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Simultaneous determination of three β-blockers at a carbon nanofiber paste electrode by capillary electrophoresis coupled with amperometric detection

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ABSTRACT

In the paper, a novel carbon nanofiber paste electrode (CFPE) was fabricated and firstly used as a sensitive amperometric detector in capillary electrophoresis (CE) for the simultaneous determination of three β-blockers: sotalol, alprenolol and atenolol. Compared with the bare carbon paste electrode, the CFPE exhibited enhanced oxidation peak current responses to the analytes due to its excellent electrocatalytic activities, high conductivity and large effective surface area. Subsequently, effects of several important factors such as detection potential, pH and concentration of running buffer, separation voltage and injection time on the analysis were investigated. Under the optimum conditions, the three analytes could be separated and detected in a phosphate buffer (pH 8.5) within 11 min. The linear ranges were 0.1–100 μM for sotalol, 0.2–150 μM for alprenolol and 0.1–50 μM for atenolol and the detection limits were as low as 10^{-8} M magnitude ($S/N=3$). Moreover, the CFPE exhibited good repeatability and long-time stability. The proposed method was applied to determine the three β-blockers in spiked urine samples with satisfactory assay results. The good performance, low cost and straightforward preparation method of CFPE demonstrated that it could be used as a detector for CE–amperometric detection system for drug analysis.

1. Introduction

β-blockers (β-adrenoceptor antagonists) are well-known compounds which are widely used in the treatment of several diseases such as hypertension, angina pectoris and arrhythmias [1]. These drugs are also consumed in sports and other stressing activities as doping agents. On the other hand, an overdose of β-blockers is toxic, leading to bradycardia, hypotension, aggravation of cardiac failure, bronchospasm, hypolyvemia, and fatigue [2]. The measurement of β-blockers in biological fluids could offer useful information in cases of intoxication or in controlling the therapy compliance of the patients. Therefore, it is necessary to develop a sensitive and selective analytical method for determining the β-blocker drugs in both pharmaceutical preparations and real urine samples. The three β-blockers here reported are sotalol (Sot), alprenolol (Alp), and atenolol (Ate), as shown in Fig. 1, they have an alkanol amine side chain terminating in a secondary amine group in the chemical structures.

Current methods for determining the β-blockers in plasma, urine, and pharmaceutical preparation have been described, including spectrophotometry [3] and colorimetry [4]. The most widely used separation method was chromatographic technique, such as conventional high performance liquid chromatography (HPLC) [5–10], and gas chromatography (GC) [11–14]. Capillary electrophoresis (CE) coupled with electrochemiluminescence (ECL) [15], CE-diode array detection (DAD) [16,17], pressure-assisted capillary electrochromatography-electrospray ionization mass spectrometry (pCEC-ESI-MS) [18] and heart cutting two dimensional CE-electrochemical detection (ED) [19] were also reported for β-blockers analysis.

CE has become an important separation technique owing to its well-recognized advantages such as rapid analysis, high resolution, flexibility, and low consumption of samples and reagents. Among a wide variety of detectors can be coupled with CE for the separation and detection of different analytes, amperometric detection (AD) offers many desirable features including remarkable sensitivity, good selectivity, without the need for derivatization, low cost and inherent miniaturization of instrument. As well known, the performance of CE–AD is strongly influenced by the working electrode materials. The detection electrode should provide not only favorable signal-to-background characteristics but also a reproducible response. Different electrodes, such as platinum, gold, and carbon materials-based electrodes, have been adopted for CE–AD detectors [20]. In the past few years, there has been an explosion of research activity in the area of nanomaterial-based electrodes since they offer significant advantages over conventional ones, such as better stability, greater sensitivity,

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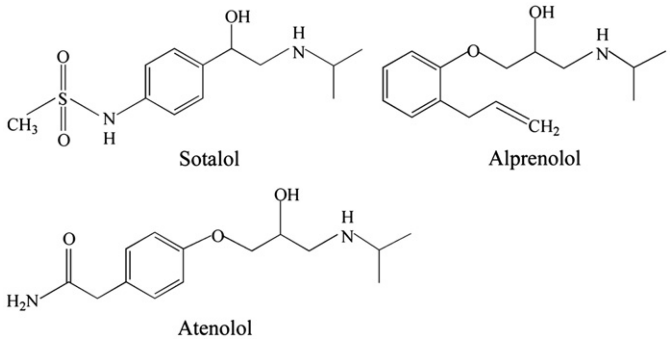

Fig. 1. Chemical structures of sotalol (Sot), alprenolol (Alp), and atenolol (Ate).

and lower detection potentials [21]. Chen's group did some excellent works in the fabrication and application of carbon nanomatericals-based AD detectors for CE. They successively developed carbon-nanotube (CNT)-alginate composite modified electrode [22], carbon nanotube/poly (ethylene-co-vinyl acetate) (CNT/EVA) composite electrode [23], and graphene/poly(urea-formaldehyde) composite electrode [24] as new sensitive amperometric detectors for CE. Recently, Nie et al. used a novel mesoporous nano-structured modified carbon material carbon disk electrode as detector in CE [25]. These new carbon nanomaterials-based CE detectors offered significantly lower operating potentials and substantially enhanced signal-to-noise characteristics. Therefore, nanomaterials have been used as highly perspective components for the construction of high performance electrochemical detectors in CE.

