



A REVIEW ON EXTRACTION SOLVENTS IN THE DISPERSIVE LIQUID-LIQUID MICROEXTRACTION

(Sebuah Ulasan Terhadap Pelarut Pengekstrakan dalam Pengekstrakan Mikro Cecair-Cecair Serakan)

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Abstract

Dispersive liquid-liquid microextraction (DLLME) is a novel sample preparation technique that has higher level of extraction efficiency by means of relying on microvolumes of solvents. It has gained considerable attention from researchers owing to several advantages such as its simplicity, shorter extraction time, lower cost and higher enrichment factor. In conventional DLLME, chlorinated solvents are widely used as the extraction solvents. Notwithstanding, most of these solvents are reportedly toxic and environmentally-unfriendly. Many related studies in recent years have focused on the use of nontoxic or low toxic extraction solvents and better practical procedures, which have helped improve the extraction efficiency. The aim of this review is to discuss the development of low toxic extraction solvent used recently in the DLLME. The possible improvement of extraction solvent from the green analytical chemistry perspectives is also discussed.

Keywords: extraction solvents, dispersive liquid-liquid microextraction, green analytical chemistry

Abstrak

Pengekstrakan mikro cecair-cecair serakan (DLLME) merupakan teknik penyediaan sampel novel yang mempunyai lebih tinggi kecekapan pengekstrakan dengan menggunakan mikroliter pelarut. Teknik ini telah mendapat perhatian daripada penyelidik kerana beberapa kelebihan seperti ringkas, masa pengekstrakan yang lebih pendek, kos yang lebih rendah dan faktor pengayaan yang lebih tinggi. Dalam DLLME konvensional, pelarut berklorin digunakan secara meluas sebagai pelarut pengekstrakan. Namun, kebanyakan pelarut ini dilaporkan toksik dan tidak mesra alam. Dalam tahun kebelakangan ini, banyak kajian yang berkaitan telah fokus kepada penggunaan pelarut pengekstrakan yang tidak bertoksik atau rendah toksik dan praktikal prosedur yang lebih baik telah meningkatkan kecekapan pengekstrakan. Tujuan kajian ini adalah untuk membincangkan perkembangan pelarut pengekstrakan rendah toksik yang digunakan dalam DLLME terkini. Penambahbaikan pelarut pengekstrakan dari perspektif kimia analisis hijau juga dibincangkan.

Kata kunci: pelarut pengekstrakan, pengekstrakan mikro cecair-cecair serakan, kimia analitik hijau

Introduction

The step involving the sample preparation is the most important one in analytical process as most of the samples are not capable of being injected directly into the analytical instruments for analysis. The main aim of sample pre-treatment is to both clean up and enrich the analytes of interest from the sample, and execute the analytes into forms that are considered suitable for instrument of analytical measurement [1].

As far as sample pre-treatment and separation are concerned, traditional methods for sample preparation such as liquid-liquid extraction (LLE) and solid-phase extraction (SPE) have mostly been used for many years. Nonetheless, some weaknesses were associated with these traditional methods such as the usage of large amount of organic solvents, which are toxic and environmentally-unfriendly, time-consuming and labour-intensive [2]. For this reason, many researchers have attempted towards better development of sample pre-treatment step that involves relatively lower solvent consumption, economic and rapid.

In the year of 2006, the dispersive liquid-liquid microextraction (DLLME), which is now one of the powerful sample pre-treatment techniques, was invented by Rezaee and his co-workers [3]. The advantages of DLLME method are inter alia simplicity, short extraction time, low cost, high enrichment factor, and high-recovery. As a result of such favourable characteristics, it has drawn considerable attention from analytical chemists. A significant number of research articles relating to DLLME having been published since its introduction bears testimony to the attention it has gained. Originally, the DLLME was established for preparation from water samples. Subsequently, it was developed for other matrices including food [4], soil [5], cosmetic products [6] and biological samples [7]. In relation to the types of analytes, they are not only limited to numerous organic compounds, but inorganic analytes were also successfully extracted from the sample using DLLME [8].

