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A new strategy for basic drug extraction in aqueous medium using electrochemically enhanced solid-phase microextraction

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ABSTRACT

This work describes an electrochemically enhanced solid-phase microextraction (EE-SPME) method using a mild negative potential (−0.6 V) for the enhanced extraction of the selected basic drugs in a pure aqueous matrix and urine samples. The EE-SPME method gave a more effective extraction of drugs (primarily via electrophoresis and complementary charge interaction) compared to that obtained with SPME (without applying a potential, and which is based on passive partitioning). The EE-SPME method eliminated the need for alkalizing, derivatizing the drugs, or modifying the fiber coating before extraction. The analysis of methamphetamine (MA) and amphetamine (AM) was selected as a typical example to demonstrate in detail the advantages of EE-SPME over SPME. Based on the results obtained, 3-min extraction efficiency for both the amphetamines using EE-SPME was better than that of 30-min using SPME. The developed EE-SPME–GC method exhibited wide linear ranges (2–1000 ng mL^{-1}) for both the amphetamines with R^2 larger than 0.99, and the method detection limits (MDLs) for AM and MA were 0.26 and 0.12 ng mL^{-1}, respectively. In addition, the EE-SPME method developed was also successfully applied to enhance the extraction of several other basic drugs (ephedrine, 3,4-methylenedioxyamphetamine (MDA), atropine, methadone, cocaine, codeine, acetylcodeine and papaverine) with preconcentration factors from 157 to 2199, indicating the potential applicability of this method in the field of forensic, clinical and pharmaceutical analysis.

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1. Introduction

Analysis of drugs and their metabolites in biological fluids is quite an important issue for forensic tests, clinical toxicology and pharmaceutical analysis [1–3], in which methodologies for rapid, cost-effective, specific and sensitive analyses are urgently demanded. Generally, biological fluids are very complex mixtures, consisting of a large number of salts, proteins and lipids, as well as other endogenous and exogenous organic molecules. Furthermore, the analytes are often presented at trace level in biological samples. As a result, sample pre-treatment steps are usually necessary to extract the analytes of interest and to eliminate the interfering compounds from the sample matrix prior to measuring procedures. Although liquid–liquid extraction and solid-phase extraction are still the most commonly adopted sample preparation methods, they are known to suffer from the drawbacks of being time-consuming, laborious and requiring a large volume of organic solvents [4].

Solid-phase microextraction (SPME) [5] is considered as a good alternative to classical methods for extracting drugs from biological samples, due to its fast, sensitive and easy-to-quantify properties [6–8]. Generally, SPME functions based on the partitioning of analytes between the sample matrix and the extracting phase coated on a fused silica fiber or metal wires. Most drugs contain polar functional groups such as amino, carboxylic acid or hydroxyl groups, and they are usually manufactured as salts (hydrochloride, sulfate or sodium salt) to facilitate the human ingestion, and so most of them predominantly exist as the ionic form in biological fluids. All these characteristics make drugs highly soluble in an aqueous matrix and therefore rather difficult to be extracted. Most reports on the application of SPME to drugs require a derivatization [9–11], alkalization [12,13] or acidification [14] step to decrease the polarity and therefore to enhance the extraction phase/water

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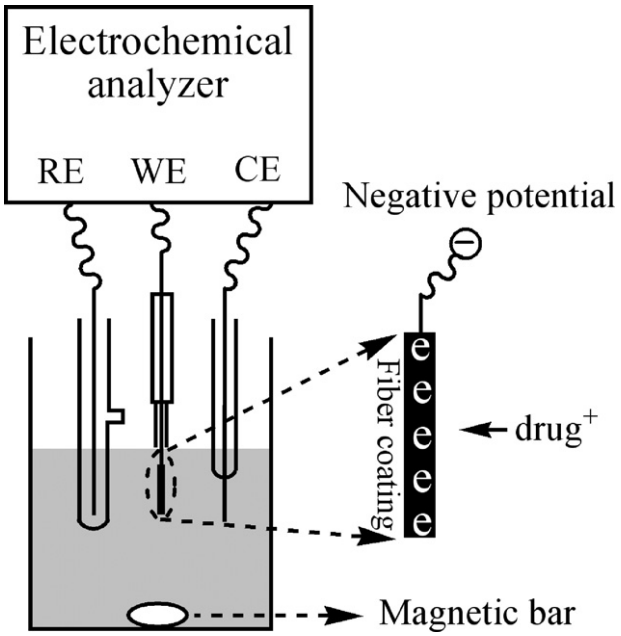

Fig. 1. Schematic of the EE-SPME device and its fundamental mechanism.

partition coefficients of the analytes. However, the derivatization pre-treatment always requires expensive and toxic reagents, and sometimes produces unstable products [15]. In some cases it is necessary to avoid alkaline or acid conditions when determining unstable drugs, such as cocaine and 4-monoacetylmorphine in alkaline or acid aqueous solution [16]. In addition, the advantages of SPME such as easy-to-handle, solventless, simple and fast, are to some extent abandoned after using these additional steps.