As a kind of new and interesting carbon nanomaterials, carbon nanofibers (CNFs) have cylindrical nanostructure with graphene layers arranged as stacked cones, cups, or plates [26]. CNFs possess unique electronic and high mechanical properties similar to CNTs [27], but compared with CNTs, CNFs have intrinsic advantages such as lower production cost, easier mass production [28], and larger surface-active group-to-volume ratio [29]. In particular, the presence of less order and more edge plane defects on the outer wall of CNFs may allow efficient and more facile electron transfer of electroactive analytes [30]. In addition, CNFs have a much larger functionalized surface area due to different stacking manners of carbon orbitals on the surface. CNFs have been used as matrix for immobilization of biomolecules such as enzymes [29–31], proteins [32] and DNA [33,34].

In this study, we synthesized CNFs by electrospinning and subsequent thermal treatment. The CNFs with large amounts of edge-plane-like defective sites were explored to mix with the mineral for the fabrication of CNFs paste electrode (CFPE). Sot, Alp and Ate were separated and detected by CE–AD at CFPE. The proposed method offered high sensitivity, wide linear range and good selectivity for the analytes. The practical utility of the present system was demonstrated by analyzing β-blockers in urine samples.

2. Experimental

2.1. Reagents and chemicals

All the reagents were of analytical grade and were used as received without further purification. Alp·HCl and Ate were purchased from Sigma (St. Louis, MO, USA). Sot was supplied by National Institutes for Food and Drug Control (Beijing, China). Na_2HPO_4, NaH_2PO_4, H_3PO_4, NaOH and mineral oil were purchased from Beijing Chemicals (Beijing, China).

The stock solutions (10 mM) of the β-blockers were prepard by dissolving these analytes in doubly distilled water. They were stored in the dark at 4 °C to avoid possible decomposition and stable for at least 1 month. Doubly distilled water was used throughout the experiment. Phosphate buffer solutions (PBS) with a series of pH were prepared with the same concentration of Na_2HPO_4 and NaH_2PO_4 solution to certain pH. Before use, all solutions were filtered through 0.22 μm cellulose acetate membrane.

2.2. Apparatus

The CE–AD system consisted of a high-voltage (0–20 kV) power supply (MPI-A, Remax Electronic Co.), a CHI 800 electrochemistry workstation (Shanghai CH instruments, China), and a fused-silica capillary (25 μm i.d., 360 μm o.d.) with a length of 45 cm (Hebei Yongnian Laser-fiber Factory, China). The construction of the AD cell used in this study has been shown in the previous work [35]. End-column CE–AD was carried out with a conventional three-electrode system, which consisted of a Ag/AgCl reference electrode, a Pt auxiliary electrode and a CFPE working electrode. The working electrode was carefully positioned directly opposite the capillary outlet with the aid of an optical microscope to reach a desired gap distance between the capillary outlet and the electrode tip. All experiments were performed at room temperature.

2.3. Preparation of CNFs and electrodes

The CNFs were prepared according to the reported method [36]. Briefly, polyacrylonitrile (PAN) fibers were firstly produced with PAN in DMF solution via an electrospinning technique. And then, the CNFs were synthesized by stabilization and subsequent carbonization of the electrospun PAN fibers in a high temperature furnace.

Graphite powder and mineral oil [70/30 (w/w)] were mixed thoroughly in a mortar to form a homogeneous carbon paste and further were packed into a pipette tube (350-μm diameter; 0.8-cm depth) and inserted copper wire for electrical contact. The surface of the resulting carbon paste electrode (CPEs) was polished with weighing paper and rinsed with double-distilled water just before use. The CFPE was prepared according to the above procedures, but the CNFs powder and mineral oil were at the ratio of 60/40 (w/w). All electrodes were stored at room temperature.

2.4. CE experiments

The capillary was treated by flushing with 0.1 M NaOH overnight before the first use. Every day before the experiments, it was rinsed with 0.1 M NaOH, doubly distilled water in turn for about 10 min and balanced with running buffer for about 15 min. Between runs, the capillary was rinsed with doubly distilled water and running buffer for 60 and 90 s respectively to ensure the good reproducibility. CE was performed at a separation voltage of 15 kV. The potential applied to the detection electrode was +1.25 V. Electrokinetic sample injection was carried out for 6 s at 15 kV. The CE buffer was 90 mM phosphate buffer at pH 8.5. 400 μL PBS was placed in the detection cell and renewed every 3 h.

