and magnetic ILs, provide greater control over extraction selectivity and phase manipulation, but often involve higher preparation complexity and cost. Moreover, low volatility alone does not ensure environmental safety, as toxicity, biodegradability, persistence, and synthesis requirements depend on the specific solvent structure. Therefore, DES/NADES may be preferable for simple and cost-effective applications, whereas ILs may be advantageous when enhanced selectivity or automation is required. However, comprehensive life-cycle, cost, and recyclability evaluations for arsenic DLLME remain limited [16, 17, 87].

The apparent differences in extraction performance among solvent systems should also be interpreted cautiously because the reported EFs and detection limits were obtained under different sample matrices, arsenic species, complexing agents, detection platforms, and optimization conditions. Consequently, a higher EF reported for one solvent system cannot be interpreted as intrinsic superiority over another solvent without controlling these variables. In practice, solvent systems tend to outperform others when their physicochemical properties are better matched to the arsenic–complex chemistry and the matrix composition. For example, selective ILs may provide an advantage when

species-specific complexation is required, whereas DES/NADES systems may be more attractive when solvent preparation, low volatility, and reduced reliance on conventional organic solvents are prioritized [28, 63, 87].

Regarding speciation strategies, both approaches address As(III)/As(V) differentiation, but through different mechanisms. The DES-based method used for rice analysis uses acidic pH control and gentle digestion to prevent species transformation. The IL-based approach employs more diverse strategies: one method uses a TSIL that selectively extracts As(III) over As(V), while another utilizes ammonium molybdate for selective As(V) chelation at pH 1.5. Finally, the matrices investigated in the reviewed studies also differ. The DES-based approach focuses on water, food, rice, and wine samples using mainly AAS-based detection whereas the IL-based approach has been applied to food, aqueous, and biological matrices, including honey, rice, blood, and urine. One study also performed simultaneous speciation of mercury and arsenic in blood [80, 82, 88].

Overall, the available evidence does not support a universal preference for either IL- or DES/NADES-based DLLME systems. Method selection requires balancing sensitivity, selectivity, environmental impact, cost, reproducibility, and operational simplicity. DES/NADES-based DLLME is attractive because of its simple preparation and reduced reliance on conventional organic solvents, whereas IL-based systems may offer advantages for selective complexation, magnetic phase manipulation, and automated extraction. However, method performance is influenced by matrix complexity, target arsenic species, solvent properties, and phase recovery, while standardization remains challenging because solvent composition and extraction conditions affect reproducibility. Therefore, DLLME systems should be selected according to the intended application and evaluated using both analytical performance and practical considerations rather than detection limits alone.

From a regulatory perspective, the analytical sensitivity achieved by many reviewed DLLME methods is sufficient for trace-level monitoring. The WHO guideline value for arsenic in drinking water is 10 µg L⁻¹, while the FDA action level for inorganic arsenic in apple juice is 10 µg L⁻¹ (10 ppb) [4]. Several of the reviewed DLLME methods report detection limits well below these concentrations, indicating adequate sensitivity for regulatory monitoring; however, compliance assessment also requires validated accuracy, precision, matrix-specific recovery, and reliable speciation where inorganic arsenic is the regulatory target. Table 2 provides a comparison of green solvent vs. ionic liquid-based DLLME for arsenic extraction.

Table 2
Comparison of green-solvent- and ionic-liquid-based DLLME methods for arsenic extraction

Parameter	Green Solvent-DLLME	Ionic Liquid-DLLME
Primary Solvents	DES, NADES (e.g., M:SA, L-menthol/octanoic acid, TAC-LA)	TSIL, MIL (e.g., [P _{6/6/6/14}]FeCl ₃ , [BMIM][PF ₆], [C ₆ MIM][PF ₆])
Green Profile	High (natural, biodegradable)	Moderate (efficient but potentially toxic)
Speciation	Limited (pH control, total As)	Advanced (selective As(III) or As(V) extraction)
Detection Method	GFAAS, FAAS, HG-AAS	ETAAS, GFAAS, ICP-MS, FI-HG-AAS
Main Advantage	Simple, low-cost, rapid, minimal solvent consumption, eco-friendly	Ultra-sensitive, selective, magnetic options, suitable for complex biological matrices
Main Limitation	Moderate sensitivity, limited speciation control, requires centrifugation	Higher cost, viscosity issues (requires back-extraction or dilution), some use toxic solvents (CCl ₄)

DES: Deep Eutectic Solvent, **NADES:** Natural deep eutectic solvent, **M:SA:** 1-menthol : salicylic acid, **TAC-LA:** Trioctylmethylammonium chloride – DL-lactic acid, **TSIL:** Task-Specific Ionic Liquid, **MIL:** Magnetic Ionic Liquid, **[BMIM]**

[PF₆]: 1-Butyl-3-methylimidazolium hexafluorophosphate, **[C₆MIM][PF₆]** 1-Hexyl-3-ethylimidazolium hexafluorophosphate, **GFAAS**: Graphite Furnace Atomic Absorption Spectrometry, **FAAS**: Flame Atomic Absorption Spectrometry, **HG-AAS**: Hydride Generation Atomic Absorption Spectrometry, **ETAAS**: Electrothermal Atomic Absorption Spectrometry, **ICP-MS**: Inductively Coupled Plasma Mass Spectrometry.

5. Conclusion and future perspectives

The accurate determination of arsenic, particularly its highly toxic inorganic species As(III) and As(V), remains an important analytical challenge due to their toxicity at trace concentrations and the complexity of real sample matrices. As demonstrated throughout this review, DLLME has evolved into an efficient and versatile sample preparation platform for arsenic analysis, providing significant advantages over conventional extraction approaches, including reduced solvent consumption, rapid phase dispersion, operational simplicity, and high enrichment factors. The combination of DLLME with advanced detection techniques such as GFAAS and ICP-MS has enabled sensitive and reliable arsenic determination in diverse matrices, including environmental waters, food products, and biological samples. Recent developments involving ionic liquids, deep eutectic solvents, natural deep eutectic solvents, and hybrid extraction strategies have further expanded the potential of DLLME by improving selectivity, analytical performance, and environmental compatibility.

