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Surfactant assisted pulsed two-phase electromembrane extraction followed by GC analysis for quantification of basic drugs in biological samples

Pegah Zahedi [a], Saied Saeed Hosseiny Davarani [a], Hamid Reza Moazami [b], Saeed Nojavan [a,*]

[a] Faculty of Chemistry, Shahid Beheshti University, G. C., 1983963113 Evin, Tehran, Iran
[b] School of Physics and Accelerators, NSTRI, P. O. Box 11365-8486, Tehran, Iran

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ABSTRACT

In this work, a simple and efficient surfactant assisted pulsed two-phase electromembrane extraction (SA-PEME) procedure combined with gas chromatography (GC) has been developed for the determination of alfentanil, sufentanil and methadone in various samples. It has been found that the addition of anionic surfactant causes the accumulation of the cationic analytes at the SLM/solution interface resulting in an easier transfer of the analytes into the organic phase. The method was accomplished with 1-octanol as the acceptor phase and supported liquid membrane (SLM) by means of an 80 V pulsed electrical driving force and the extraction time of 20 min. The model analytes were extracted from 3.0 mL sample solution (pH 4.0) containing 0.02% w/v surfactant (sodium dodecyl sulfate). The duty cycle of 92% and frequency of 0.357 Hz gave the best performance. Extraction recoveries in the range of 70.5–95.2% and satisfactory repeatability ($7.6 < RSD < 13.7$) were obtained. The limits of detection were 1.5, 1.5 and 0.6 ng mL^{-1} for sufentanil, alfentanil and methadone, respectively. The method offers an acceptable linearity (2.0–1000.0 ng mL^{-1}) for each analyte with coefficient of determination higher than 0.998. Furthermore, the figures of merit of SA-PEME were compared with the results from the conventional two-phase EME which confirm the advantages of the proposed technique. The method was applied for the determination and quantification of the model compounds in the wastewater, plasma, breast milk and urine samples.

1. Introduction

In 2006, Pedersen-Bjergaard and Rasmussen made an innovative modification to a previously known extraction method, hollow fiber liquid phase microextraction (HF-LPME) [1]. The modification was the insertion of two platinum electrodes, connected to a direct current DC power supply, to electrically enhance the movement of the analyte through the supported liquid membrane (SLM). Electrically assisted migration of the analytes significantly improved the performance of the extraction by reducing the extraction time as well as increasing the enrichment factor [2]. Electromembrane extraction (EME) was the name coined by the authors to represent the novel method. It was successfully utilized thereafter to extract a great variety of analytes in different matrices [3–8]. Despite the high potential of EME method for efficient extraction of ionizable compounds in a relatively short time, it was associated with some drawbacks. The main trouble of EME is that high potential differences were found to be inappropriate due to the bubble formation at the electrodes, instability problems, punctuation of the SLM and sparking [9]. The problems were found to be more serious in analyses of real samples containing large amounts of ionic components [10,11]. On the other hand, the mass transfer resistance and built-up of a boundary layer of ions at the interfaces at both sides of the SLM could cause a reduction in extraction recovery over time [12]..

Two different methods were suggested to overcome the instability problems of EME including the application of a stabilizer circuit to prevent malignant increasing of current [13], and pulsed voltage instead of constant DC supply [14–16]. In the first pulsed configuration, the applied potential was managed to be switched off in short periods of time. The duration of the pulse was long enough for the analytes to migrate from the sample solution, through the

Abbreviations: SA-PEME, surfactant assisted pulsed electromembrane extraction; HF-LPME, hollow fiber liquid phase membrane extraction; SLM, supported liquid membrane; DC, direct current.

* Corresponding author. Fax: +98 21 22431662.
E-mail addresses: s_nojavan@sbu.ac.ir, s_nojavan3479@yahoo.com (S. Nojavan).

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SLM into the acceptor phase, but so short to effectively minimize the thickness of the boundary layer [14].

Hence, the pulsed electromembrane extraction (PEME) could increase stability by decreasing the thickness of the boundary layer at the interfaces and improve extractability by eliminating the mass transfer barrier. The PEME could be introduced as an efficient microextraction technique with higher preconcentration factors, relatively short extraction time, higher precision, and a more stable system in comparison with conventional EME [9].

We have recently used a totally different potential function to improve the extraction [17]. The new function comprises precise periodical reversing of the field polarity. As described, the reversing of the field polarity induces large transient current in the SLM that leads to a significant improvement in the performance via a dual charge transfer mechanism.

It is a challenge to combine three-phase EME with GC determinations due to difficulties arising from direct injection of aqueous solutions [9]. The GC is a simple and fast analysis technique which can be easily coupled with different types of sensitive detectors such as flame ionization detector (FID) and mass spectrometer (MS). The two phase EME was proved to be the method of choice to make compatibility between EME and GC [18], hence, the proposed method could have the benefits of two-phase LPME and three-phase EME procedures simultaneously. Another advantage of two-phase over three-phase EME is excluding the optimization of pH in the acceptor phase [18]. In comparison with other conjugated methods, direct injection of the acceptor phase to the GC injection port helps the overall procedure to end up in a shorter time.

