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Review

# Evolution of dispersive liquid–liquid microextraction method

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ABSTRACT

Dispersive liquid–liquid microextraction (DLLME) has become a very popular environmentally benign sample-preparation technique, because it is fast, inexpensive, easy to operate with a high enrichment factor and consumes low volume of organic solvent. DLLME is a modified solvent extraction method in which acceptor-to-donor phase ratio is greatly reduced compared with other methods. In this review, in order to encourage further development of DLLME, its combination with different analytical techniques such as gas chromatography (GC), high-performance liquid chromatography (HPLC), inductively coupled plasma-optical emission spectrometry (ICP-OES) and electrothermal atomic absorption spectrometry (ET AAS) will be discussed. Also, its applications in conjunction with different extraction techniques such as solid-phase extraction (SPE), solidification of floating organic drop (SFO) and supercritical fluid extraction (SFE) are summarized. This review focuses on the extra steps in sample preparation for application of DLLME in different matrixes such as food, biological fluids and solid samples. Further, the recent developments in DLLME are presented. DLLME does have some limitations, which will also be discussed in detail. Finally, an outlook on the future of the technique will be given.



**Contents**



*Abbreviations:* DLLME, dispersive liquid-liquid microextraction; SFO, solidification of floating organic drop; GC, gas chromatography; HPLC, high-performance liquid chromatography; ET-AAS, electrothermal atomic absorption spectrometry; SPE, solid phase extraction; SFE, supercritical fluid extraction; LLE, liquid-liquid extraction; SPME, solid-phase microextraction; LPME, liquid-phase microextraction; SDME, single-drop microextraction; HF-LPME, hollow fiber liquid-phase microextraction; CPE, cloud point extraction; HLLE, homogeneous liquid-liquid extraction; USAEME, ultrasound-assisted emulsification-microextraction; US, ultrasound; PF, preconcentration factor; ER, extraction recovery; PAHs, polycyclic aromatic hydrocarbons; OPPs, organophosphorus pesticides; ECD, electron capture detection; FPD, flame photometric detection; CBs, chlorobenzenes; THMs, trihalomethanes; MS, mass spectrometric detection; LODs, limits of detections; PFBAY, pentafluorobenzaldehyde; CPs, chlorophenols; OSPs, organosulphur pesticides; NPD, nitrogen-phosphorus detection; FID, flame ionization detection; $NaBEt_4$, sodium tetraethylborate; TCS, triclosan; MTCS, methyltriclosan; MTBSTFA, N-methyl-N(tert-butyldimethylsilyl) trifluoroacetamide; DAD, diode array detection; VWD, variable wavelength detection; UHPLC, ultra-high pressure liquid chromatography; TUV, tunable ultraviolet detection; TCC, triclocarban; M-TCS, methyl-triclosan; OAD, orthogonal array design; CCD, central composite design; EDTA, ethylendiaminetetraacetic acid; DMF, N, N-dimethyl formamide; FAAS, flame atomic absorption spectrometry; FO-LADS, fiber optic–linear array detection spectrophotometer; PAN, 1-(2-pyridylazol)-2-naphthol; ICP-OES, inductively coupled plasma-optical emission spectrometry; Sm, samarium; Eu, europium; Gd, gadolinium; Dy, dysprosium; LC-ES-MS/MS, liquid chromatography–electrospray-tandem mass spectrometry; 7-amino FM2, 7-aminoflunitrazepam; LOQs, limits of quantification; LC-APCI-MS-MS, liquid chromatography–atmospheric-pressure chemical ionization tandem mass spectrometry; CAP, chloramphenicol; THA, thiamphenicol; FLD, fluorescence detection; PCBs, polychlorinated biphenyls; MUSE, miniaturized ultrasonic solvent extraction; RTILS, room temperature ionic liquids; IL-DLLME, ionic liquid based dispersive liquid-liquid microextraction; PDLLME, partitioned dispersive liquid–liquid micro extraction; TCE, tetrachloroethylene; THF, tetrahydrofuran; PUHs, phenylurea herbicides; IBMK, isobutyl methyl ketone; IL-based USA-DLLME, ionic liquid-based ultrasound-assisted dispersive liquid-liquid microextraction; DLLME-LSC, DLLME technique with little solvent consumption; TBME, tert-butyl methyl ether; OCPs, organchlorine pesticides; PBDEs, polybrominated diphenyl ethers; DSPE, dispersive solid–phase extraction; HOCs, halogenated organic compounds; CE, capillary electrophoresis.

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## 1. Introduction

In spite of substantial technological advances in analytical field, most instruments cannot directly handle complex sample matrixes yet. As a result, a sample-preparation step is commonly involved before instrumental analysis. The main aim of sample preparation is to clean up and concentrate the analytes of interest, while rendering them in a form that is compatible with the analytical system. Liquid–liquid extraction (LLE), based on the transfer of analyte from the aqueous sample to a water-immiscible solvent, is widely employed for sample preparation. Nevertheless, some shortcomings such as emulsion formation, use of large sample volumes and toxic organic solvents and hence, generation of large amounts of pollutants make LLE labour to be intensive, expensive, time-consuming and environmentally unfriendly. Another popular sample-preparation approach is solid-phase extraction (SPE). Although it uses much less solvent than LLE, the usage can still be considered significant, and normally an extra step of concentrating the extract down to a small volume is needed. SPE can be automated but this entails complexity and additional cost [1,2]. There have been substantial efforts in the past two decades to adapt the existing sample-preparation methods and develop new approaches to save time, labour and materials. Miniaturization has been a key factor in the pursuit of these objectives.