In this paper, we proposed a simple and effective approach, electrochemically enhanced SPME (EE-SPME), to the direct extraction of drugs in aqueous medium. This approach eliminated the need of a derivatization, acidification or alkalization step. The EE-SPME device recently developed by our group [17], is constructed based on a three-electrode system using a multi-walled carbon nanotubes (MWCNTs)/Nafion-coated SPME fiber as the working electrode (WE). The schematic of EE-SPME device and its fundamental mechanism is shown in Fig. 1. For example, when a suitable negative potential is applied on the WE, the positively charged analytes (e.g. protonated drug) are then driven to the surface of the WE by the generated electrical field via electrophoresis, and subsequently adsorbed by the WE via complementary charge attraction. Similarly, by simply switching the applied potential to a suitable positive magnitude, the enhanced extraction of negatively charged analytes could also be readily obtained. Accordingly, the EE-SPME is considered naturally and ideally suited for the extraction of drugs in aqueous solutions, since most of them predominantly exist in their ionic form as discussed above. In this study, the enhanced extraction of methamphetamine (MA) and amphetamine (AM) in a pure aqueous matrix and in urine samples was chosen as a typical example in order to evaluate in detail the extraction performance of the EE-SPME method. Additionally, so as to extend the application field of EE-SPME, it was used for the enhanced extraction of several other basic drugs in a pure aqueous matrix and in urine samples.

2. Experimental

2.1. Reagents and solutions

AM sulfate, MA hydrochloride, 3,4-methylenedioxyamphetamine (MDA) hydrochloride, codeine phosphate, cocaine hydrochloride, methadone hydrochloride, acetylcodeine hydrochloride and papaverine hydrochloride were provided from the Institute of Forensic Science of the Ministry of Public Security P.R.C. (Beijing, China). Atropine sulfate and ephedrine hydrochloride were obtained from the National Institute for the Control of Pharmaceutical and Biological Products (Beijing, China). Each individual stock solution was prepared with water at a concentration of 1 mg mL^{-1}. All the standard solutions used for SPME extraction were prepared to the required concentration by diluting the stock solution with water, and the deionized water was used throughout all the experiments. Nafion (a 5% by wt. solution in lower aliphatic alcohols and water) was purchased from Sigma–Aldrich (Milwaukee, WI, USA) and directly used. MWCNTs of less than 10 nm in diameter and 1–2 μm in length were provided by Shenzhen Nanotech Port (Shenzhen, China). A commercial manual sampling SPME device with 85 μm polyacrylate (PA) were obtained from Supelco (Bellefonte, PA, USA) and used for data comparison. Before use, the commercial fiber was conditioned in the GC inlet according to the manufacturer's recommendation.

2.2. Instrumentation

An electrochemical analyzer (LabNet VA5021) provided by the Najing Corporation (Xiamen, China) was used for the EE-SPME experiments. A Shimadazu GC-2010 gas chromatograph (GC) system equipped with a 30 m × 0.25 mm I.D., 0.25 μm DB-5 capillary column and a flame ionization detector (FID) were employed for all SPME–GC experiments. The following column temperature program was used for the separation of amphetamines: an initial temperature of 100 °C was held for 1 min, then it was increased to 110 °C at 5 °C min^{-1}, and held there for 2 min, and finally it was ramped to 120 °C at 5 °C min^{-1} and held there for 2 min, The column temperature for the other drugs was maintained at 100 °C for 1 min, then raised to 260 °C at 20 °C min^{-1} and kept for 4 min, and then ramped to 280 °C at 10 °C min^{-1} and held for 4 min, before being finally raised to 300 °C at 10 °C min^{-1} and held for 1 min. High-purity nitrogen (99.99%) was used as the carrier gas and kept at a flow rate of 1.64 and 1.25 mL min^{-1} for the analysis of amphetamines and the other drugs. Detector flow rates were set to 30 mL min^{-1} for nitrogen (makeup gas), 47 mL min^{-1} for hydrogen, and 400 mL min^{-1} for air. The inlet and detector temperatures were at 260 °C and 300 °C.