The surfactants have been applied as the extraction-enhancing agent in LPME procedure [19,20]. As described in the literature, the mechanism of the improvement includes the accumulation of surfactant on the surface of the membrane via the interaction with the hydrophobic tails of the surfactant molecule that leads to the concentration of the analytes on the hydrophilic heads. Also, there is a recent report on the application of nonionic surfactant for the enhancement of performance in three-phase EME [21]. The same effect could be expected for the two phase EME systems, but to the best of our knowledge, it has not been studied yet.

In this work, for the first time, a new pulsed two-phase EME combined with gas chromatography (GC) procedure has been developed. The applicability of the procedure for the determination of some model compounds (alfentanil, sufentanil and methadone) has been investigated. Also, the effect of surfactant in EME system was studied and a mechanism has been proposed to illustrate the effect of the surfactant on the observed improvement. The two phase EME provided direct introduction of the acceptor phase for gas chromatographic determination of the analytes. The results showed that the addition of surfactant could also improve the performance of the extraction. The developed method was successfully applied to the fast and efficient determination of mentioned analytes in different complex matrices.

2. Experimental

2.1. Chemicals and reagents

The hollow fiber was PP Q3/2 with an internal diameter of 0.6 mm, wall thickness of 200 μm and pore size of 0.2 μm (Membrana, Wuppertal, Germany). Alfentanil, sufentanil and methadone were kindly supplied by Tofigh Daru Pharmaceutical Company (Tehran, Iran) and were used without any further purification. 1-Heptanol, 1-octanol and 2-ethylhexanol were purchased from Fluka (Buchs, Switzerland). Analytical grade HCl and 1-nonalol were purchased from Merck (Darmstadt, Germany). The HPLC grade water was obtained through the Millipore water purification system (Bedford, MA, USA). Sodium dodecyl sulfate (SDS) was purchased from Sigma–Aldrich (Steinheim, Germany).

2.2. Standard solutions and samples

The stock solution containing 1 mg mL^{-1} of each model compound was prepared in distilled water and stored at 4 °C in a light protected container. Sample solutions were prepared by dilution of the stock solution by distilled water. The stock solutions were also utilized to spike human plasma, breast milk, and wastewater samples. The pH of sample solution was adjusted using HCl (1.0 M) and NaOH (1.0 M) solutions.

The breast milk sample was collected from a woman at the start of the lactation. The drug-free human plasma was obtained from Taleghani Hospital (Tehran, Iran). The wastewater samples were collected from Tofigh Daru Pharmaceutical Company (Tehran, Iran).

A urine sample was obtained from a volunteer who had been treated with methadone (3 tablets in 24 h and each tablet contains 10 mg methadone).

2.3. EME procedure

The equipment used for EME procedure was similar to our previous works [17,18]. The simple platinum wires with a diameter of 0.25 mm were obtained from Pars Platin Co. (Tehran, Iran). The hollow fibers were cut into 25 mm pieces, washed with acetone in an ultrasonic bath and then dried in air for 4 h. Every piece was dipped in an organic solvent for 15 s to immobilize the organic solvent in the pores of the hollow fiber. Then, the lumen was filled with the same organic solvent by means of an HPLC syringe. The lower end of the hollow fiber was closed by thermal and mechanical pressure, and the external part of hollow fiber was rinsed with water. The effective volume of the organic solvent in the lumen of hollow fiber was 6 μL. One of the electrodes was then placed into the hollow fiber lumen. Subsequently, 3.0 mL sample solution (containing SDS) was introduced into a glass vial in which the second platinum electrode was placed.

As described in our previous work [17], the pulsing circuit was a homemade digital function generator capable of reversing the polarity of external power supply at desired frequency and duty cycle. The duty cycle of the function generator was adjusted to 100% during the optimization of extraction voltage and time. After completion of the extraction, 1.0 μL of the acceptor solution (organic solvent) was withdrawn from the lumen and directly injected into the GC system.

2.4. Chromatographic determination procedure

GC determinations were performed using a Varian CP-3800 system (Palo Alto, CA, USA) equipped with an FID detector. The separation column was a Chrompack CP-Sil 8CB (25m × 0.32 mm id, 0.25 μm film thickness) (Raritan, NJ, USA). The initial temperature of the oven was 150 °C. The oven temperature was increased at a rate of 25 °C min^{-1} to 300 °C and was kept constant for 1 min. The temperatures of the injector and detector were set to 270 °C and 300 °C, respectively. The carrier gas was highly pure nitrogen (purity > 99.999%) with the constant pressure of 17 psi. The injection mode was splitless.