Despite these advances, several challenges continue to limit the widespread application of DLLME for routine arsenic monitoring. Matrix-dependent extraction behavior, potential interconversion among arsenic species, solvent-related variability, and insufficient methodological harmonization remain critical issues requiring systematic investigation. Future validation studies should therefore focus on representative and challenging matrices, particularly food samples such as grains, seafood, vegetables, dairy products, and processed foods. Such evaluations should include matrix-matched recovery experiments, assessment of species stability during sample preparation, estimation of measurement uncertainty, and the use of certified reference materials whenever available. Establishing standardized protocols and interlaboratory validation approaches will be essential to ensure reproducibility and comparability of DLLME-based analytical data across laboratories.

Future developments in DLLME should move beyond laboratory-scale optimization toward integrated, automated, and high-throughput analytical platforms. Microfluidic systems, lab-on-a-chip devices, continuous-flow extraction, magnetic phase-assisted approaches, and lab-in-syringe configurations represent promising strategies for improving extraction control, phase separation, solvent handling, and compatibility with automated workflows. At the same time, the development of advanced task-specific green solvents should continue, with particular attention to solvent stability, preparation reproducibility, toxicity, detector compatibility, and the feasibility of solvent recovery and reuse. Data-driven approaches, including artificial intelligence and machine learning, may further facilitate the optimization of multiple DLLME parameters; however, their practical value will depend on the robustness and independent validation of the developed models.

Overall, the future success of DLLME for arsenic monitoring will depend on the integration of analytical reliability with engineering innovation and environmental sustainability. Priorities should include matrix-specific validation, standardized analytical procedures, greener and more selective extraction phases, and automated extraction architectures capable of supporting routine analysis. Such advances will be critical for translating DLLME from a highly efficient laboratory technique into a reliable and widely applicable platform for arsenic surveillance in food, environmental, and biological samples.

Declarations

Ethics approval and consent to participate:

This article does not contain any studies with human participants or animals performed by any of the authors.

Conflict of Interest:

The authors declare that they have no conflict of interest.

Funding:

This research received no funding.

Author Contribution

A. Moharrami: Management and coordination responsibility for the research activity planning and execution; E. Pourbasheer: Ideas; Writing Original Draft, and Conceptualization; L. Farhoudi: Writing Original Draft & Handling Revisions; F. Fathi: Oversight and leadership responsibility for the research activity planning and execution, Writing - Critical review.

Acknowledgement:

Authors are grateful from University of Mohaghegh Ardabili, Ardabil, Iran and Ardabil University of Medical Sciences, Ardabil, Iran.

Availability of data and material:

"Not Applicable"

References

1. Genchi G, Lauria G, Catalano A, Carocci A, Sinicropi MS (2022) Arsenic: a review on a great health issue worldwide. *Appl Sci* 12(12):6184
2. Campbell KM, Nordstrom DK (2014) Arsenic speciation and sorption in natural environments. *Rev Mineral Geochem* 79(1):185–216
3. Hall AH (2002) Chronic arsenic poisoning. *Toxicol Lett* 128(1–3):69–72
4. Organization WH Guidelines for drinking-water quality, World health organization 2006
5. Raju NJ (2022) Arsenic in the geo-environment: A review of sources, geochemical processes, toxicity and removal technologies. *Environ Res* 203:111782
6. Rekhi H, Rani S, Sharma N, Malik AK (2017) A Review on Recent Applications of High-Performance Liquid Chromatography in Metal Determination and Speciation Analysis. *Crit Rev Anal Chem* 47(6):524–537
7. Lata S, Ansari NG (2024) Analytical techniques for heavy metal analysis. *Heavy Metal Contamination in the Environment*, CRC, pp 180–202

8. Wang X, Xu G, Chen P, Sun Y, Yao X, Lv Y, Guo W, Wang G (2018) Fully-automated magnetic stirring-assisted lab-in-syringe dispersive liquid–liquid microextraction for the determination of arsenic species in rice samples. *RSC Adv* 8(30):16858–16865
9. Rezaee M, Assadi Y, Milani Hosseini MR, Aghaee E, Ahmadi F, Berijani S (2006) Determination of organic compounds in water using dispersive liquid-liquid microextraction. *J Chromatogr A* 1116(1–2):1–9
10. J.M.J.L.-p.e. Kokosa, Dispersive liquid-liquid microextraction, (2020) 473–497
11. Rastegarzadeh S, Kalantaripour M, Pourreza N (2023) Development of a fluorescent probe for cefazolin detection based on solvent-based de-emulsification dispersive liquid–liquid microextraction of silver nanoparticles. *Anal Sci* 39(3):257–266
12. Tay KSJ, See HH (2025) Recent Advances in Dispersive Liquid-Liquid Microextraction for Pharmaceutical Analysis. *Crit Rev Anal Chem* 55(3):559–580
13. Sorouraddin SM, Parvizzad K, Farajzadeh MA (2023) Development of a pH-induced dispersive solid-phase extraction method using folic acid combined with dispersive liquid–liquid microextraction: application in the extraction of Cu(II) and Pb(II) ions from water and fruit juice samples. *Anal Sci* 39(1):23–31
14. Salah ARM (2025) Green Solvents in Sustainable Organic Synthesis: Ionic Liquids and Deep Eutectic Systems
15. Foorginezhad S, Ji XJCT, Policy E (2025) Immobilized ionic liquids/deep eutectic solvents in carbon capture: current progress and future potential. 27(11):5991–6007
16. Quintana AA, Sztapka AM, Santos Ebinuma VC, Agatemor C (2022) Enabling Sustainable Chemistry with Ionic Liquids and Deep Eutectic Solvents: A Fad or the Future? *Angewandte Chemie (International ed. in English)* 61(37) e202205609
17. Magina S, Barros-Timmons A, Ventura SPM, Evtuguin DV (2021) Evaluating the hazardous impact of ionic liquids - Challenges and opportunities. *J Hazard Mater* 412:125215
18. Viñas P, Campillo N, López-García I, Hernández-Córdoba M (2014) Dispersive liquid-liquid microextraction in food analysis. A critical review. *Anal Bioanal Chem* 406(8):2067–2099
19. Llorente-Mirandes T, Rubio R, López-Sánchez JF (2017) Inorganic Arsenic Determination in Food: A Review of Analytical Proposals and Quality Assessment Over the Last Six Years. *Appl Spectrosc* 71(1):25–69
20. Jagirani MS, Soylak M (2023) Arsenic speciation by using emerging sample preparation techniques: a review. *Turk J Chem* 47(5):991–1006
21. Notardonato I, Avino PJS (2024) Dispersive liquid–liquid micro extraction: An analytical technique undergoing continuous evolution and development—A review of the last 5 years. 11(7):203
22. Patel KS, Pandey PK, Martin-Ramos P, Corns WT, Varol S, Bhattacharya P, Zhu Y (2023) A review on arsenic in the environment: contamination, mobility, sources, and exposure. *RSC Adv* 13(13):8803–8821
23. Lorenzo-Parodi N, Kaziur W, Stojanović N, Jochmann MA, Schmidt TC (2019) Solventless microextraction techniques for water analysis. *TRAC Trends Anal Chem* 113:321–331
24. Piri-Moghadam H, Alam MN, Pawliszyn J (2017) Review of geometries and coating materials in solid phase microextraction: Opportunities, limitations, and future perspectives. *Anal Chim Acta* 984:42–65
25. Smith RM (2003) Before the injection—modern methods of sample preparation for separation techniques. *J Chromatogr A* 1000(1–2):3–27
26. Soares da Silva Burato J, Vargas Medina DA, de Toffoli AL (2020) Vasconcelos Soares Maciel, F. Mauro Lancas, Recent advances and trends in miniaturized sample preparation techniques. *J Sep Sci* 43(1):202–225
27. Poole C, Mester Z, Miró M, Pedersen-Bjergaard S, Pawliszyn J (2016) Glossary of terms used in extraction (IUPAC Recommendations 2016). *Pure Appl Chem* 88(5):517–558