2.3. Preparation of MWCNTs/Nafion-coated fiber

A MWCNTs/Nafion-coated fiber was prepared based on our previous report [17] with little modification: MWCNTs were packed into a Teflon tube (with 6 mm inner diameter and the length of MWCNTs in the tube was kept as 1.5 cm). An aliquot of 200 μL Nafion solution was placed into a Teflon tube so as to make the depth of Nafion solution in the tube 1.5 cm. Before coating, the stainless steel wire (O.D. 0.15 mm) was sequentially cleaned with acetone, ethanol and water, and dried at ambient temperature. The treated stainless steel wire was dipped into the Nafion solution, then immediately drawn out and placed into the MWCNTs. The MWCNTs-coated wire was instantly withdrawn and carefully spun to detach the loose MWCNTs. Subsequently, it was placed into an oven at 120 °C for 30 min to ensure that the MWCNTs were tightly attached to the stainless steel base. Finally, the coated stainless steel wire was immersed into the Nafion solution again and immediately pulled out. The MWCNTs/Nafion fiber coating was obtained with a length of 1.5 cm and an average thickness of about 20 μm. The MWCNTs/Nafion-coated fiber was mounted into a self-assembly SPME holder. Prior to use, the MWCNTs/Nafion-coated fiber was conditioned at 260 °C for 1 h to remove possible contaminants.

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2.4. SPME sampling

A 10-mL aliquot of standard or sample solution with varying concentrations of analytes was placed in a 20-mL sample vial with a magneton. Three electrodes, a MWCNTs/Nafion-coated fiber as the WE, a saturated calomel electrode as the reference electrode (RE) and a platinum wire as the counter electrode (CE), were placed in the sample vial and connected to the electrochemical analyzer. A potential of −0.6 V was applied on the WE for the EE-SPME of amphetamines and the other drugs. The EE-SPME experiments were performed at room temperature for 10 min at a stirring rate of 750 rpm unless otherwise mentioned. The SPME experiments were carried out using identical procedures to those for EE-SPME, only without applying a potential. It should be emphasized that all the comparative experiments between EE-SPME and SPME were carried out using the same MWCNTs/Nafion-coated fiber, except where indicated. After extraction, the fiber was immediately removed from the solution and introduced into the GC inlet and desorbed at 260 °C for 4 min.

2.5. Urine samples

All urine samples were collected from drug-free volunteers and used without any further pre-treatment steps. Urine samples (5 mL) were directly spiked with amphetamines or other drugs, and diluted with an equal volume of deionized water for EE-SPME and SPME. The obtained urine samples spiked with amphetamines at concentrations of 1.0, 0.5 and 0.25 μg mL^{-1} were used for both EE-SPME and SPME experiments but, for the other drugs, 1.0 μg mL^{-1} was used.

3. Results and discussion

3.1. Comparison between SPME and EE-SPME of the amphetamines

According to a recent official report [18], MA is one of the most prevalently abused drugs worldwide, and is associated with psychosis, violence and paranoia. The popularity of MA, and its hazardous effects, has led to a requirement for rapid, low-cost and sensitive methodologies for its analyses in biological fluids. Accordingly, in this study, MA and AM (the major metabolite of MA after ingestion into the human body) were selected as representative compounds to investigate the potential of EE-SPME for the application of this series of drugs. Typically, MA is manufactured as hydrochloride to facilitate its ingestion into the human body. Consequently, the predominant forms of MA and AM in aqueous solution are MA^+ and AM^+, which makes them more difficult to be extracted. Fig. 2a shows that a PA fiber, which is known to have a good affinity towards polar analytes among the commercial SPME fibers [19,20], could hardly extract either of the amphetamines from aqueous solution. Fig. 2b shows that the extraction efficiency for MA and AM was obviously improved using a MWCNTs/Nafion-coated fiber. The higher extraction efficiency of the MWCNTs/Nafion-coated fiber for amphetamines is attributed to the fact that Nafion presents special affinity for polar and ionic analytes [21], and MWCNTs possess a high surface area-to-volume ratio and exhibit a strong π–π conjugated interaction with the benzene rings in AM and MA [22,23]. Furthermore, Fig. 2c shows that, with the application of a negative potential (−0.6 V), the peak areas for AM and MA greatly increased by 3.5 and 8.7 fold compared to those obtained using the same MWCNTs/Nafion-coated fiber without any applied potentials (Fig. 2b). The enhanced extraction efficiency was attributed to the fact that the applied electrical field promoted the movement of protonated amphetamines via electrophoresis. Therefore, more protonated amphetamines, which are originally more soluble in aqueous medium, came into contact with the surface of the WE and were adsorbed by the fiber coating via complementary charge interaction. In this process, the partitioning coefficients of the analytes between fiber coating and aqueous solution (K_{fw}) were enhanced. These results initially demonstrated the suitability of the EE-SPME for the enhanced extraction of amphetamines. To test more precisely the improvement of extraction efficiency with EE-SPME, the pH of the standard mixture was adjusted to 11 using 1 mol L^{-1} NaOH to neutralize the amphetamines and to obtain the maximum extraction efficiency for SPME [13]. Fig. 2d shows that, compared to those in Fig. 2b, the peak areas of A and 4-MA were enlarged by a factor of 1.5 and 4.3 after pH adjustment. Nevertheless, compared to the optimal results from SPME, EE-SPME was still 2.4 and 2.1 fold higher for AM and MA in terms of enrichment capability.