A comprehensive review of literature has pointed to many excellent reviews discussing the development and applications of DLLME [9-12]. Some of the reviews were found to summarise various strategies for improving dispersion liquid-liquid microextraction [13, 14] and application with different analytical instruments [15, 16]. Notwithstanding such reviews, none of the reviews meticulously discussed the different types of extraction solvents used in DLLME. The present study therefore fills such a gap in the literature. Specifically, it presents the review of extraction solvents used in the conventional DLLME and modified DLLME. In addition, future trend of extraction solvents used in DLLME is also discussed from the perspective of green analytical chemistry.

Principle of DLLME

It has to be noted that the DLLME is based on the ternary solvent system, in which miniaturized volume of solvents are used. In a typical procedure, extraction solvent is mostly used to extract the analytes of interest from the samples. In the event of promoting the rapid transfer of analytes of interest from the samples, dispersion solvent is used. Upon injecting the mixture of extraction solvent and dispersion solvent into the sample solution, microdroplets of extraction solvent is rapidly dispersed into the aqueous sample and a cloudy solution is formed. As a large surface area is formed between extraction solvent and the aqueous sample in the cloudy solution, the transfer of analytes of interest to extraction phase is therefore rapid. As the extraction equilibrium is rapidly achieved, the extraction time is therefore relatively shorter. The mixture is then separated by centrifugation and the extraction solvent containing analytes of interest is collected by means of using microsyringe. This is followed by the identification of analytes in the extraction solvent, which can be performed using analytical instrument [3].

In order to obtain high extraction efficiency, several parameters have to be looked into. In such processes, the selection of appropriate extraction solvent is considered very important. In the DLLME, extraction solvent should have the following requirements: the extraction solvent is required to have low solubility with water and miscible with the dispersive solvent. In addition, it is also required to have the potential for extracting analytes of interest and suitable chromatographic behaviour. Besides, the extraction solvent must have different densities with the water so that it can be phase separated. In the conventional DLLME, the extraction solvent usually have relatively higher density than water. As a result, it is able to form sedimented phase in the bottom of the tube after phase separation [3]. Chlorinated solvents such as chloroform, chlorobenzene, carbon tetrachloride, and tetrachloroethylene are commonly selected as extraction solvent as they fulfil such requirements [17]. These chlorinated solvents show the advantages in DLLME such as producing high enrichment factor, short extraction time, ease of operation and high

sensitivity [18-20]. However, these solvents are highly toxic. Most of them have low lethal dose and carcinogenic [21].

Extraction solvents used in DLLME

With the aim of minimizing the drawbacks associated with using chlorinated solvents, other types of solvents including heavy-density, low density and ionic liquid were introduced. Table 1 shows a summary of these extraction solvents. Heavy-density solvents including brominated and iodinated solvents have been introduced. The results revealed that extraction efficiencies of these solvents were comparable and higher than using the chlorinated solvents. Good sensitivity with relatively lower limit of detection was also obtained [22-26]. Compared to chlorinated solvents, some of the brominated and iodinated solvents have lower toxicity [22, 26, 27]. In addition, higher recovery efficiency with lower relative standard deviation can also be achieved by means of using only 1-methyl-3-bromobutane as extraction solvent without having to rely on dispersive solvent, which is capable of reducing the use of organic solvent [28]. Nevertheless, not all brominated and iodinated solvents have lower toxicity. In this regard, some solvents such as 2-iodopropane [29] and 1, 2-dibromoethane [21] are as toxic as chlorinated solvents. Furthermore, there are only limited number of brominated or iodinated solvents with low toxicity [30].