28. Rezaee M, Yamini Y, Faraji M (2010) Evolution of dispersive liquid-liquid microextraction method. *J Chromatogr A* 1217(16):2342–2357
29. Wang W-X, Yang T-J, Li Z-G, Jong T-T, Lee M-R (2011) A novel method of ultrasound-assisted dispersive liquid-liquid microextraction coupled to liquid chromatography-mass spectrometry for the determination of trace organoarsenic compounds in edible oil. *Anal Chim Acta* 690(2):221–227
30. Yu X, Pawliszyn J (2000) Speciation of alkyllead and inorganic lead by derivatization with deuterium-labeled sodium tetraethylborate and SPME-GC/MS. *Anal Chem* 72(8):1788–1792
31. Arthur CL, Pawliszyn J (1990) Solid phase microextraction with thermal desorption using fused silica optical fibers. *Anal Chem* 62(19):2145–2148
32. Sevgen S, Kara G, Kir AS, Sahin A, Boyaci E (2025) A critical review of bioanalytical and clinical applications of solid phase microextraction. *J Pharm Biomed Anal* 252:116487
33. Hou J, Hu C, Li H, Liu H, Xiang Y, Wu G, Li Y (2025) Nanomaterial-based magnetic solid-phase extraction in pharmaceutical and biomedical analysis. *J Pharm Biomed Anal* 253:116543
34. Jiao C, Li X, Zhang Z, Wu Y, Ren X, Pawliszyn J, Zeng J (2025) Field-Deployable Immuno-Solid-Phase Microextraction Coupled with Photothermal Imaging for Rapid Pathogen Surveillance in Environmental and Clinical Matrices. *Anal Chem* 97(37):20602–20610
35. Grafit A, Muller D, Kimchi S, Avissar YY (2018) Development of a Solid-phase microextraction (SPME) Fiber protector and its application in flammable liquid residues analysis. *Forensic Sci Int* 292:138–147
36. Kokosa JM, Przyjazny A (2022) Green microextraction methodologies for sample preparations. *Green Anal Chem* 3:100023
37. Li P, Zhang X-q, Chen Y-j, Lian H-z, Hu XJAM (2014) A sequential solid phase microextraction system coupled with inductively coupled plasma mass spectrometry for speciation of inorganic arsenic. *6(12):4205–4211*
38. Nisyriou S, Zacharis CK (2025) Microextraction-based techniques for the determination of beta-blockers in biological fluids: A review. *Separations* 12(1):14
39. Rutkowska M, Płotka-Wasyłka J, Sajid M, Andruch V (2019) Liquid-phase microextraction: A review of reviews. *Microchem J* 149:103989
40. Sarafraz-Yazdi A, Amiri A (2010) Liquid-phase microextraction. *TRAC Trends Anal Chem* 29(1):1–14
41. Câmara JS, Perestrelo R, Olayanju B, Berenguer CV, Kabir A, Pereira JA (2022) Overview of different modes and applications of liquid phase-based microextraction techniques. *Processes* 10(7):1347
42. de la Calle I, Pena-Pereira F, Lavilla I, Bendicho C (2016) Liquid-phase microextraction combined with graphite furnace atomic absorption spectrometry: A review. *Anal Chim Acta* 936:12–39
43. Pedersen-Bjergaard S, Rasmussen KE (2008) Liquid-phase microextraction with porous hollow fibers, a miniaturized and highly flexible format for liquid-liquid extraction. *J Chromatogr A* 1184(1–2):132–142
44. Rezaee M, Assadi Y, Hosseini M-RM, Aghae E, Ahmadi F, Berijani S (2006) Determination of organic compounds in water using dispersive liquid-liquid microextraction. *J Chromatogr A* 1116(1–2):1–9
45. Zuloaga O, Olivares M, Navarro P, Vallejo A, Prieto A (2015) Dispersive liquid-liquid microextraction: Trends in the analysis of biological samples. *Bioanalysis* 7(17):2211–2225
46. Grau J, Azorin C, Benede JL, Chisvert A, Salvador A (2022) Use of green alternative solvents in dispersive liquid-liquid microextraction: A review. *J Sep Sci* 45(1):210–222
47. Leong MI, Fuh MR, Huang SD (2014) Beyond dispersive liquid-liquid microextraction. *J Chromatogr A* 1335:2–14
48. Namera A, Saito T (2013) Recent advances in unique sample preparation techniques for bioanalysis. *Bioanalysis* 5(8):915–932