2.5. Sample preparation

The new urine sample was collected from a healthy female volunteer and filtered through 0.22 μm membranes prior to analysis. And then, it was dilluted with running buffer by 20 times to decrese the interference of the ion strength of the sample matrix. Finally, it was spiked with a series of concentrations of analytes for detection.

3. Results and discussion

3.1. Electrochemistry experiments

The electrochemical behaviors of the three anlytes were investigated at the CPE and CFPE using cyclic voltammetry (CV). Illustrated in Fig. 2 were CV curves of 0.5 mM Sot (A), Alp (B), and Ate (C) in 0.1 M PBS (pH 7.0) at the bare CPE and CFPE, respectively. As an example, from Fig. 2A it could be seen that there was a weak anodic peak current response of Sot at about 0.87 V at the bare CPE (green line), while a remarkable increase in the oxidation current response can be obtained at the CFPE (blue line) in comparison with that at the bare CPE. In addition, a 20 mV negative shift in the peak potential together with increased sharpness of the anodic wave was observed at the CFPE. Alp and Ate had lower electrochemical activity compared with Sot both at CPE and CFPE. The oxidation peaks of Alp and Ate could hardly be observed at CPE, but obvious oxidation peaks at about 1.1 V were observed at CFPE. The phenomenon can be attributed to the use of nano-dimensional CNF with better electrical conduction, higher electrochemical active area as well as its cross-linked structure, which facilitates the kinetics of the electrochemical reaction.

3.2. Effect of the potential applied to the working electrode

The potential applied to the working electrode directly affected the sensitivity and stability, so hydrodynamic voltammetry (HDV) experiments of the analytes at a CFPE were performed in the range of 0.7–1.3 V at the following conditions: separation voltage, 15 kV; sample injection, 10 kV × 10 s; running buffer, 20 mM PBS (pH 7.0). And then, the peak current of the sample was measured from electropherograms under different detection potentials. As shown in Fig. 3, it was found that the peak current responses of all analytes increased with higher applied potential in the range of 0.7–1.25 V, while the detection potential exceeded 1.25 V the responses decreased slightly. Compared with the peak current, the background noise increased slowly from 0.068 nA to 0.15 nA. When applied potential was 1.25 V, the three analytes could be determined with the highest signal-to-noise ratio. Therefore, 1.25 V was selected as the most suitable detection potential in this experiment.

3.3. Optimization of capillary electrophoresis conditions

3.3.1. Effect of buffer pH and concentration

Since the physico-chemical properties of Sot, Alp, and Ate are similar, simultaneous separation of them is a challenge. The manipulation of buffer pH value is usually a key strategy, since it affects the zeta potential (ξ), the electroosmotic flow (EOF) in the capillary as well as the overall charge of the analytes, which determines the migration time and separation of the analytes. PBS was employed as the running buffer. The influence of pH on the separation was investigated within the pH range from 2 to 10.5. The results showed buffer pH affected the migration time and the separation resolution of the three analytes. The lower the pH, the longer the migration time of all analytes. When pH was lower than 7.0 or higher than 9.0, only one overlapped peak was obtained in electropherogram. It is well known that when buffer pH is close to the p*K*a value, the buffer capacity is maximum and best separation efficiency could be achieved [37]. The p*K*a values of β-blockers vary from 9.2 to 9.8 [38]. Therefore, the pH effects were studied in detail from 7.5 to 9.0. Results showed that from pH 7.5 up to pH 8.5, the separation of Sot, Alp, and Ate was getting

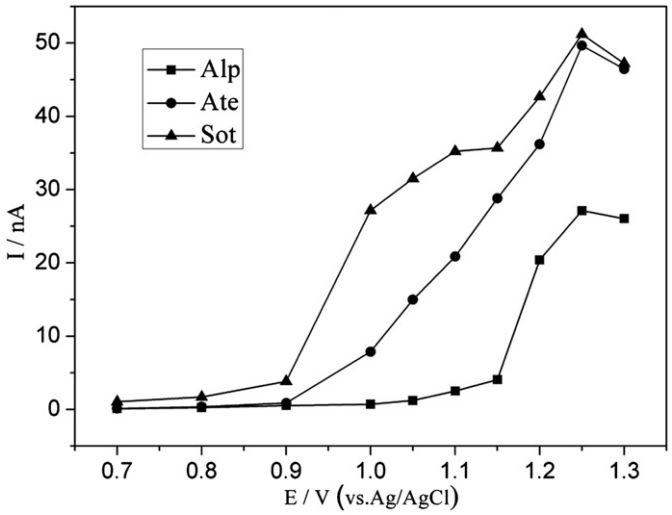

Fig. 3. Hydrodynamic voltammograms of 10 μM Sot, Ate, and Alp at the CFPE. Conditions: separation capillary, 45 cm length (25 μm i.d.); sample injection, 10 kV × 10 s; separation voltage, 15 kV; running buffer, 20 mM PBS (pH 7.0).

