Colloids and Surfaces B: Biointerfaces 78 (2010) 217–221

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: www.elsevier.com/locate/colsurfb

Voltammetric sensor for buzepide methiodide determination based on TiO_2 nanoparticle-modified carbon paste electrode

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A R T I C L E I N F O

Article history:
Received 17 February 2010
Accepted 8 March 2010
Available online 12 March 2010

Keywords:
TiO_2 nanoparticles
Buzepide methiodide
Carbon paste electrode
Voltammetric determination
Biological fluids

A B S T R A C T

In this work, we have prepared nano-material modified carbon paste electrode (CPE) for the sensing of an antidepressant, buzepide methiodide (BZP) by incorporating TiO_2 nanoparticles in carbon paste matrix. Electrochemical studies indicated that the TiO_2 nanoparticles efficiently increased the electron transfer kinetics between drug and the electrode. Compared with the nonmodified CPE, the TiO_2-modified CPE greatly enhances the oxidation signal of BZP with negative shift in peak potential. Based on this, we have proposed a sensitive, rapid and convenient electrochemical method for the determination of BZP. Under the optimized conditions, the oxidation peak current of BZP is found to be proportional to its concentration in the range of 5×10^{-8} to 5×10^{-5} M with a detection limit of 8.2×10^{-9} M. Finally, this sensing method was successfully applied for the determination of BZP in human blood serum and urine samples with good recoveries.

1. Introduction

The electrochemical methods using chemically modified electrodes have been widely used as sensitive and selective analytical methods for the detection of trace amounts of biologically important compounds [1]. Recently, the conjugation of nanoparticles with biomaterials has become a tempting research project that provides a route into nanobiotechnology. It is reported that the incorporation of metal nanoparticles on carbon electrodes enhances the electron transfer rate [2]. So, the metal nanoparticle-modified electrodes are increasingly employed in many electrochemical applications. The large surface-to-volume ratio and active sites of these nano-sized metal particles, in electrocatalysis, constitute a part of the driving force in developing the nanosized electrocatalysts. Unlike bulk films, metal nanoparticles exhibit an unusual property of quantized double-layer charging effects [2].

Titanium dioxide (TiO_2) is a versatile material with a wide range of uses from pigments [3] to photocatalysts [4] and dimensionally stable electrode [5] applications. Recently, TiO_2 nanoparticles are being used as film-forming materials. Hence, there is a considerable interest in using TiO_2 nanoparticles as a modifier since they have high surface area, optical transparency, good biocompatibility and relatively good conductivity. The application of the carbon paste electrodes modified with nanostructure exhibit considerable improvements in electrochemical behavior of biologically important compounds [6,7]. Further, they show rather low background current compared to the solid graphite or noble metal electrodes [8].

BZP is an antidepressant [9], chemically known as 1-(4-amino-4-oxo-3,3-diphenylbutyl)hexahydro-1-methyl-1-hazepinium iodide. It is used in the treatment of functional intestinal disorders in combination with haloperidol [10]. In a metaanalysis of Randomized Clinical Trial (RCT) it was concluded that the antidepressants might be effective in reducing Irritable Bowel Syndrome (IBS) symptoms in about one-third of patients [11]. Since BZP is an antidepressant, attempts have been made to assess its effect to treat the IBS [12].

In our previous study [13], we have investigated the electrochemical behavior of BZP at GCE and its analytical applications. No attempt has been made so far to study the electrochemical behavior of BZP at bare or modified CPE. In view of this, we have investigated the electrochemical behavior of BZP at TiO_2 nanoparticle-modified CPE in detail. Further, we have successfully applied this sensing method for the determination of BZP in human blood serum and urine samples. The proposed method is observed to more sensitive and accurate than the previously reported methods [13].

2. Experimental

2.1. Apparatus

Electrochemical studies were carried out on a CHI-1110a electrochemical Analyzer (CH Instruments Ltd. Co., USA, version 4.01)

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doi:10.1016/j.colsurfb.2010.03.003

electrode system, including a CPE as the working electrode, a platinum wire as a counter electrode and an Ag/AgCl (3 M KCl) as reference electrode. All reported potentials are against Ag/AgCl (3 M KCl).

2.2. Reagents

A stock solution of BZP (2.5 mM) was prepared in Milli-Q water and acetonitrile mixture (70:30) and is stored in a refrigerator at 4 °C. In the present work, Britton–Robinson (BR) buffer of different pH was used as supporting electrolyte. All other chemicals used were of analytical reagent grade and Milli-Q water is used throughout.