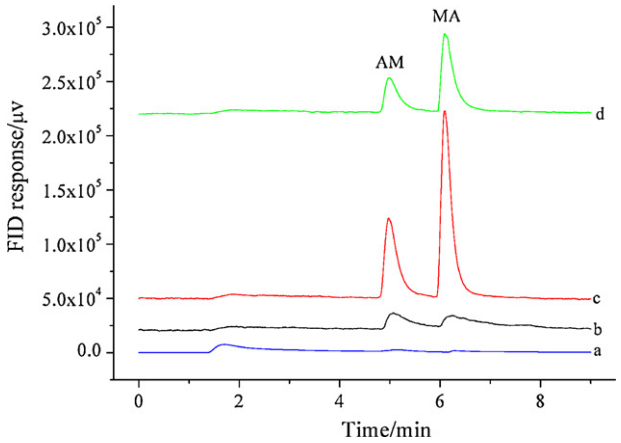

Fig. 2. Chromatographic comparison of a 1.0 μg mL^{-1} amphetamine standard mixture with (a) SPME at pH 7 using a PA fiber; (b) SPME at pH 7 using the MWCNTs/Nafion-coated fiber; (c) EE-SPME at pH 7 using the MWCNTs/Nafion-coated fiber; and (d) SPME at pH 11 using the MWCNTs/Nafion-coated fiber. SPME conditions: applied potential for EE-SPME, −0.6 V; extraction time, 10 min; stirring rate, 750 rpm.

3.2. Optimization of EE-SPME

To achieve the best extraction efficiency for EE-SPME, several parameters such as applied potential, extraction time, stirring rate and pH was optimized. In EE-SPME applications, the applied potential is considered as a vital parameter [17]. The effect of applied potential on EE-SPME extraction efficiency was investigated by plotting analyte peak area as a function of applied potential. Potentials from −0.8 to 0.5 V (vs. SCE) were applied for the EE-SPME of the amphetamines. Fig. 3 shows that the extraction efficiency for the amphetamines obviously increased as the potential varied from 0.5 to −0.6 V and tended to level off thereafter. With the application of positive potentials, the positively charged fiber coating repelled the protonated amphetamines and thus resulted in lower extraction efficiency. In contrast, the application of negative potentials made the fiber coating negatively charged and therefore enhanced the extraction of protonated amphetamines via electrophoresis and complementary charge interaction. For the following EE-SPME experiments, an optimum applied potential of −0.6 V was selected.

The extraction time profiles for EE-SPME and SPME were both constructed by plotting the peak areas for the amphetamines versus extraction time. Fig. 4 shows that, for the SPME mode, the peak areas for the amphetamines slowly increased as the extraction time varied from 1 to 10 min and tended to reach equilibrium at 10 min. However, for the EE-SPME mode, the peak areas for the amphetamines rapidly increased as the extraction time ramped