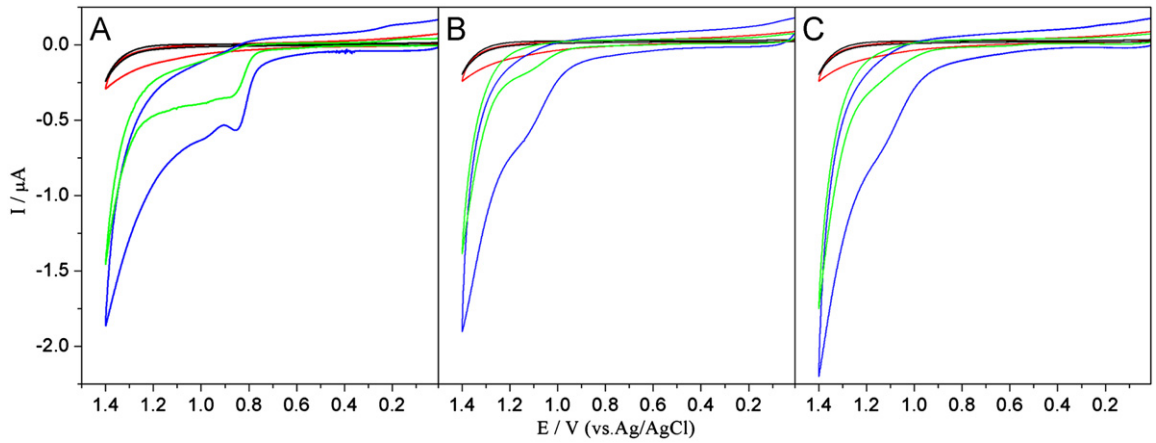

Fig. 2. Cyclic voltammograms (CVs) of 0.5 mM Sot (A), Alp (B), and Ate (C) in 0.1 M PBS (pH 7.0) at bare CPE and CFPE. Black line: blank buffer at bare CPE; red line: blank buffer at CFPE; green line: the analytes at bare CPE; blue line: the analytes at CFPE. Scan rate: 100 mV s^{-1}. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

better. When pH was at 8.5, the separation performance was best although the peaks of Alp and Ate were still overlapped partially. Considering of the peak height, separation resolution and the migration time, we selected pH 8.5 as the optimum pH value.

In addition, the running buffer concentration is also an important parameter. As it influences the viscosity coefficient of the solution, the diffusion coefficient of analytes and the effective zeta-potential of the inner surface of capillary tube are influenced as well, thus it affects the migration time and resolution of all analytes. Fig. 4 depicts the effect of concentrations of running buffer between 10 and 120 mM on the resolution. With the increase of the PBS concentration ranging from 10 to 90 mM, the EOF decreased, the analysis time increased, and the resolution was increased. Both the maximum resolutions of Sot and Alp, Alp and Ate were observed when the PBS concentration was 90 mM. When the PBS concentration exceeded 90 mM, the resolutions began to decrease because high buffer concentrations would result in high Joule heating. Hence, 90 mM PBS was employed as the optimum running buffer concentration with the biggest resolution and fairly short migration time. Under this condition, three β-blockers could be separated within 11 min.

3.3.2. Effect of the separation voltage and injection time

The separation efficiency of CE was investigated at the separation voltage in the range of 10–18 kV. The migration time of analytes was significantly shortened and the current signals increased gradually with the increase of separation voltage. However, higher separation voltages resulted in higher Joule heating because of the higher current inside the capillary, which caused peak broadening and directly affected the separation efficiency. As a compromise, 15 kV was selected as the optimum separation voltage in this experiment.

The injection time determines the amount of sampling, and thus affects both peak current and peak shape. Electrokinetic injection was used in our experiment. The effect of sample injection time on peak current was investigated by changing the injection times interval of 2, 4, 6, 8, and 10 s at a voltage of 15 kV. When the injection time was prolonged, the peak current increased correspondingly. However, the peak current responses of the analytes nearly levels off and peak broadening becomes more severe if the injection time exceeded 8 s. In this experiment, 6 s was chosen as the optimum injection time.

