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Development and evaluation of electromembrane extraction across a hollow polymer inclusion membrane

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ABSTRACT

In this work, a new variation of the electromembrane extraction (EME) approach employing a hollow polymer inclusion membrane (HPIM) was developed. In this method, a HPIM was prepared by casting a solution of the desired proportions of cellulose acetate (CTA), tris(2-ethylhexyl)phosphate (TEHP) and di-(2-ethylhexyl)phosphoric acid (D2EHPA) in dichloromethane on glass capillary tubing. Three basic drugs namely amphetamine, methamphetamine, and 3,4-methylenedioxy-*N*-methylamphetamine (MDMA) were selected as model analytes to evaluate the extraction performance of this new approach. The drugs were extracted from human plasma samples, through a 20 μm thickness HPIM, to an aqueous acceptor solution inside the lumen of the hollow membrane. Parameters affecting the extraction efficiency were investigated in detail. Under the optimized conditions, enrichment factors in the range of 97–103-fold were obtained from 3 mL of sample solution with a 10 min extraction time and an applied voltage of 300 V across the HPIM. The detection limits of the method for the three drugs were in the range of 1.0–2.5 ng/mL (at a signal/noise ratio of three), with relative standard deviations of between 6.4% and 7.9%. When the method was applied to spiked plasma samples, the relative recoveries ranged from 99.2% to 100.8%. Enrichment factors of 103, 99 and 97 were obtained for amphetamine, methamphetamine, and MDMA, respectively. A comparison was also made between the newly developed approach and EME using supported liquid membranes (SLM) as well as standard sample preparation methods (liquid–liquid extraction) used by the Toxicology Unit, Department of Chemistry, Malaysia.

1. Introduction

Many analytical methods dealing with samples in complex matrices require a pretreatment step for matrix removal prior to quantification by instrumental measurement. Liquid–liquid extraction (LLE) is the traditional approach but it is considered a time-consuming technique. Solid phase extraction (SPE) has successfully redressed the limitations inherent in the classical LLE method with reduced analysis times and reduced organic solvent consumption. In recent years several miniaturized sample pretreatment methods have been introduced to speed up and simplify the procedures as well as to minimize organic solvent usage. These include solid phase micro extraction (SPME) [1], single drop microextraction (SDME) [2–4], liquid phase microextraction (LPME) [4–7], micro-SPE [8], thin-film microextraction (TFME) [9], and mixed-matrix membrane microextraction [10].

Several new approaches based on the use of an electric field as the driving force to enhance the extraction of charged analytes from aqueous samples are currently also receiving attention (see reviews) [11–14]. The technique termed 'electromembrane extraction' (EME), has been based on supported liquid membranes (SLM) consisting of a porous polymeric membrane impregnated with a water-immiscible organic solvent [15]. Only charged analytes (either positive or negative) are transported across the membrane according to the polarity of the applied field. In addition, the membrane also functions as a cleanup filter that obstructs the transportation of neutral and high molecular mass compounds such as humic acid and proteins. This procedure has been intensively explored and found to be applicable to various charged species (see the reviews [16–20]). Nevertheless, as the SLMs have limited

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mechanical stability due the leaching of the liquid phase from the membrane [21,22], the use of polymer inclusion membranes (PIM) as an alternative for electric field driven membrane extraction has recently been investigated in our laboratory [23–26]. PIMs are homogeneous, self-supporting plasticized polymeric membranes, which for these investigations consisted of cellulose triacetate as base polymer, a plasticizer, and usually an ion carrier. This robust material was proven to be suitable for the extraction of lipophilic organic ions [24,25], including pesticides [26] as well as inorganic anions [27].

Here, we report a new variation of the EME approach in which a hollow polymer inclusion membrane (HPIM) is prepared and used as sample/acceptor interface to extract selected drugs of abuse from human plasma samples. The membrane was prepared by casting a solution (on the microliter scale) of the desired proportions of base polymer, plasticizer and carrier in dichloromethane on glass capillary tubing. Extraction parameters influencing EME–HPIM were investigated and optimized. The performance of the proposed method was evaluated by comparing with the results of EME–SLM and LLE, the standard protocol for drug analysis.

2. Experimental

2.1. Chemicals and reagents

Amphetamine, methamphetamine, and 3,4-methylenedioxy-*N*-methylamphetamine (MDMA) were obtained from Cerilliant (TX, USA). Cellulose triacetate (CTA), tris(2-ethylhexyl)phosphate (TEHP), *o*-nitrophenyl octyl ether (NPOE), and Selectophore-grade dichloromethane (DCM) were purchased from Fluka (Buchs, Switzerland). Di-(2-ethylhexyl)phosphoric acid (D2EHPA) was purchased from Aldrich (Buch, Switzerland). Sodium chloride (NaCl), glacial acetic acid, sodium hydroxide (NaOH), potassium chloride (KCl), and 1-chlorobutane were purchased from Merck (Damstardt, Germany). Ultrapure deionized (DI) water was produced on a Direct-Q3 ultrapure water system (Merck Millipore, Darmstadt, Germany). All other reagents were of analytical grade and used without any further purification.