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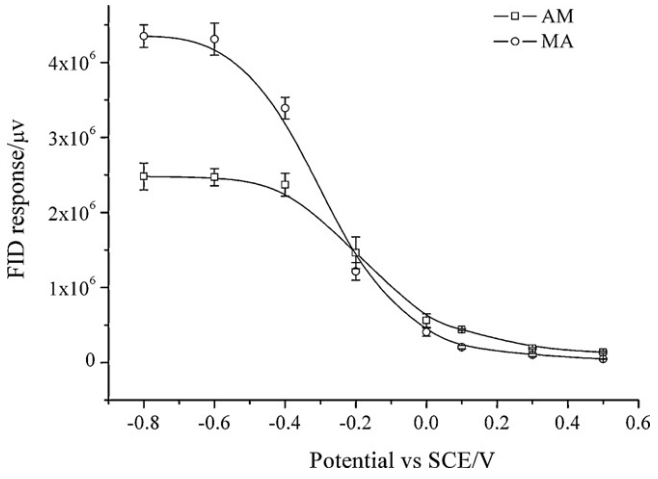

Fig. 3. Effect of applied potentials on the EE-SPME of a 1.0 μg mL^{-1} amphetamine standard mixture. SPME conditions: extraction time, 10 min; stirring rate, 750 rpm; no pH adjustment. Error bars represent the standard deviations for triplicate extractions.

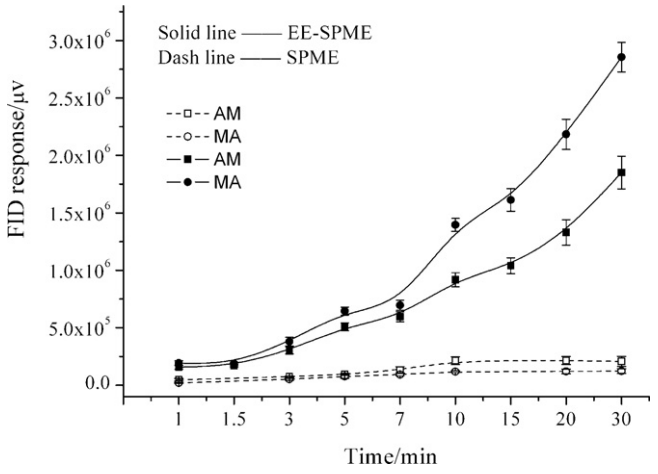

Fig. 4. Effect of extraction time on EE-SPME and SPME of a 0.5 μg mL^{-1} amphetamine standard mixture. SPME conditions: applied potential for EE-SPME, −0.6 V; stirring rate, 750 rpm; no pH adjustment. Error bars represent the standard deviations for triplicate extractions.

from 1 to 30 min, and no equilibrium was reached even at 30 min. This longer equilibrium time indicates the enhanced K_{fw} and the improved extraction capacity of EE-SPME for the analytes [24,25]. It is worth noting that the 3-min extraction efficiency for the selected analytes using EE-SPME was even better than that of 30-min using SPME. This result demonstrated the advantages of EE-SPME over SPME in terms of extraction efficiency and extraction speed. Due to the high extraction efficiency of EE-SPME, a 10-min extraction was chosen in an attempt to optimize the method with respect to minimum time.

In our previous study, agitation of the sample proved to facilitate the electro-kinetic immigration of the charged analytes through the boundary layers and thus improve the extraction efficiency [17]. Based on the results (not shown), a stirring rate of 750 rpm was selected for the following experiments.

As discussed above, most drugs predominantly exist in their ionic form in aqueous solutions. In this study, the EE-SPME was directly carried for the extraction of selected drugs in pure matrix or urine sample without adjusting sample pH. This is one of the advantages of the EE-SPME application for this series of compounds.

3.3. Analytical performance of the method

In order to investigate the performance of the EE-SPME–GC method, the linearity, method detection limits (MDLs), preconcentration factors, extraction efficiency and repeatability were studied for the amphetamines. The results were summarized in Table 1. The linearity of the developed method was studied using water samples spiked with the amphetamines over the range 2–1000 ng mL^{-1} (2, 5, 10, 25, 50, 100, 250, 500 and 1000 ng mL^{-1}), and three replicates were analyzed for each concentration level. Good linearity was obtained with determination coefficients (R^2) larger than 0.99 for both the amphetamines, indicating the developed method was suitable for external quantification of amphetamines. The MDLs (defined as the lowest analyte concentration that could be quantified and confirmed with a signal-to-noise ratio of 3) were found to be 0.26 and 0.12 ng mL^{-1} for AM and MA. The preconcentration factors on the basis of fiber coating volume (0.3 μL) are defined as the concentration of analyte in the extraction phase over that in the sample matrix, and were calculated to be 433 for AM and 1333 for MA. The extraction efficiency, determined by comparing the amount of analyte extracted with the total amount of analyte in the sample, was 1.3% for AM and 4.0% for MA. Extraction efficiency around 1% is typical for EE-SPME due to its non-exhaustive extraction property [26], and the extraction efficiency for amphetamines obtained in this study was higher than that previously reported (0.5–1.5%) [13]. For the determination of method precision, six replicates of spiked water sample containing both amphetamines at a concentration of 500 ng mL^{-1} were extracted and analyzed, and the results, calculated as relative standard deviation (RSD), were lower than 8.1%.