Introduction of solid-phase microextraction (SPME) by Pawliszyn and co-worker [3] basically initiated the interest for microextraction techniques in analytical chemistry. With the SPME technique, target analytes of low or medium polarity are extracted from aqueous or gaseous samples onto a solid polymeric fiber. Extraction occurs by passive diffusion and the extraction yield is essentially determined by the fiber to sample partition coefficient. It is a portable, simple to use, relatively fast method and can be automated and coupled on-line to analytical instrumentation. However, the coated fibers are generally expensive, and for some applications, have limited lifetimes.

Liquid-phase microextraction (LPME) as an alternative miniaturized sample-preparation approach, emerged in the mid-to-late 1990s [4,5]. As its name suggests, in LPME, only a microliter volume of the solvent is needed to extract analytes from the aqueous samples. It overcomes many disadvantages of LLE as well as some of those of SPME (e.g. independence of a commercial supplier and sample carryover or cross-contamination) [6,7]. Single drop microextraction (SDME) was developed as a solvent-minimized sample pretreatment procedure. It is inexpensive, and since very little solvent is used, there is minimal exposure to toxic organic solvents [8,9]. However, some disadvantages of this method are as follows: fast stirring would tend to break up the organic drop; air bubble formation [10]; extraction is time-consuming and equilibrium could not be attained after a long time in most cases [9]. As a solution to improve the stability and reliability of LPME, Pedersen-Bjergaard and Rasmussen introduced hollow fiber based LPME in 1999. Hollow fiber liquid-phase microextraction (HF-LPME) allows extraction and preconcentration of analytes from complex samples in a simple and inexpensive way. In general, the extraction efficiency achieved by HF-LPME is higher than direct-SDME, since hydrophobic hollow fibers allow the use of vigorous stirring rates to accelerate the extraction kinetics. Moreover, the use of hollow fibers provides protection of the extractant phase and hence, the analysis of dirty samples is feasible. Further, the small pore size of hollow fibers allows microfiltration of the samples, thus yielding very clean extracts [11].

Recent research has focused on the development of efficient, economical and miniaturized sample-preparation methods. Cloud point extraction (CPE) is based on phase separation, which occurs in aqueous solutions of non-ionic surfactants, when heated above the so-called cloud point temperature [12]. Besides of the many benefits of CPE, the choice of surfactants often brings the nuisance to the analysis of analytes by analytical instruments such as GC and HPLC [13,14]. In addition, the use of anionic surfactants as effective extractants in CPE often requires salts and adjustment of pH [15,16]. Homogeneous liquid–liquid extraction (HLLE) utilizes the phase separation phenomenon from a homogeneous solution, and the target solutes are extracted into a sedimented phase. Ternary component solvent system and perfluorinated surfactant system are the two usual modes of HLLE [17–19].

Recently, a new mode of LPME based on solidification of floating organic droplet (LPME-SFO) was developed [20,21]. In this method, specific holders such as the needle tip of microsyringe, the hollow fiber and polychloroprene rubber (PCR) tube are not required for supporting the organic microdrop due to the use of organic solvents with low density and proper melting point. Combination of microextracting systems and ultrasound (US) radiation provides an efficient preconcentration technique such as ultrasound-assisted emulsification-microextraction (USAEME) for determining of analytes at trace levels. This preconcentration technique was first developed by Regueiro et al. [22]. The US radiation is an efficient tool to facilitate the emulsification phenomenon and accelerates the mass-transfer process between two immiscible phases, leading to an increment in the extraction efficiency of the technique in a minimum amount of time [23,24].

Dispersive liquid–liquid microextraction (DLLME) was introduced by Assadi and co-workers in 2006 [25]. It is based on the ternary component solvent systems such as HLLE and CPE. It is a simple and fast microextraction technique based on the use of an appropriate extractant, i.e., a few microliters of an organic solvent such as chlorobenzene, chloroform or carbon disulfide with high density and a disperser solvent such as methanol, acetonitrile or acetone with high miscibility in both extractant and aqueous phases. When the mixture of extractant phase and disperser is rapidly injected into the sample, a high turbulence is produced. This turbulent regimen gives rise to the formation of small droplets, which are dispersed throughout the aqueous sample. Emulsified droplets have interfacial area. After the formation of cloudy solution, the surface area between the extracting solvent and the aqueous sample becomes very large, so the equilibrium state is achieved quickly and, therefore, the extraction time is very short. In fact, this is the principal advantage of DLLME. After centrifugation of the cloudy solution, a sedimented phase is settled in the