49. Zgoła-Grześkowiak A, Grześkowiak T (2011) Dispersive liquid-liquid microextraction. *TRAC Trends Anal Chem* 30(9):1382–1399
50. Zarei AR, Gholamian F (2011) Development of a dispersive liquid–liquid microextraction method for spectrophotometric determination of barbituric acid in pharmaceutical formulation and biological samples. *Anal Biochem* 412(2):224–228
51. Saraji M, Khalili Boroujeni M, Hajialiakbari AA, Bidgoli (2011) Comparison of dispersive liquid–liquid microextraction and hollow fiber liquid–liquid–liquid microextraction for the determination of fentanyl, alfentanil, and sufentanil in water and biological fluids by high-performance liquid chromatography. *Anal Bioanal Chem* 400(7):2149–2158
52. Fernández P, González C, Pena MT, Carro AM, Lorenzo RA (2013) A rapid ultrasound-assisted dispersive liquid–liquid microextraction followed by ultra-performance liquid chromatography for the simultaneous determination of seven benzodiazepines in human plasma samples. *Anal Chim Acta* 767:88–96
53. Ranjbari E, Golbabanezhad-Azizi A-A, Hadjmohammadi MR (2012) Preconcentration of trace amounts of methadone in human urine, plasma, saliva and sweat samples using dispersive liquid–liquid microextraction followed by high performance liquid chromatography. *Talanta* 94:116–122
54. Soltani S, Ramezani AM, Soltani N, Jouyban A (2012) Analysis of losartan and carvedilol in urine and plasma samples using a dispersive liquid–liquid microextraction isocratic HPLC–UV method. *Bioanalysis* 4(23):2805–2821
55. Simões RA, Barth T, Bonato PS (2013) Enantioselective analysis of ranolazine and desmethyl ranolazine in microsomal medium using dispersive liquid–liquid microextraction and LC–MS/MS. *Bioanalysis* 5(2):171–183
56. Rezaee M, Yamini Y, Faraji M (2010) Evolution of dispersive liquid–liquid microextraction method. *J Chromatogr A* 1217(16):2342–2357
57. Eldin A, Ismaiel O, Hassan W, Shalaby A (2016) Green analytical chemistry: Opportunities for pharmaceutical quality control. *J Anal Chem* 71(9):861–871
58. Lili L, Xu H, Song D, Cui Y, Hu S, Zhang G (2010) Analysis of volatile aldehyde biomarkers in human blood by derivatization and dispersive liquid–liquid microextraction based on solidification of floating organic droplet method by high performance liquid chromatography. *J Chromatogr A* 1217(16):2365–2370
59. Ranjbari E, Biparva P, Hadjmohammadi MR (2012) Utilization of inverted dispersive liquid–liquid microextraction followed by HPLC–UV as a sensitive and efficient method for the extraction and determination of quercetin in honey and biological samples. *Talanta* 89:117–123
60. Moradi M, Yamini Y, Baheri T (2011) Analysis of abuse drugs in urine using surfactant-assisted dispersive liquid–liquid microextraction. *J Sep Sci* 34(14):1722–1729
61. Gałuszka A, Migaszewski Z, Namieśnik J (2013) The 12 principles of green analytical chemistry and the SIGNIFICANCE mnemonic of green analytical practices. *TRAC Trends Anal Chem* 50:78–84
62. Sajid M, Plotka-Wasyłka J (2022) Green analytical chemistry metrics: A review. *Talanta* 238(Pt 2):123046
63. Notardonato I, Avino P (2024) Dispersive liquid–liquid micro extraction: an analytical technique undergoing continuous evolution and development—a review of the last 5 years. *Separations* 11(7):203
64. Yang Y, Liu Z, Chen H, Li S (2019) Low-density solvent-based dispersive liquid-liquid microextraction followed by HPLC–ICP–MS for speciation analysis of phenylarsenics in lake water. *Int J Environ Anal Chem* 99(1):87–100
65. Hatami M, Karimnia E, Farhadi K (2013) Determination of salmeterol in dried blood spot using an ionic liquid based dispersive liquid–liquid microextraction coupled with HPLC. *J Pharm Biomed Anal* 85:283–287
66. Xiao C, Tang M, Li J, Yin C-r, Xiang G, Xu L (2013) Determination of sildenafil, vardenafil and aildenafil in human plasma by dispersive liquid–liquid microextraction-back extraction based on ionic liquid and high performance