3.4. Application to urine samples

In forensic and clinical analysis, urine remains as the preferred drug screening medium due to its merits of noninvasive collection, stability of specimens and longer detection period for most illicit drugs. To evaluate its applicability for the analysis of amphetamines in biological samples, the optimized EE-SPME–GC method was applied to urine samples. All urine samples were extracted using SPME and EE-SPME, and were found to be AM and MA free. To visualize the enhancement effect of EE-SPME, spiked urine samples (1.0, 0.5 and 0.25 μg mL^{-1}) were extracted with EE-SPME and SPME. These values correspond to an original amphetamine concentration in urine of 2.0, 1.0 and 0.5 μg mL^{-1}, since the urine samples were diluted with an equal volume of water for all EE-SPME and SPME experiments. These concentration levels were chosen since the U.S. Department of Health and Human Services

Table 1
Analytical figures of merit of the EE-SPME–GC-FID method for the determination of selected amphetamines[a].

Analyte	LDR (ng mL^{-1})	R^2	Preconcentration factor	Extraction efficiency (%)	Precision (%RSD, n = 6)	MDL (ng mL^{-1})
AM	2–1000	0.994	433	1.3	3.3	0.26
MA	2–1000	0.998	1333	4.0	8.0	0.12

[a] Experimental conditions: sample volume, 10 mL; applied potential, −0.6 V; extraction time, 10 min; stirring rate, 750 rpm; no pH adjustment; desorption temperature, 260 °C; desorption time, 4 min.

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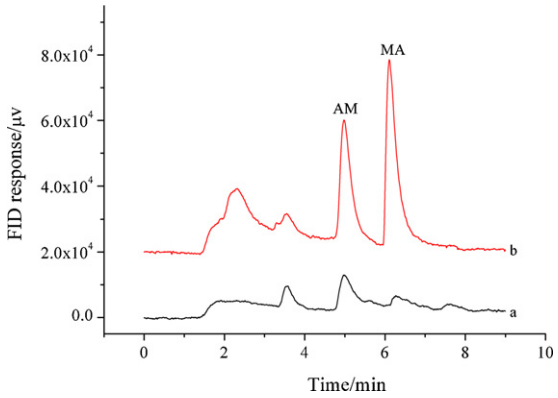

Fig. 5. Chromatograms obtained for spiked urine samples containing each amphetamine at 1.0 μg mL^{-1}, with (a) SPME and (b) EE-SPME. SPME conditions: applied potential for EE-SPME, −0.6 V; extraction time, 10 min; stirring rate, 750 rpm; no pH adjustment.