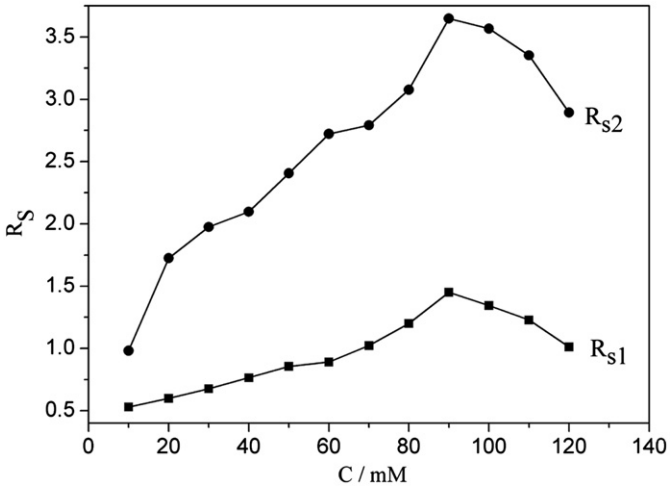

Fig. 4. Effect of buffer concentration on resolution (R_S) of three β-blockers. R_{S1}: resolution of 5 μM Alp and 2.5 μM Ate; R_{S2}: resolution of 2.5 μM Ate and 5 μM Sot. Conditions: detection potential: 1.25 V; running buffer, PBS (pH 8.5); other conditions as in Fig. 3.

3.4. Analytical performance

Under the optimized conditions: detection voltage at 1.25 V (vs. Ag/AgCl), 90 mM PBS (pH=8.5) as running buffer, electrokinetic injection 6 s at 15 kV, separation voltage at 15 kV, the CE–AD method based on CFPE was successfully applied for the separation and detection of the three β-blockers. Fig. 5 shows the representative electropherograms of a mixture for (a) 5 μM Alp, (b) 2.5 μM Ate, and (c) 5 μM Sot recorded at CPE (Fig. 5A) and CFPE (Fig. 5B). The three analytes can be well separated and detected within 11 min. It can be seen that under the same conditions, the peak current responses obtained at CFPE were about 3 times higher than that at the bare CPE. Thus, the CFPE was promising as a new amperometric detector for CE allowing a more sensitive detection.

3.5. Repeatability, linearity, and detection limits

The repeatability of the current response and migration time for Sot, Alp, and Ate was estimated by making repetitive injections of a standard mixture solution (5.0 μM for Sot and Alp, 2.5 μM for Ate) under the optimum conditions. The relative standard deviations (RSDs) of peak current and migration time were 0.53% and 2.31% for Sot, 0.38% and 3.54% for Alp, 0.45% and 3.43% for Ate respectively, which indicated a good reproducibility of the method.

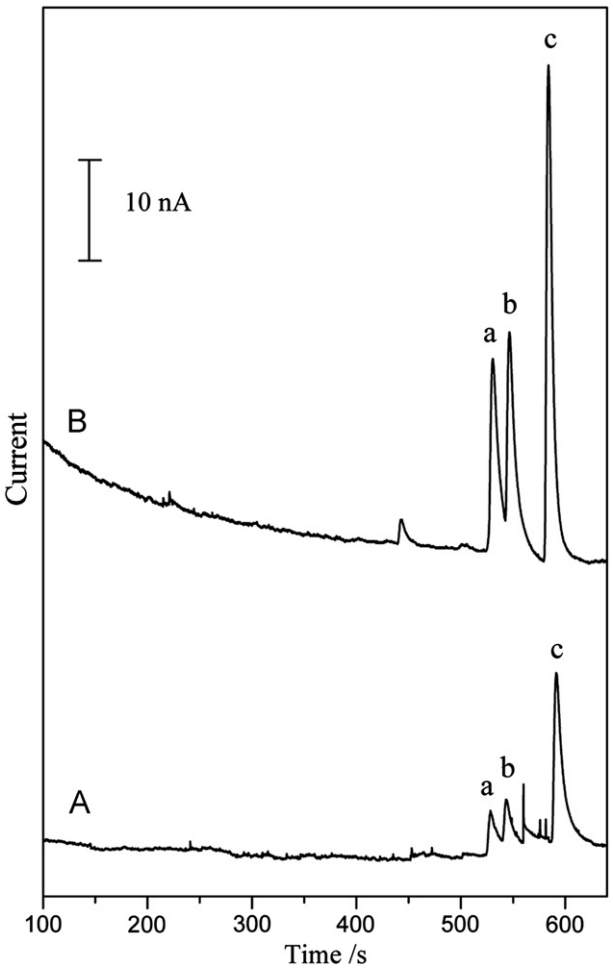

Fig. 5. Electropherograms for a mixture containing (a) 5 μM Alp, (b) 2.5 μM Ate and (c) 5 μM Sot at a bare CPE (A) and CFPE (B). Conditions: detection potential: 1.25 V; sample injection, 15 kV × 6 s; running buffer, 90 mM PBS (pH 8.5); other conditions as in Fig. 3.