liquid chromatography-ultraviolet detection. *J Chromatogr B* 931:111–116

67. Anthemidis AN, Ioannou K-IG (2012) Sequential injection ionic liquid dispersive liquid–liquid microextraction for thallium preconcentration and determination with flame atomic absorption spectrometry. *Anal Bioanal Chem* 404(3):685–691
68. Berton P, Wuilloud RG (2010) Highly selective ionic liquid-based microextraction method for sensitive trace cobalt determination in environmental and biological samples. *Anal Chim Acta* 662(2):155–162
69. Zhang J, Li M, Li L, Li Y, Peng B, Zhang S, Gao H, Zhou W (2012) Investigation of the ultrasound effect and target analyte selectivity of dispersive liquid–liquid microextraction and its application to a quinocetone pharmacokinetic study. *J Chromatogr A* 1268:1–8
70. He L, Zhang K, Wang C, Luo X, Zhang S (2011) Effective indirect enrichment and determination of nitrite ion in water and biological samples using ionic liquid-dispersive liquid–liquid microextraction combined with high-performance liquid chromatography. *J Chromatogr A* 1218(23):3595–3600
71. Nageswara Rao R, Mastan Vali R, Vara Prasada Rao A (2012) Determination of rifaximin in rat serum by ionic liquid based dispersive liquid–liquid microextraction combined with RP-HPLC. *J Sep Sci* 35(15):1945–1952
72. Yan H, Wang H (2013) Recent development and applications of dispersive liquid–liquid microextraction. *J Chromatogr A* 1295:1–15
73. Mostafa A, Shaaban H, Alqarni AM, Alghamdi M, Alsultan S, Al-Saeed JS, Alsaba S, AlMoslem A, Alshehry Y, Ahmad R (2022) Vortex-assisted dispersive liquid–liquid microextraction using thymol based natural deep eutectic solvent for trace analysis of sulfonamides in water samples: assessment of the greenness profile using AGREE metric, GAPI and analytical eco-scale. *Microchem J* 183:107976
74. Shaaban H (2023) Sustainable dispersive liquid–liquid microextraction method utilizing a natural deep eutectic solvent for determination of chloramphenicol in honey: assessment of the environmental impact of the developed method. *RSC Adv* 13(8):5058–5069
75. Xia Y, Zhi X, Wang X, Chen M, Cheng J (2012) Ultrasound-enhanced surfactant-assisted dispersive liquid–liquid microextraction and high-performance liquid chromatography for determination of ketoconazole and econazole nitrate in human blood. *Anal Bioanal Chem* 402(3):1241–1247
76. Mudiam MKR, Ratnasekhar C (2013) Ultra sound assisted one step rapid derivatization and dispersive liquid–liquid microextraction followed by gas chromatography–mass spectrometric determination of amino acids in complex matrices. *J Chromatogr A* 1291:10–18
77. Seeger TS, Vecchia PD, Machado EQ, Reinke K, Mesko MF, Duarte FA (2017) Feasibility of DLLME for the Extraction and Preconcentration of As and Cd in Sugar for Further Determination by ICP-MS. *J Braz Chem Soc* 28(9):1691–1697
78. Fiorentini EF, Canizo BV, Wuilloud RG (2019) Determination of As in honey samples by magnetic ionic liquid-based dispersive liquid-liquid microextraction and electrothermal atomic absorption spectrometry. *Talanta* 198:146–153
79. Mafakheri N, Shamsipur M, Babajani N (2024) Development of a dispersive liquid–liquid microextraction procedure based on a natural deep eutectic solvent for ligand-less preconcentration and determination of heavy metals from water and food samples. *Microchem J* 199:110010
80. Fattahi N, Ahmed HL, Nematifar Z, Hashemi N, Moradi M, Soltani S, Akbari S (2024) Acid-based deep eutectic solvents followed by GFAAS for the speciation of As (III), As (V), total inorganic arsenic and total arsenic in rice samples. *Food Addit Contaminants: Part A* 41(6):617–628
81. Ji Y, Zhao M, Li A, Zhao L (2021) Hydrophobic deep eutectic solvent-based ultrasonic-assisted dispersive liquid-liquid microextraction for preconcentration and determination of trace cadmium and arsenic in wine samples. *Microchem J* 164:105974

82. Ali J, Tuzen M, Kazi TG (2017) Determination of total arsenic in water and food samples by pressure-induced ionic liquid-based dispersive liquid-liquid microextraction method prior to analysis by hydride generation atomic absorption spectrometry
83. Cruz-Vera M, Lucena R, Cárdenas S, Valcárcel M (2009) One-step in-syringe ionic liquid-based dispersive liquid-liquid microextraction. *J Chromatogr A* 1216(37):6459–6465
84. Safdarian M, Hashemi P, Naderlou M (2012) In-line cold column trapping of organic phase in dispersive liquid-liquid microextraction: Enrichment and determination of curcumin in human serum. *J Chromatogr A* 1244:14–19
85. Hashemi Z, Ranjbari F, Ranc V, Fathi F (2026) Multiplexed biosensing: A review of surface plasmon resonance platforms for biomarker analysis. *Talanta* 304:129564
86. Saad SM, Aling NA, Miskam M, Saaïd M, Mohamad Zain NN, Kamaruzaman S, Raoov M, Mohamad Hanapi NS, Wan Ibrahim WN, Yahaya N (2020) Magnetic nanoparticles assisted dispersive liquid-liquid microextraction of chloramphenicol in water samples. *Royal Soc open Sci* 7(4):200143
87. Smith EL, Abbott AP, Ryder KS (2014) Deep eutectic solvents (DESS) and their applications. *Chem Rev* 114(21):11060–11082
88. Ashouri V, Adib K, Fariman GA, Ganjali MR, Rahimi-Nasrabadi M (2021) Determination of arsenic species using functionalized ionic liquid by in situ dispersive liquid-liquid microextraction followed by atomic absorption spectrometry. *Food Chem* 349:129115
89. Ashouri V, Adib K, Fariman GA, Ganjali MR, Rahimi-Nasrabadi M (2021) Determination of arsenic species using functionalized ionic liquid by in situ dispersive liquid-liquid microextraction followed by atomic absorption spectrometry. *Food Chem* 349:129115
90. Shirkhanloo H, Khaligh A, Mousavi HZ, Eskandari MM, Miran-Beigi AA (2015) Ultra-trace arsenic and mercury speciation and determination in blood samples by ionic liquid-based dispersive liquid-liquid microextraction combined with flow injection-hydride generation/cold vapor atomic absorption spectroscopy. *Chem Pap* 69(6):779–790
91. Shirkhanloo H, Rouhollahi A, Mousavi HZ (2011) Ultra-trace arsenic determination in urine and whole blood samples by flow injection-hydride generation atomic absorption spectrometry after preconcentration and speciation based on dispersive liquid-liquid microextraction. *Bull Korean Chem Soc* 32(11):3923–3927
92. Elci L, Elci A, Berg TA, Tyson JF (2013) Dispersive liquid-liquid microextraction and microsample injection system coupled with inductively coupled plasma-mass spectrometry for inorganic arsenic speciation in natural waters. *Int J Environ Anal Chem* 93(10):1065–1073
93. Shamsipur M, Fattahi N, Assadi Y, Sadeghi M, Sharafi K (2014) Speciation of As (III) and As (V) in water samples by graphite furnace atomic absorption spectrometry after solid phase extraction combined with dispersive liquid-liquid microextraction based on the solidification of floating organic drop. *Talanta* 130:26–32
94. Liang P, Peng L, Yan P (2009) Speciation of As (III) and As (V) in water samples by dispersive liquid-liquid microextraction separation and determination by graphite furnace atomic absorption spectrometry. *Microchim Acta* 166(1):47–52
95. Chen S, Liu Y, Wang C, Yan J, Lu D (2022) Speciation of As (III) and As (V) in food by magnetic dispersive microsolid phase extraction with dispersive liquid-liquid microextraction with graphite furnace atomic absorption spectrometry (GFAAS) detection. *Anal Lett* 55(2):269–280
96. Domínguez-Álvarez J (2020) Capillary electrophoresis coupled to electrospray mass spectrometry for the determination of organic and inorganic arsenic compounds in water samples. *Talanta* 212:120803