Workplace Drug Testing Program requires a limit of quantitation of at least 1 μg mL^{-1} for initial screening for AM and MA in urine and 0.5 μg mL^{-1} for a confirmatory test [13]. Based on our previous report, salts and other coexisting cations in the urine matrix probably interfere in the approach of target ions to the WE and thus lower the EE-SPME efficiency [17]. As expected, the absolute response of the analytes was 2.1–3.2 times lower for EE-SPME with urine samples than with a pure aqueous matrix. Nevertheless, the enhancement effect of the extraction efficiency could also be obtained between SPME and EE-SPME. Fig. 5 shows that, compared with those of SPME (Fig. 5a), enhancement factors of 3.0 and 11.3 for AM and MA were obtained with EE-SPME (Fig. 5b) in the spiked urine sample containing both amphetamines at 1.0 μg mL^{-1}. A similar phenomenon was observed at a spiked level of 0.5 μg mL^{-1} (see Fig. 1 in Supplementary Data). When the spiked concentration level was down to 0.25 μg mL^{-1}, neither amphetamine could be detected with SPME due to its insufficient sensitivity (Fig. 6a). Comparatively, with EE-SPME (Fig. 6b), the peaks for both amphetamines clearly appeared, indicating the higher enrichment ability of EE-SPME. For different urine samples, an enhancement effect between EE-SPME and SPME could be obtained, which confirmed the applicability of the EE-SPME method in urinary analysis. However, as was the case of the other method in real sample analysis, the enhancement effect varied from urine sample to sample due to the varied composition of the matrix derived from the different urine samples. An isotopically labeled internal standard could be utilized to overcome this problem [12,13], but this requires the use of a mass spectral detector. Since the main goal of this study was to test the applicability of EE-SPME for drug extraction and to develop a method using inexpensive equipment, this option was not pursued in this study. It should be emphasized that the EE-SPME method developed was also applicable for the enhanced extraction of amphetamines in urine samples without dilution (see Fig. 2 in Supplementary Data), and the sensitivity was comparable to that after dilution. However, dilution of the urine sample with water was recommended for the EE-SPME, in order to avoid the possible aggravating adsorption of the analytes by the urine matrix and to decrease the risks of fiber contamination. The intraday precision of the method was determined by extracting a urine sample with both amphetamines spiked at 1 μg mL^{-1} (five replicates) over a day. The RSD was calculated to be 4.8% for AM and 8.3% for MA, revealing good method precision and stability of the fiber in urinary analysis. Interday precision was accessed using 6 analyses of a spiked urine sample (1 μg mL^{-1}) over 3 days and were less than 11.2%. Based on the results obtained, the MWCNTs/Nafion-coated fiber could be used more than 100 times without obvious decline in its extraction performance (including 50 times in urinary analysis).

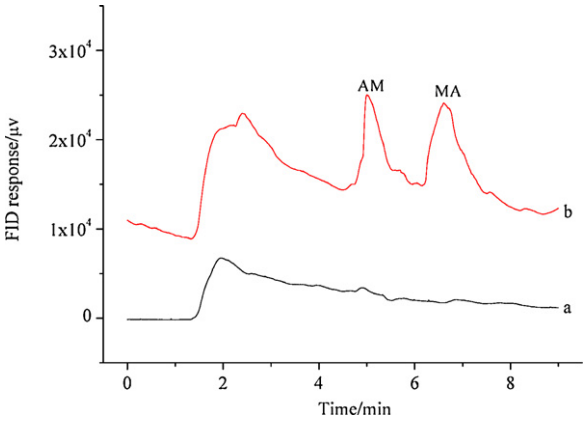

Fig. 6. Chromatograms obtained for spiked urine samples containing each amphetamine at 0.25 μg mL^{-1}, with (a) SPME and (b) EE-SPME. SPME conditions as in Fig. 5.

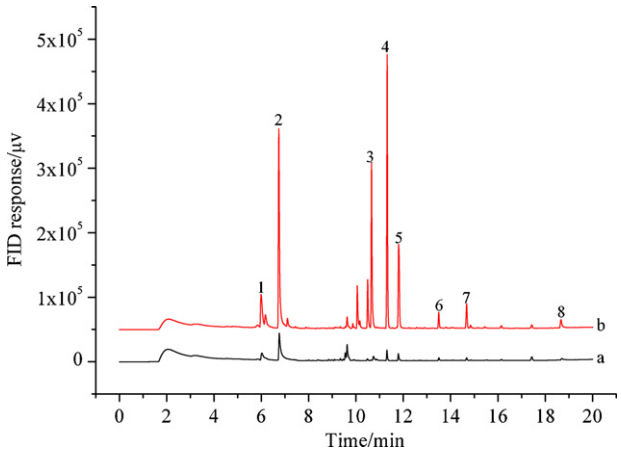

Fig. 7. Chromatographic comparison of a standard mixture containing each drug at 1.0 μg mL^{-1} with (a) SPME and (b) EE-SPME. Peak identification: 1. ephedrine, 2. MDA, 3. atropine, 4. methadone, 5. cocaine, 6. codeine, 7. acetylcodeine, and 8. papaverine. SPME conditions: applied potential for EE-SPME, −0.6 V; extraction time, 15 min; stirring rate, 750 rpm; no pH adjustment.