Table 1
Linear ranges, detection limits and reproducibility of β-blockers detection.

Analytes	Linear ranges (μM)	Regression equation $Y^a=BX^b+A$	Correlation coefficients	Detection limits (nM)	Reproducibility (RSD, %)[c]	
					Migration time	Peak intensity
Sot	0.1–100	$Y=2.75+8.02X$	0.9989	50	0.53	2.31
Alp	0.2–150	$Y=0.66+3.04X$	0.9979	100	0.38	3.54
Ate	0.1–50	$Y=1.00+6.98X$	0.9985	70	0.45	3.43

[a] Y represents the peak current responses (nA).
[b] It represents the concentration of Sot, Alp and Ate (μM).
[c] The concentrations of Sot, Alp and Ate used are 5.0 μM, 5.0 μM, and 2.5 μM.

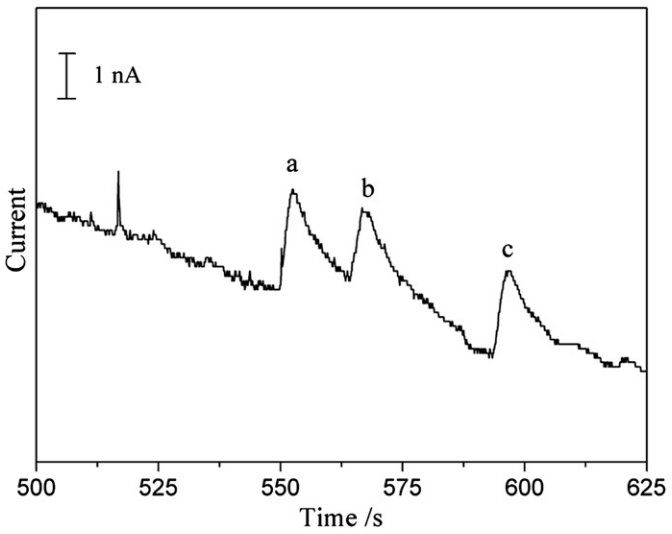

Fig. 6. Typical electropherograms of (a) Alp, (b) Ate and (c) Sot corresponding to the LOQ measurements at a CFPE. Other conditions were the same as in Fig. 5.

A series of standard mixture solutions of Sot, Alp, and Ate ranging from 1.0×10^{-8} to 2.0×10^{-4} M were tested to determine the linearity of this method. The peak current and concentration of each analyte was subjected to regression analysis to calculate the calibration equations and correlation coefficients. The results of regression analysis on linear ranges, regression equations, and correlation coefficients were summarized in Table 1. The detection limits of Sot, Alp, and Ate were 5.0×10^{-8} M, 1.0×10^{-7} M, and 7.0×10^{-8} M ($S/N=3$), respectively. Fig. 6 shows the electropherogram of 0.12 μM Sot, 0.27 μM Alp and 0.18 μM Ate corresponding to the LOQ ($S/N=10$) measurements at a CFPE. The results indicated that the CFPE was suitable for detection of the three analytes, enabling repeatable and sensitive quantification of mixtures containing the three β-blockers.

The detection of Sot, Alp, and Ate by CE–AD based on CFPE was compared with other methods. The detection limit was lower than those by spectrophotometry [3], colorimetry [4], HPLC-ECL [7] and CE-DAD [16,17], and was comparable to that achieved in CE-ECL [15], HPLC-photodiode-array UV detection [5], GC-MS-MS (ion trap)-electronic impact ionization (EI) [12], heart cutting two dimensional CE-ED [19], but was higher than HPLC-UV/fluorescence (FL) detection [6] and pCEC-ESI-MS [18]. Wide linear ranges were obtained as most of the methods.

3.6. Sample analysis

The proposed CE–AD method was utilized for the detection of Sot, Alp, and Ate in human urine. In order to examine the validity of the method, recoveries of the three β-blockers were determined by injecting the standard samples into a diluted urine samples. It can be observed from the electropherogram of 20-fold diluted urine spiked with 5 μM Sot and Alp, 2.5 μM Ate (Fig. 7B) that the unknown compounds from the urine matrix did not interfere with the peaks of the analytes.