2.2. HPIM preparation

A solution of 60 mg CTA as base polymer, 15 mg of TEHP as plasticizer, and 40 mg of D2EHPA as an anionic carrier in 1.5 mL of DCM was prepared. A glass capillary (10 cm long, 1 mm internal diameter (I.D.), single-end open) was first cleaned with a lint-free tissue and immersed in solution (to a length of approximately 3 cm at the closed end side) for 10 s. The glass capillary was dried for 10 s at room temperature follow by re-immersion in the same solution for another 10 s and subsequently dried at room temperature for 20 min. The HPIM was removed from the glass capillary after soaking the capillary in cold deionized water for 60 min. A Hitachi SU-70 field emission scanning electron microscope (Hitachi-Hitech, Tokyo, Japan) was used for the investigation of the surface morphology of the membrane. The membrane was fixed on the stub with double-sided sticky tape and then coated with platinum for 15 s. The membrane thickness was measured with a digital micrometer (MDC-1, Mitutoyo Corporation, Kawasaki, Japan) and was determined to be approximately 20 μm.

2.3. Sample preparation

Stock solutions of amphetamine, methamphetamine, and MDMA at a concentration of 50 μg/mL were prepared in methanol and stored in a refrigerator. Standard solutions for studying the extraction performance contained the target analytes at a concentration of 500 ng/mL and contained a background of 100 μM KCl. Human pooled plasma was purchased from Biowest SAS (Nuaillé, France). The targeted drugs were spiked into the blank plasma at trace level and all spiked plasma samples were kept in a freezer at −20 °C until the experiments were performed. Prior to the extraction procedures, 1 mL of spiked plasma samples were mixed with 3 mL of methanol and vortexed for 3 min. The mixture was centrifuged at 6000 rpm for 5 min. The supernatant (approximately 3 mL) was then transferred into a sample vial and 3 μL of 0.1 M KCl was added to a concentration of 100 μM before finally being used for extraction.

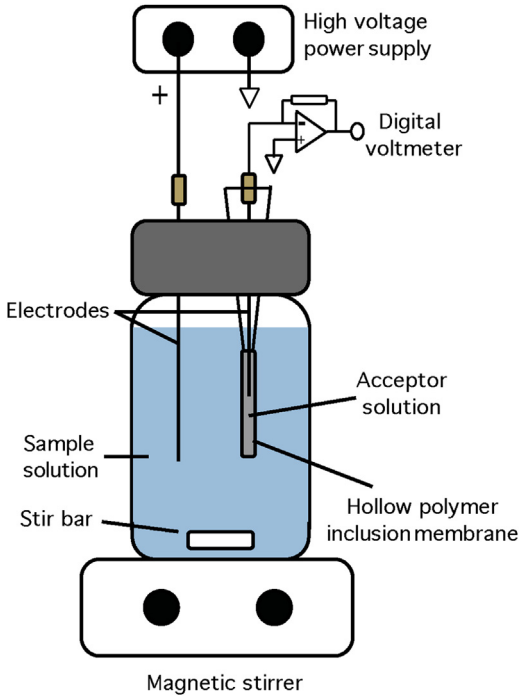

Fig. 1. Schematic illustration of the EME–HPIM setup.

2.4. Extraction procedure

2.4.1. EME–HPIM

The setup is illustrated in Fig. 1. The experiment was performed according to the following procedure: 3 mL of sample solution was put into a 4 mL glass vial (sample compartment). A 1 cm piece of prepared HPIM was closed in the lower end by heat sealing, while the upper end was connected to a 2.5 cm length pipette tip (Eppendorf 200 μl tip, Germany) as a guiding tube. The hollow polymer inclusion membrane and the guiding tube were then inserted through the cap of a glass vial. With a microsyringe, 20 μL of acceptor solution was filled into the lumen of the HPIM. Platinum wires (0.5 mm diameter) were used as electrodes. Positive voltages were applied at the sample side using a high voltage DC power supply (GM12-1K5P, Advance Hilt, Woburn, MA, USA). The electrode connected to the acceptor solution was at ground potential but connected to the input of an operational amplifier in the current-to-voltage converter configuration to allow monitoring of the current passed through the membrane. The sample solution was well stirred at a constant rate of 800 rpm throughout the experiments which were performed at room temperature (25–28 °C). After extraction, the acceptor solution was collected with a microsyringe, and then transferred to a micro insert vial for the capillary electrophoresis with contactless conductivity detection system (CE–C^4D). For comparison, electromembrane