3.5. Application to other drugs

The method developed for amphetamines was applied to the extraction of several other basic drugs (atropine, codeine, cocaine, ephedrine, methadone, acetylcodeine, MDA and papaverine). As these drugs are all manufactured as their salts, the EE-SPME method should also be applicable for their extraction. A standard aqueous solution containing all drugs was directly prepared for comparison of the SPME and EE-SPME methods. Fig. 7a shows that all drugs were difficult to extract from aqueous solution with SPME due to their highly hydrophilic properties. For EE-SPME, compared to those of SPME, enhancement factors of 4.3–23.6 for all selected drugs were observed as seen in Fig. 7b. The preconcentration factors and extraction efficiency of the EE-SPME for the selected drugs are summarized in Table 2. The preconcentration factors ranged from 157 to 2199, indicating that the concentrations of analytes were 157–2199 times higher in the fiber coating than in the original sample. The extraction efficiency for all the drugs was calculated to be in the range 0.47–6.6%. These data are supposed to be larger in the equilibrium situation, since they were obtained from a non-equilibrium extraction (15 min). Finally, a urine sample directly spiked with all drugs was prepared for comparison of SPME and

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Table 2
Preconcentration factors and extraction efficiency of the EE-SPME for the selected drugs in pure aqueous sample[a].

Analyte	(Mean ± SD, $n = 3$)	
	Preconcentration factors	Extraction efficiency (%)
Ephedrine	616 ± 46	1.8 ± 0.14
MDA	2199 ± 134	6.6 ± 0.40
Atropine	1436 ± 46	4.3 ± 0.14
Methadone	1575 ± 97	4.7 ± 0.29
Cocaine	870 ± 133	2.6 ± 0.40
Codeine	157 ± 11	0.47 ± 0.03
Acetylcodeine	239 ± 19	0.72 ± 0.06
Papaverine	445 ± 29	1.3 ± 0.09

[a] Experimental conditions: sample volume, 10 mL; applied potential, −0.6 V; extraction time, 15 min; stirring rate, 750 rpm; no pH adjustment; desorption temperature, 260 °C; desorption time, 4 min.

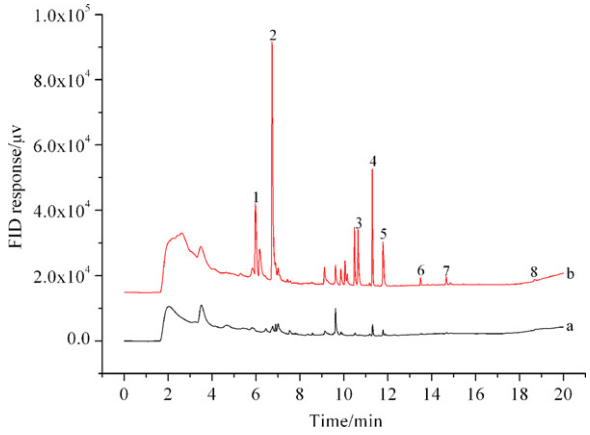

Fig. 8. Chromatographic comparison of a spiked urine sample containing each drug at 1.0 μg mL^{-1} with (a) SPME and (b) EE-SPME. SPME conditions and peak identification as in Fig. 7.

EE-SPME. Similar results were obtained in that peaks of ephedrine (peak 1) and atropine (peak 3), which could hardly be found with SPME (Fig. 8a), appeared with EE-SPME (Fig. 8b); additionally, the peak areas of the other drugs increased with enhancement factors in the range 3.2–26.0. These results verified the aforementioned hypothesis that the EE-SPME method could be used for the enhanced extraction of a series of drugs, revealing further the extensive applicability of this approach.

4. Conclusions

An EE-SPME method was successfully applied for the enhanced extraction of amphetamines, as well as several other basic drugs, in a pure aqueous matrix and in urine samples. By applying a mild negative potential (−0.6 V) on the constructed EE-SPME device, an enhanced extraction of basic drugs in the aqueous medium was achieved via electrophoresis and complementary charge interaction. Based on the results obtained, the EE-SPME method developed would be appealing for drug analysis in clinical, forensic and pharmaceutical fields as it is simple, straightforward and sensitive, and does not require sample pretreatment such as derivatization, acidification or alkalization steps. This EE-SPME technique, coupled with a sophisticated chromatographic system such as GC/MS, may become a powerful drug-screening method which can quickly identify positive biological specimens of drugs. Further work will focus on the enhanced extraction of negatively charged drugs in aqueous medium (e.g., drugs containing a carboxylic or phenolic group) with EE-SPME using positive potentials. In addition, we also aim to miniaturize the EE-SPME device by integrating the three electrodes into a sample vial, which will allow for the analysis of biological samples when only small volumes are available.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.chroma.2010.11.020.

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