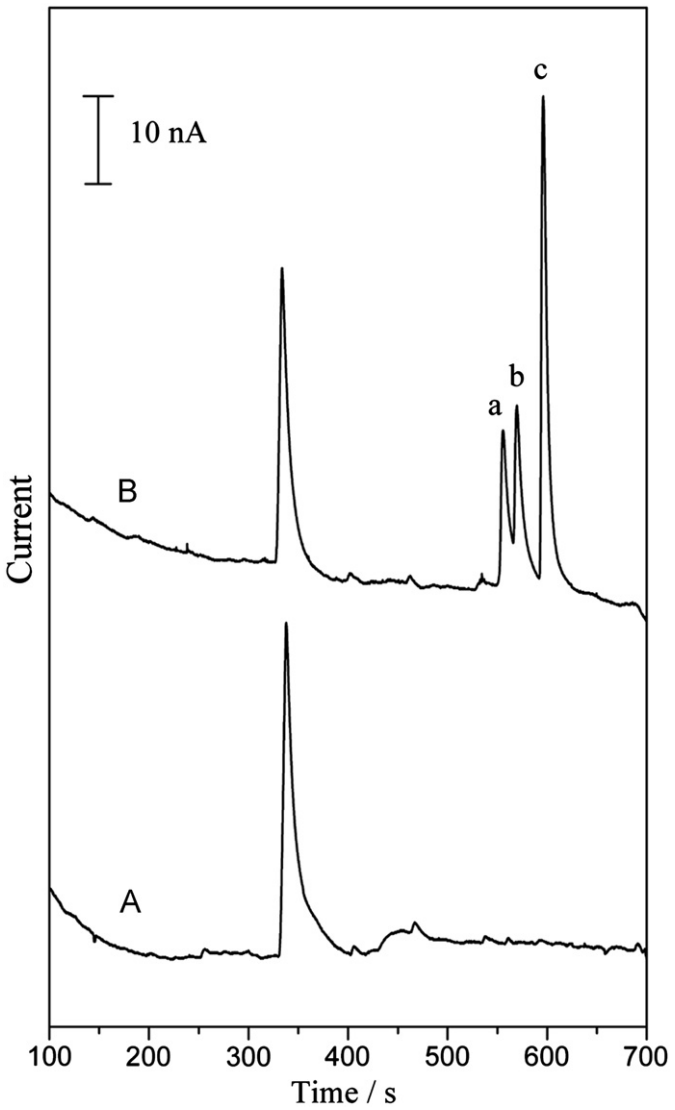

Fig. 7. Electropherograms of 20-fold diluted blank urine sample at a CFPE (A), 20-fold diluted urine spiked with (a) 5 μM Alp, (b) 2.5 μM Ate and (c) 5 μM Sot at a CFPE (B). Conditions were the same as in Fig. 5.

The results of recovery were shown in Table 2. The recoveries of the three β-blockers with different concentrations in urine varied from 94.6% to 104.0%. The RSD ($n=3$) of the migration time and the peak intensity were 0.44%–0.91% and 2.19%–4.62%, respectively.

Table 2
Determination of β-blockers in urine ($n=3$).

Analytes	Added (μM)	Found (μM)	Recovery (%)	RSD (%)	
				Migration time	Peak intensity
Sot	2.5	2.60	104.0	0.59	3.98
	5	5.16	103.3	0.90	2.19
	10	9.72	97.2	0.91	2.93
Alp	2.5	2.41	96.4	0.44	3.81
	5	4.86	97.2	0.86	4.62
	10	9.78	97.8	0.72	3.47
Ate	1.25	1.28	102.1	0.47	4.16
	2.5	2.37	94.6	0.78	3.92
	5	4.82	96.4	0.77	2.70

4. Conclusion

This work demonstrated that CE–AD based on a carbon nanofiber paste working electrode could be successfully used to simultaneous separate and determin Sot, Alp, and Ate in spiked human urine. By optimizing the separation and detection conditions, the three β-blockers could be separated completely within 11 min with high sensitivity, wide linear range, good reproducibility and satisfactory recovery. Moreover, it is an efficient approach for the routine study of Sot, Alp, and Ate in urine, and it may promisingly pave a way for applications in clinics and sports.

