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Comparison of hollow fiber liquid-phase microextraction and ultrasound-assisted low-density solvent dispersive liquid–liquid microextraction for the determination of drugs of abuse in biological samples by gas chromatography–mass spectrometry

Liang Meng[a,*], Wenwen Zhang[b], Pinjia Meng[c], Binling Zhu[a], Kefang Zheng[a]

[a] Department of Forensic Science, Fujian Police College, Fuzhou 350007, PR China
[b] Traffic Management Bureau, Beijing Municipal Public Security Bureau, Beijing 100037, PR China
[c] College of Forensic Science, People's Public Security University of China, Beijing 100038, PR China

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ABSTRACT

Two microextraction techniques based on hollow fiber liquid-phase microextraction (HF-LPME) and ultrasound-assisted low-density solvent dispersive liquid–liquid microextraction (UA-LDS-DLLME) had been applied for the determination of drugs of abuse (methamphetamine, amphetamine, 3,4-methylenedioxymethamphetamine, 3,4-methylenedioxyamphetamine, methcathinone, ketamine, meperidine, and methadone) in urine and blood samples by gas chromatography–mass spectrometry. Parameters affecting extraction efficiency have been investigated and optimized for both methods. Under the optimum conditions, linearities were observed for all analytes in the range 0.0030–10 μg/ml with the correlation coefficient (R) ranging from 0.9985 to 0.9995 for HF-LPME and in the range 0.0030–10 μg/ml with the R ranging from 0.9985 to 0.9994 for DLLME. The recovery of 79.3–98.6% with RSDs of 1.2–4.5% was obtained for HF-LPME, and the recovery of 79.3–103.4% with RSDs of 2.4–5.7% was obtained for DLLME. The LODs (S/N = 3) were estimated to be in the range from 0.5 to 5 ng/ml and 0.5 to 4 ng/ml, respectively. Compared with HF-LPME, the UA-LDS-DLLME technique had the advantages of less extraction time, suitability for batches of sample pretreatment simultaneously, and higher extraction efficiency, while HF-LPME has excellent sample clean-up effect, and is a robust and suitable technique for various sample matrices with better repeatability. Both methods were successfully applied to the analysis of drugs of abuse in real human blood sample.

1. Introduction

Fighting against drugs of abuse and addiction is an ongoing struggle for society and public health systems [1]. In order to control drug crime effectively, it is necessary to develop selective analytical methods suitable for unambiguous identification and determination of drugs in illicit samples and biological matrices. This has traditionally been carried out using gas chromatography (GC) [2,3], high-performance liquid chromatography (HPLC) [4], and capillary electrophoresis (CE) [5–7]. In recent years, the mixing use of drugs is becoming one of the epidemiological characteristics of the drug abuse pattern [1]. For example, a new type of mixed drug oral solution has become prevalent in China [8]. The simultaneous screening and confirmation of drugs of abuse present in the body are of considerable importance for the investigation of intoxications, withdrawal, and clinical treatment.

Recently, miniaturized modification of the traditional extraction methods termed liquid-phase microextraction (LPME) [9] has up-to-date development. Hollow fiber LPME (HF-LPME) [10] and dispersive liquid–liquid microextraction (DLLME) [11] can be regarded as different operational modes of LPME. HF-LPME uses a porous hollow fiber to stabilize, protect, and extend the extraction solvent, which has the advantages of low-cost, excellent sample clean-up effect, high extraction recovery, and enrichment factor

Abbreviations: UA-LDS-DLLME, ultrasound-assisted low-density solvent dispersive liquid–liquid microextraction; HF-LPME, hollow fiber liquid-phase microextraction; SPME, solid-phase microextraction; AM, amphetamine; MA, methamphetamine; MDA, 3,4-methylenedioxyamphetamine; MDMA, 3,4-methylenedioxyamphetamine; MACT, methcathinone; K, ketamine.

* Corresponding author. Department of Forensic Science, Fujian Police College, Shoushan Road 59, Cangshan District, Fuzhou 350007, PR China.
Tel.: +86 0591 88037670; fax: +86 0591 88037670.
E-mail address: mlatfy@hotmail.com (L. Meng).

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[10]. DLLME is based on cloudy solution extraction like cloud point extraction and has been developed in many categories [11]. The initial mode of DLLME combines a heavier density solvent than water with the dispersant to form a cloudy solution. After extraction, phase separation is performed by centrifugation and the enriched analyte in the sedimented phase is collected. Obviously, it is suitable for the clean sample, but not for complex ones, such as blood or urine samples [12], while ultrasound-assisted low-density solvent DLLME (UA-LDS-DLLME) uses the ultrasound energy for assisting in the emulsification process without any disperser solvent. This avoids the extraction solvent loss and reduces organic solvent consumption significantly, which improves the extraction efficiency. Moreover, the lower density extraction solvent than water was easily collected after de-emulsification. It can eliminate the effect of complex sample matrix and be suitable for the biological sample. The outstanding advantages of DLLME are its simplicity, rapidity, and inexpensiveness, especially suitable for the biological sample preparation [11]. Both technologies have been widely used in environmental, food, fragrance, flavor, forensic, pharmaceutical, and biological analyses [9–13], which also showed good performance for the determination of drugs of abuse [14,15].