Table 1. Summary of advantages and disadvantages of heavy-density, low density and ionic liquid

Type of Extraction Solvent	Advantages	Disadvantages
Heavy-density solvent	High extraction recovery Some solvents can extract analytes without dispersive solvents	Limited choice of solvent. Some solvents are as toxic as chlorinated solvents.
Low-density solvent	Higher extraction recovery Lower toxicity extraction solvent Choices of solvent are broader than heavy density solvent Extract is cleaner Some methods do not required centrifugation	Some require specially designed tools to collect organic phase It can be difficult to differentiate the interphase between the floating organic phase and the aqueous phase Choice of solvents for DLLME-SFO is limited
Ionic liquid	Lower melting point, lower vapor pressure, higher thermal stability and good solubility in organic and inorganic compounds Higher extraction recovery and sensitivity Choices of solvent are broader than low-density and high-density solvents	Not suitable for analysis with GC Toxicity to environment is not well understood

*DLLME-SFO: Dispersive liquid liquid microextraction based on solidification of floating drop
GC: gas chromatography

Low-density solvents were used recently as extraction solvent in DLLME. The choice of lower-density organic solvent is more popular than high-density solvents [31]. The low-density solvents such as n-hexane [30], toluene [32], 2-ethyl-1-hexanol [31], 1-heptanol [34], 1-octanol [35], isooctane [36], and 1-dodecanol [37] and 1-undecanol [38] have been used as extraction solvents in low-density solvents (LDS) DLLME. In addition, they have been proven to possess low LOD and LOQ, high recovery and higher linearity. Unlike in the conventional DLLME, the low-density solvents do not sediment at the bottom of the tubes as the low-density extraction solvent floats on the top of the aqueous phase after phase separation is carried out. The floated extraction solvent is much easier to collect and the extract is cleaner since any matrix components will be sedimented at the bottom of the extraction vessel [4]. Therefore, a good chromatogram can be easily achieved. It is also worthy of note that some methods do

not require centrifugation for phase separation and thus extraction time is relatively shorter. Low-density extraction solvent droplets float on the surface of the aqueous phase after the samples and solvents are mixed and shaken [35]. Then, the floating extraction phase was collected by means of employing different techniques. This method is useful for preventing analytes from being degraded by excessive centrifugation or ultrasonic energy [39]. However, to draw off the floating solvents, some required the use of specially designed devices [40].

Leong & Huang [41] and Xu et al. [42] developed the new DLLME method based on solidification of a floating organic drop (DLLME-SFO). Specifically, the mixture of low-density extraction solvent and dispersive solvent are injected into aqueous samples and as a result, a cloudy solution is formed. The mixture is then centrifuged and placed in the ice bath to solidify the floated extraction solvent. Following the solidification stage, the solidified solvent is taken by spatula and melted prior to sending it for analysis. In DLLME-SFO, extraction solvent must fulfil several requirements, namely low melting point below room temperature, low solubility in water, lower density than water, and high affinity towards analytes of interest and compatible for instrument analysis. Good extraction efficiencies such as low LOQ, LOD and high recovery were successfully obtained by means of using the DLLME-SFO [37, 43-45]. In comparison with the conventional DLLME, this method uses low-toxic extraction solvents. The drawbacks of this method are limited to the solvent selected, which must have low melting point of below room temperature. This method may not be considered as suitable for use if the laboratory is not air conditioned and located in warm climate [13]. Apart from that, spatula is used for transfer solidified solvent, which may result in the loss of analytes. Guíñez and his teammates [45] tried using Hamilton syringe to collect floating or solidified extraction solvent but the efficiency was low since the interphase between the floating organic phase and the aqueous phase was rather hard to differentiate. Besides, Nojavan and his colleagues [46] indicated that high-density solvents had revealed better performance and reproducibility than lower-density solvents in extraction of seven basic pharmaceutical compounds.