Figures

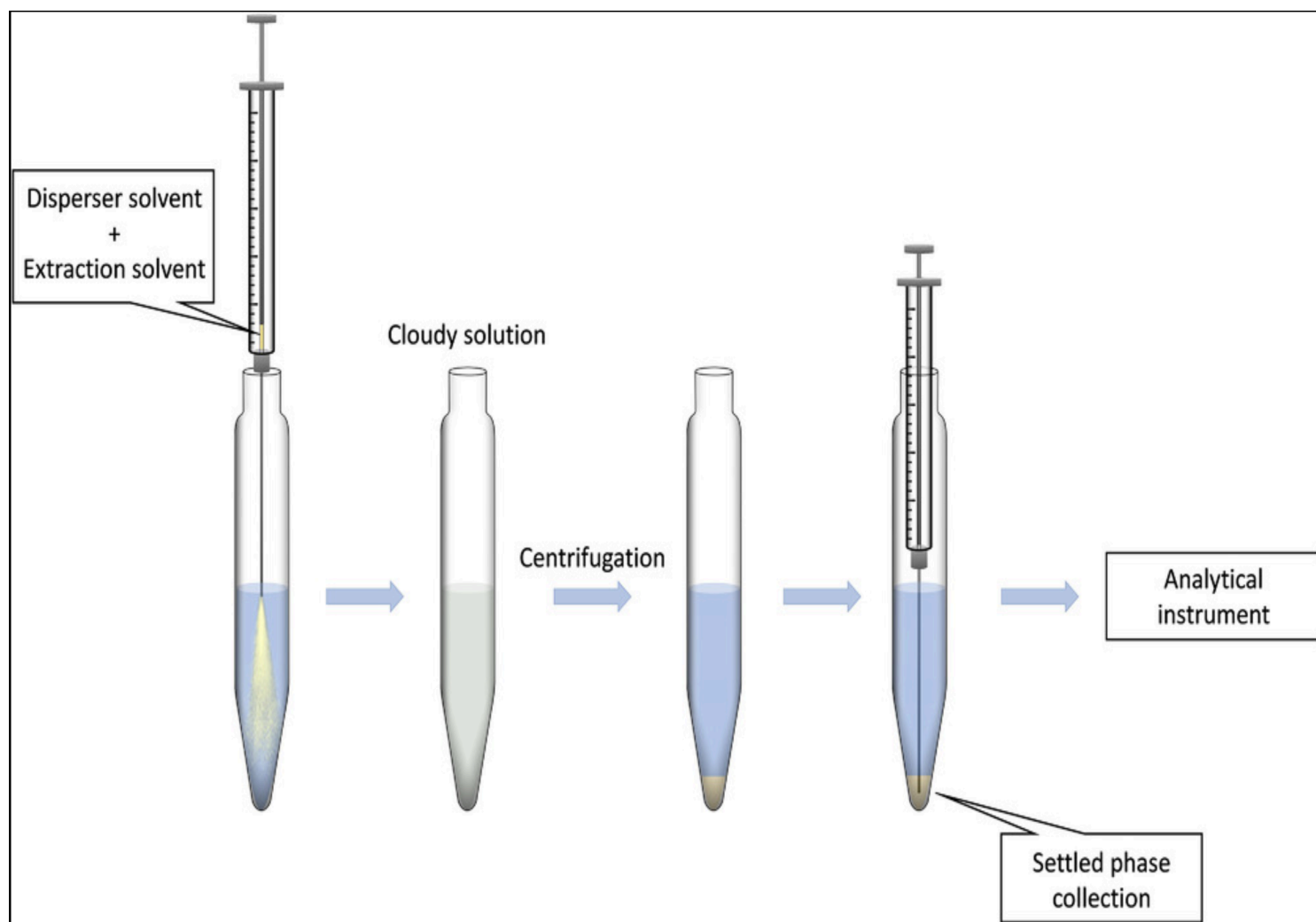


Figure 1

The general scheme of the traditional dispersive liquid-liquid microextraction (DLLME) procedure. Reprinted with permission from [46].