In the present work, two approaches based on HF-LPME and UA-LDS-DLLME have been developed for the determination of eight drugs of abuse (methamphetamine, amphetamine, 3,4-methylenedioxymethamphetamine, 3,4-methylenedioxyamphetamine, methcathinone, ketamine, meperidine, and methadone) in urine and blood samples by GC–MS. Different parameters affecting the extraction process such as extraction solvent, solvent volume, pH of sample, extraction time, and temperature were studied and optimized in detail for both methods. The UA-LDS-DLLME method was firstly used for the biological sample preparation. The advantages and disadvantages of both methods have also been discussed. The recommended methods were successfully employed to determine the trace levels of target analytes in human blood samples.

2. Experimental

2.1. Reagents and materials

Methamphetamine hydrochloric (MA), amphetamine sulfate (AM), 3,4-methylenedioxymethamphetamine hydrochloric (MDMA), 3,4-methylenedioxyamphetamine hydrochloric (MDA), methcathinone hydrochloric (MACT), ketamine hydrochloric (K), meperidine hydrochloric, and methadone hydrochloric, were purchased from the Institute of Forensic Science (China Ministry of Public Security, Beijing). 1-(2-Methoxyphenyl) piperazine (2-MeOPP) was purchased from J&K Scientific Ltd (Beijing, China) for internal standard (IS). Toluene, benzene, o-xylene, cyclohexanone, butyl acetate, octyl acetate, n-hexane, and cyclohexane, were purchased from Sinopharm (Beijing, China), all of analytical grade and redistilled in a glass distillation system to remove trace impurities. All other analytical grade reagents used for experiments were purchased from Sinopharm. All standard solutions were prepared with double distilled water and stored in the refrigerator at 4 °C prior to use.

The Q 3/2 Accurel polypropylene hollow-fiber membrane (600 μm ID, wall thickness 200 μm, with 0.2 μm pore size) was purchased from Membrana GmbH (Wuppertal, Germany). The hollow fiber was cut into 4.0 cm pieces. The approximate internal volume of each section was 10 μl. The hollow fiber sections were ultrasonicated for 5 min in acetone to remove the contaminants in the fiber. Then the fibers were removed from the acetone and dried in the air.

Table 1
Qualitative and quantitative selective detection of ions by GC/MS.

Analytes	Selective detection of ions (*m*/*z*)
Methamphetamine	44, 65, 91
Amphetamine	58, 65, 91
MDMA	58, 77, 135
MDA	44, 77, 136
Methcathinone	51, 58, 77
Ketamine	152, 180, 209
Meperidine	71, 172, 247
Methadone	57, 72, 165
1-(2-Methoxyphenyl) piperazine	135, 150, 192

The blank samples were obtained from the volunteers in our college ($n = 10$), who were confirmed drug free.

2.2. Apparatus

The analyse was performed by an Agilent 6890A GC coupled to a single quadrupole 5973 C mass spectrometer (MS) instrument (CA, USA). The separation of the extracted compounds was carried out on a DB-5MS capillary column (30 m × 0.32 mm ID, 0.25 μm film thickness, J & W, Folsom, CA, USA). The column was initially maintained for 2 min at 100 °C, and the temperature was then increased to 300 °C at a rate of 20 °C/min, and finally held for 6 min. Helium (99.99%) was used as a carrier gas with a constant flow rate of 1.2 ml/min. The injection was made in the splitless mode at 260 °C. The injection volume was 1 μl. The EI (70 eV) source was at 230 °C, and the quadrupole mass analyzer was at 150 °C. Solvent delay time was 3.5 min. The instrument was operated in the scan mode for qualitative analysis, and selected ion monitoring mode (SIM) for quantitative analysis. Retention times and *m*/*z* ratios of characteristic ion in the mass spectrum were selected for quantification, as seen in Table 1.

2.3. Extraction procedures

2.3.1. HF-LPME

A 1.0 ml of sample (urine and blood) was placed in a 10 ml vial containing an 8 mm stir bar and diluted with 7 ml of 100 mmol/L NH_3 solution. Two conventional 0.8 mm O.D. medical syringe needles were inserted through a silicon septum in the screw top. The ends of two needles were inserted into the ends of a 4 cm piece of hollow fiber at a depth of 2 mm, respectively. Then, the hollow fiber was first dipped in toluene for about 10 s to immobilize the solvent in the pores. A 25 μl syringe was used to fill the hollow fiber with 10 μl of toluene (containing 15 μg/ml of 2-MeOPP for IS). The hollow fiber was placed into the sample immediately. The extraction unit was sealed and placed in a constant temperature water bath magnetic stirrer (Aibote, Henan, China) to vibrate (500 rpm) for 10 min at 30 °C. After extraction, the extractant was withdrawn and injected into the GC–MS for analysis. Each piece of fiber was used only once.

2.3.2. UA-LDS-DLLME

A 1.0 ml of sample (urine and blood) was placed in a 2 ml centrifuge tube and adjusted pH with 0.1 ml of NH_3 solution. Then, a 100 μl of toluene (containing 15 μg/ml of 2-MeOPP for IS) as extractant was dropped into the sample solution. The mixture was sonicated vigorously in an ultrasonic bath (Kunshan, Shanghai) for 3 min with occasional manual shaking to form a cloudy suspension, facilitating mass transfer of target analytes into extractant solvent. Subsequently, the tube was centrifugated for 3 min at 10,000 rpm. For the blood sample, 10 mg of NaCl was added to break emulsion. Finally, the upper layer of low-density extractant was withdrawn and injected into the GC–MS for analysis.