Room temperature ionic liquids or ionic liquids (ILs, not all ILs are room temperature ILs.) are one of the extraction solvents that have been widely discussed in the literature. ILs are the salts that are made of substituted organic cation with an organic or inorganic anion that exist in liquid state at room temperature [47]. They possess outstanding physical properties such as low melting point, low vapour pressure, high thermal stability and good solubility in organic and inorganic compounds. As ILs are non-flammable and non-volatile, they are therefore classified as green solvent [9, 48]. Quite a number of studies related to IL-DLLME and a few review pieces have been published since IL-DLLME was first introduced in the year of 2008 [9, 47, 48]. Based on cation segment, ILs can be categorized into four types, which are alkylammonium-based, dialkylimidazolium-based, phosphonium-based and N-alkylpyridinium-based [49]. Most of the works have been found to have used dialkylimidazolium-based ILs as extraction solvents. In this regard, Hu et al. [50] employed three different dialkylimidazolium-based ILs as extraction solvent for determination of urinary 3-hydroxybenzo [a] pyrene. The recovery was found to be much higher than chlorinated solvents. IL-DLLME revealed excellent sensitivity with relatively lower LOD within a range of pg/mL [50, 51] or ng/mL [52-54] was obtained. Moreover, the types of ionic liquid are broader as many kinds of cations and anions can be combined [55]. By means of changing the structure and interaction of ions, their chemical and physical properties can vary and thus, ILs can be designed to exhibit target-selective [47]. Nonetheless, ILs have several drawbacks. Low volatility of ILs make them not suitable for gas chromatography. Hence, most IL-DLLME reported in related studies were coupled with high performance liquid chromatography (HPLC). However, ILs will be retained in the column or injector, which can result in distorted chromatograms [56, 57]. In order to overcome such problems, special design of injectors are required such as the combination of programmed temperature vaporization injector and thermal desorption unit, which can directly inject the analytes and prevent the entering of ILs into GC system [51].

Future trend based on green analytical chemistry

As a result of the limitless and almost never-ending human activities, there have been growing concerns about the potential negative influences on the environment. The side effects of the environment must be taken into consideration in the chemistry activities. The ideas of “green analytical chemistry” was originally proposed in the year of 2008 [58]. Green analytical chemistry can be applied in many forms, one of the segments is the reduction of the amount and toxicity of the solvents and reagent used. Thus, high toxicity solvents especially halogenated solvents have to be avoided from being used in sample preparation. Some interesting alternatives such as ILs, agro-

solvents and lipid structures could be greener solution for replacement of high toxicity solvents [59]. Nevertheless, their strengths, weaknesses, threats to the environment and compatibility to the analytical instruments should be explicitly identified due to the fact that their detrimental effects are not well understood.

The concept of three Rs (reduce, replace, recycle) has often been mentioned in the green analytical chemistry [60]. The reuse of chemicals or materials in process with minimum interferences from extraction efficiency is considered necessary. For instance, Wang and colleagues [61] applied such concepts in their attempts to extract three endocrine disrupting compounds from food packaging. Specifically, IL used as extraction solvent, was successfully recovered by modifying the pH and it can be reused three times without any significant loss of extraction efficiencies. In addition, Sheikhan and Shirafkan [62] also successfully separated ILs from analytes by changing pH and reused ILs at least four times. These methods are capable of minimizing the cost of extraction solvents and the environment and safety issues. In addition, recycle of ILs can help prevent the problem of ILs remaining in the column of HPLC. Hence, future works may have to zoom in on identifying ways to recycle and reuse the solvents.

One of the growing trends in analytical chemistry is the automation of extraction and analytical procedures. Automation is capable of minimizing the operator risks, waste generation, energy and solvent consumption [59]. In this regard, many innovative ideas for automated DLLME including automated agitation-assisted demulsification DLLME [63], effervescence assisted DLLME [64] and DLLME-switchable polarity dispersive solvent (DLLME-SPDS) [65] have over the years been introduced. The former method used agitation for the phase separation and the whole automated process requires only a total of 160 μL of solvents. The latter two approaches are automated and they have also excluded the negative impact of dispersive solvents on the solubility of analytes in aqueous sample. However, DLLME-SPDS has some limitations; it is only able to extract analytes in neutral and alkaline medium. Other automated techniques including flow, batch, flow-batch and in-syringe modes were also reported in the literature [66].

Conclusion

DLLME is considered as a powerful sample preparation for extraction of analytes from aqueous samples. It is worthy of note that the selection of appropriate extraction solvent is a critical parameter with the aim of acquiring a good extraction efficiency. Several types of extraction solvents such as the heavy-density solvents, low-density solvent and ionic liquids are discussed in the paper. In addition, the future trend for development of extraction solvents based on green chemistry was also intensively discussed. Overall, the exploitation of new extraction solvents and improvement of extraction performance in DLLME based on green analytical chemistry can be the main focus in future.

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