Acknowledgments

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References

[1] J.V. Okopski, J. Clin. Pharm. Ther. 12 (1987) 369–388.
[2] C.P. Snook, K. Sigvaldason, J. Kristinsson, J. Toxicol. Clin. Toxicol. 38 (2000) 661–665.
[3] S.M. Al-Ghannam, J. Pharm. Biomed. Anal. 40 (2006) 151–156.
[4] A.S. Amin, G.H. Ragab, H. Saleh, J. Pharm. Biomed. Anal. 30 (2002) 1347–1353.
[5] M. Delamoye, C. Duverneuil, F. Paraire, P. Mazancourt, J. Alvarez, Forensic Sci. Int. 141 (2004) 23–31.
[6] V.P. Ranta, E. Toropainen, A. Talvitie, S. Auriola, A. Urttia, J. Chromatogr. B 772 (2002) 81–87.
[7] Y.J. Park, D.W. Lee, W.Y. Lee, Anal. Chim. Acta 471 (2002) 51–59.
[8] P. Vázquez, M. Galera, A. Guirado, M.M. Vázquez, Anal. Chim. Acta 666 (2010) 38–44.
[9] I. Baranowska, S. Magiera, J. Baranowski, J. Chromatogr. B 879 (2011) 615–626.
[10] S. Fan, J.H. Zou, H. Miao, Y.N. Wu, Y.F. Zhao, Chin. J. Anal. Chem. 39 (2011) 1153–1158.
[11] K. Hartonen, M. Riekkola, J. Chromatogr. B 676 (1996) 45–52.
[12] L. Amendola, F. Molaioni, F. Botrè, J. Pharm. Biomed. Anal. 23 (2000) 211–221.
[13] S. Magiera, C. Uhlschmied, M. Rainer, Ch.W. Huck, I. Baranowska, G.K. Bonn, J. Pharm. Biomed. Anal. 56 (2011) 93–102.
[14] M.M. Galera, P.P. Vázquez, M.M. Vázquez, Va´zquez, M.G. García, C.F. Amate, J. Sep. Sci. 34 (2011) 1796–1804.
[15] J.S. Huang, J.Y. Sun, X.G. Zhou, T.Y. You, Anal. Sci. 23 (2007) 183–188.
[16] R. Ariasa, R. Jiménez, R. Alonso, M. Télez, I. Arrieta, P. Flores, E. Ortiz-Lastra, J. Chromatogr. A 916 (2001) 297–304.
[17] D. Dogrukol-Ak, A.G. Dal, M. Tuncel, Chromatographia 66 (2007) 159–163.
[18] M.H. Lu, L. Zhang, B. Qiu, Q. Feng, S.F. Xi, G.N. Chen, J. Chromatogr. A 1193 (2008) 156–163.
[19] X.W. Zhang, Z.X. Zhang, Chin. J. Anal. Chem. 5 (2010) 648–652.
[20] L.A. Holland, A.M. Leigh, Electrophoresis 23 (2002) 3649–3658.
[21] M. Pumera, A. Escarpa, Electrophoresis 30 (2009) 3315–3323.
[22] B.G. Wei, J. Wang, Z. Chen, G. Chen, Chem. Eur. J. 14 (2008) 9779–9785.
[23] Z. Chen, L.Y. Zhang, G. Chen, Electrophoresis 30 (2009) 3419–3426.
[24] B. Chen, L.Y. Zhang, G. Chen, Electrophoresis 32 (2011) 870–876.
[25] D.X. Nie, P. Li, D. Zhang, T.S. Zhou, Y. Liang, G.Y. Shi, Electrophoresis 31 (2010) 2981–2988.
[26] A. Arvinte, F. Valentini, A. Radoi, F. Arduini, E. Tamburri, L. Rotariu, G. Palleschi, C. Balaa, Electroanal. 19 (2007) 1455–1459.
[27] M. Endo, Y.A. Kim, T. Fukai, T. Hayashi, K. Oshida, M. Terrones, T. Yanagisawa, S. Higaki, M.S. Dresselhaus, Appl. Phys. Lett. 80 (2002) 1267–1269.
[28] J. Jang, J. Bae, M. Choi, S.H. Yoon, Carbon 43 (2005) 2730–2736.
[29] V. Vamvakaki, K. Tsagaraki, N. Chaniotakis, Anal. Chem. 78 (2006) 5538–5542.
[30] H. Chen, L. Ding, X.J. Zhang, H.X. Ju, Anal. Chem. 79 (2007) 4442–4447.
[31] J. Zhang, J.P. Lei, Y.Y. Liu, I.W. Zhao, H.X. Ju, Biosens. Bioelectron. 24 (2009) 1858–1863.
[32] V. Stavyiannoudaki, V. Vamvakaki, N. Chaniotakis, Anal. Bioanal. Chem. 395 (2009) 429–435.
[33] D. Peckys, A. Melechko, M. Simpson, T. McKnight, Nanotechnol. 20 (2009) 145304–145311.
[34] D. Mann, T. McKnight, A. Melechko, M. Simpson, G. Sayler, Biotechnol. Bioeng. 97 (2007) 680–688.
[35] J.Y. Sun, C.Y. Zheng, X.L. Xiao, L. Niu, T.Y. You, E.K. Wang, Electroanal. 17 (2005) 1675–1680.
[36] Y. Liu, H.Q. Hou, T.Y. You, Electroanal. 20 (2008) 1708–1713.
[37] S.Q. Dong, L.Z. Chi, S. Zhang, P.G. He, Q.J. Wang, Y.Z. Fang, Anal. Bioanal. Chem. 391 (2008) 653–659.
[38] D.A. Garteiz, T. Walle, J. Pharm. Sci. 61 (1972) 1728–1731.