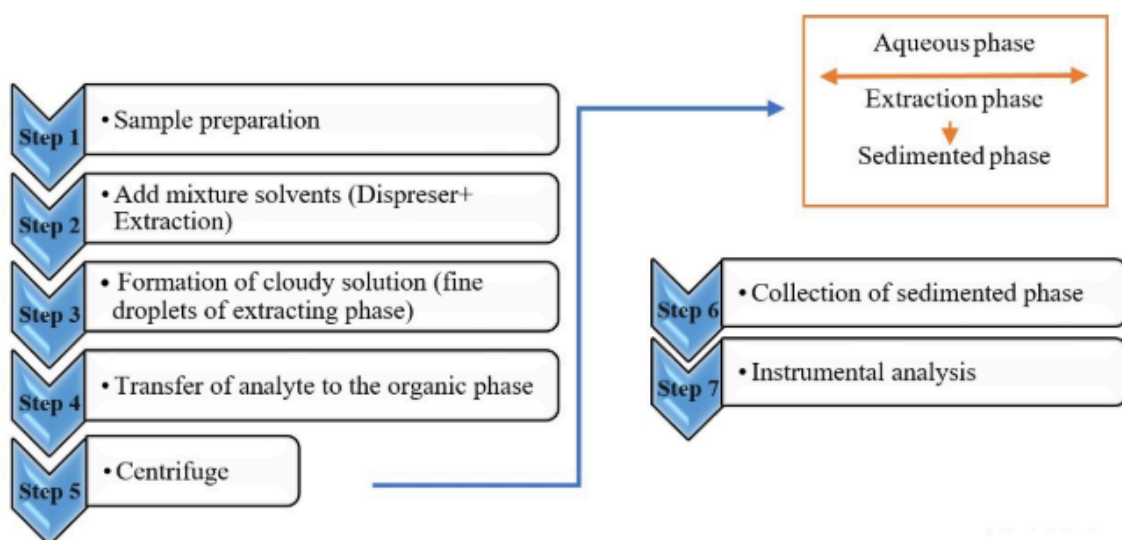


Figure 2

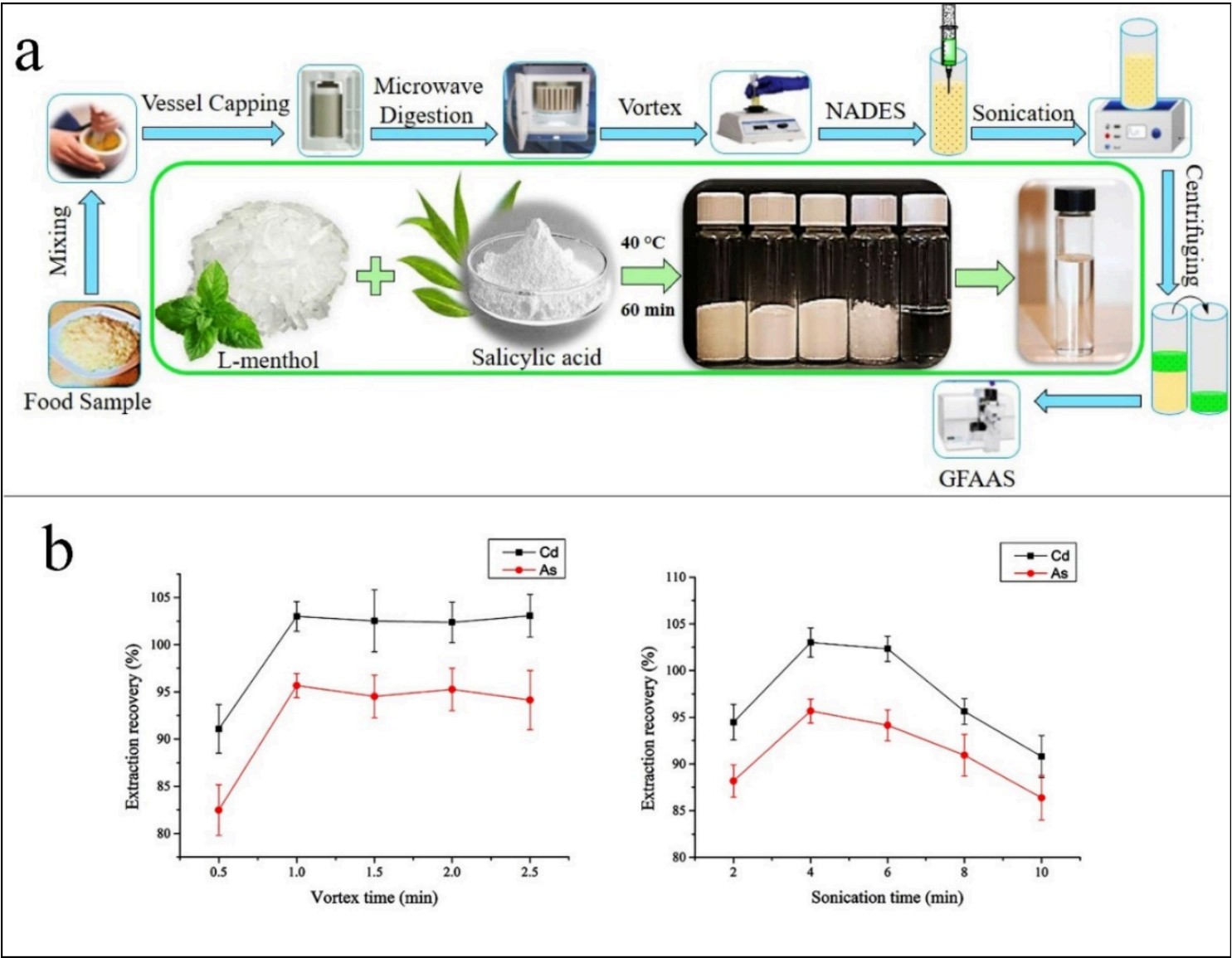


Figure 3

Schematic image of the **a)** for M:SA NADES synthesis and extraction process. Reprinted with permission from [79] **b)** Effect of vortex time and sonication time organic solvents in extraction recovery. Reprinted with permission from [81].

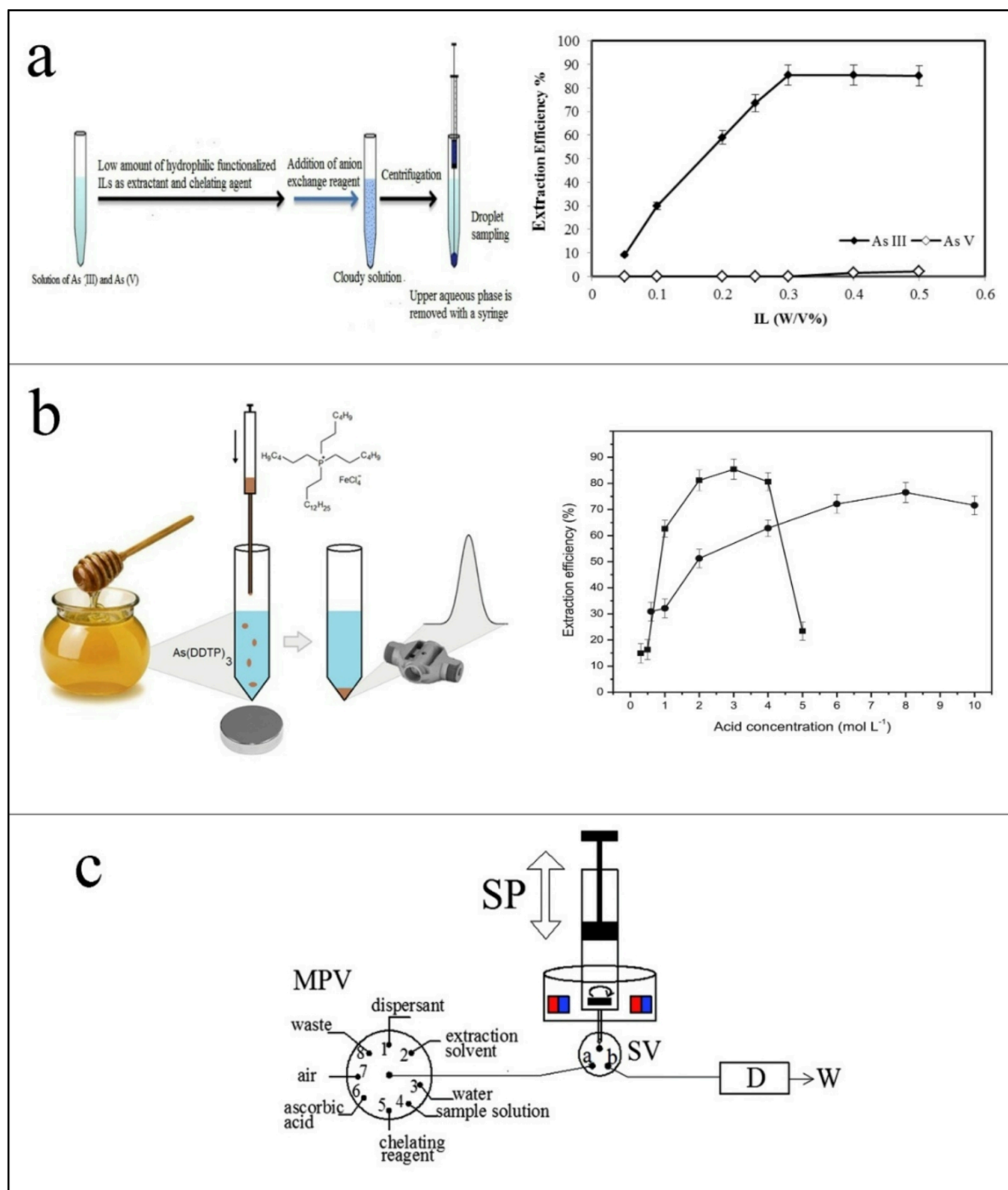


Figure 4

a) The schematic of the determination arsenic using functionalized ionic liquid by in situ DLLME followed by atomic absorption spectrometry & the effect of amount TSILs in extraction efficacy. Reprinted with permission from [88]. **b)** The schematic of the preconcentration of As traces in honey samples by DLLME with the use of MIL and direct determination by ETAAS and effect of acid concentration on As extraction efficiency of the MIL-DLLME method. Hydrochloric acid (■) and Sulfuric acid (●). Reprinted with permission from [78]. **c)** The schematic of the MAS-LIS-DLLME

system. D, detection system; SP, syringe pump; SV, three-way solenoid valve; W, waste; MPV, multiposition valve. Reprinted with permission from [8].

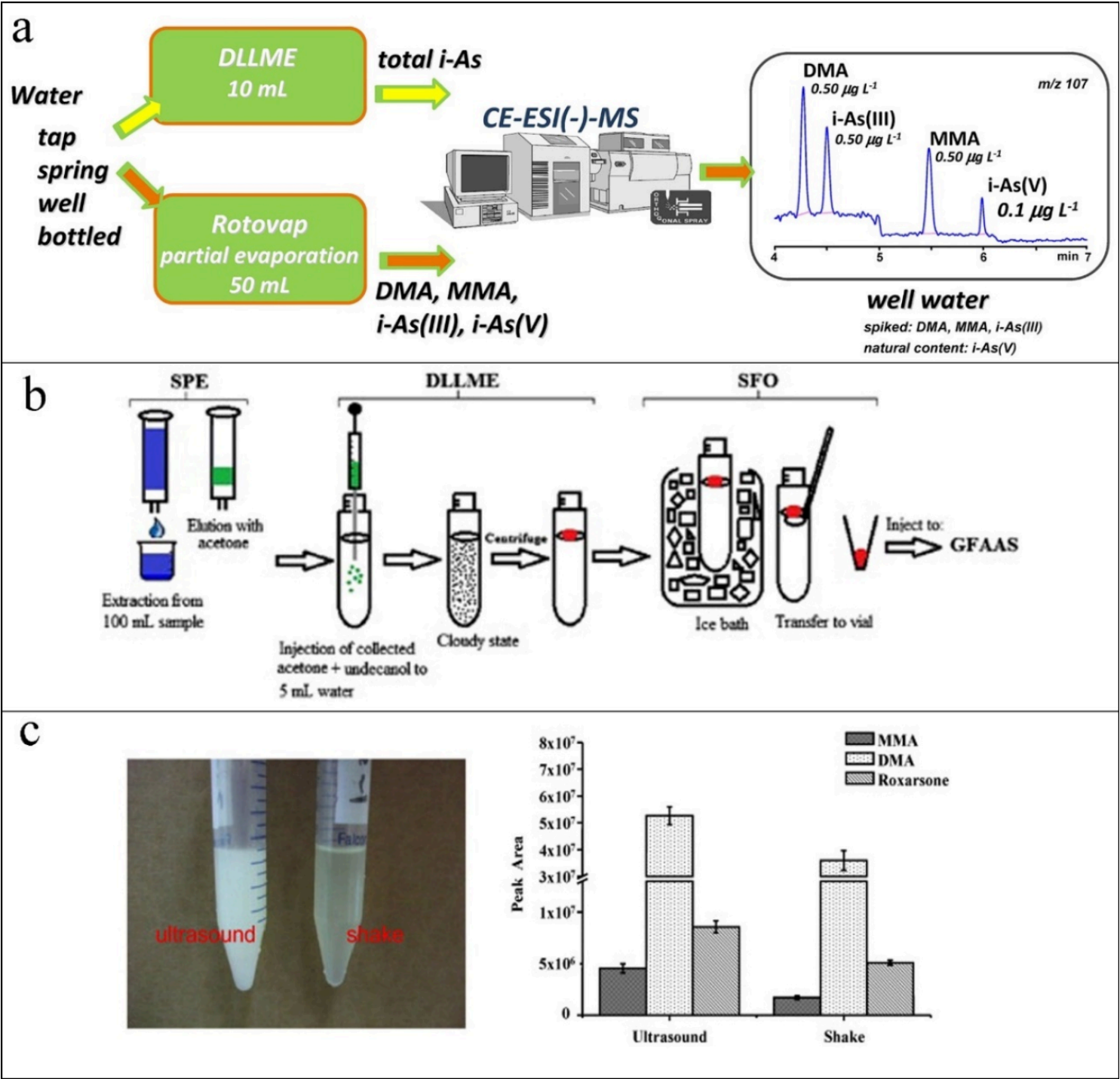


Figure 5

The schematic of **a)** CE-ESI-MS for determination of organic and inorganic arsenic compounds [96] **b)**speciation of As in water samples by GFAAS after SPE combined with DLLME [93] **c)**Comparison of ultrasound-assisted DLLME with shake-assisted-DLLME [29].

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [floatimage1.jpeg](#)