2.3. Preparation of TiO_2-modified CPE

TiO_2 nanoparticle-modified CPE (TiO_2-CPE) is prepared [14,2] by mixing 20 mg TiO_2 nanoparticle with 500 mg graphite powder and 86 mg of paraffin oil. The paste was carefully mixed and homogenized in an agate mortar for 1 h. After that, the resulting carbon paste was tightly pressed into the end cavity (2-mm in diameter) of working electrode body. The electrode surface was gently smoothed by rubbing on a piece of weighing paper just prior to use. The electrical connection was implemented by a copper wire. Whenever necessary, a new surface was obtained by pushing out an excess of paste and polishing it on weighing paper. The unmodified CPE was prepared by the same procedure without addition of TiO_2 nanoparticle.

2.4. Working procedure

Working solutions were prepared by diluting the known amount of drug with the BR buffer of different pH. Before measurement, CPE is activated in blank supporting electrolyte by using successive cyclic scans from −0.10 to 1.2 V until stable voltammograms are obtained. After each measurement, the used paste was carefully removed from the end cavity and another new TiO_2-CPE was fabricated as mentioned above.

2.5. Determination of BZP in human urine and plasma samples

Spiked urine sample was obtained by treating 1.0 mL aliquot of urine with 100 µL BZP standard solution (2.5 mM). A suitable aliquot of spiked urine was diluted with phosphate buffer, without any pre-treatment, to prepare appropriate sample solutions and the DPV was recorded under optimized conditions.

Spiked serum samples were prepared as reported earlier [15]. Serum samples, obtained from healthy individuals (after having obtained their written consent), were stored frozen until assay. For the determination of BZP in plasma, 500 µL aqueous BZP solutions (10 µM) were added to 500 µL of untreated plasma. The mixture was vortexed for 30 s. In order to precipitate the plasma proteins, the plasma samples were treated with 250 µL of 15% $HClO_4$. After that, the mixture was vortexed for further 30 s and then centrifuged at 5000 rpm for 5 min. An appropriate volume of supernatant liquor was transferred in the voltammetric cell containing BR buffer of pH 7 and voltammograms were recorded. The voltammograms of samples without BZP did not show any signal that can interfere with the direct determination. The content of the drug in plasma was determined referring to the calibration graph or regression equation.

3. Results and discussion

3.1. Voltammetric behavior of BZP at TiO_2-CPE

Fig. 1 shows the CV of BZP at the bare and TiO_2-CPE, in BR buffer of pH 7.0 at the scan rate of 100 mV s^{-1}. BZP showed a quasireversible peak with oxidation peak potential at 0.649 V (a_1) and its corresponding reduction peak potential at 0.459 V (c_1) at TiO_2-CPE. Further, one irreversible oxidation peak at 0.945 V (a_2) is also observed. It is clear from the figure that the peak currents of all the peaks are observed to be increased with negative shift in peak potential at TiO_2-CPE compared to bare CPE. The shift in peak potential is about 0.045, 0.018 and 0.02 V for peaks a_1, c_1 and a_2, respectively.

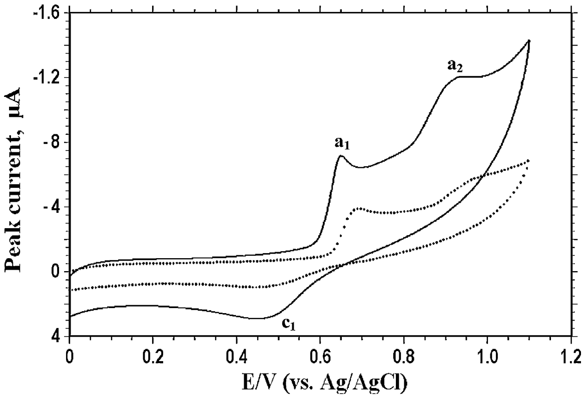

Fig. 1. CV of 5×10^{-5} M BZP at CPE-TiO_2 (solid line) and at bare CPE (dotted line) in phosphate buffer of pH 7 at a scan rate of 100 mV s^{-1}.

From the comparison of voltammograms of BZP at bare and TiO_2-CPE, it is clear that the TiO_2 nanoparticles significantly enhance the oxidation peak current of BZP. TiO_2 nanoparticles with regular and specific channels offer huge surface area and numerous active sites. Therefore, the TiO_2-CPE is more active for BZP and results in the remarkable enhancement of peak current. This behavior is consistent with a very strong electrocatalytic effect [2]. The peaks a_1 and c_1 are well defined and sharp while peak a_2 is broad and ill-defined. Therefore, all the measurements were made referring to peak a_1 and c_1 only.

3.2. Effect of pH

Influence of pH on electrochemical behavior of 50 µM BZP at TiO_2-CPE is investigated in the pH range of 2.1–10. The effect of pH on peak potential and peak current of a_1 and c_1 is demonstrated in Fig. 2a and b. The peak current of a_1 and c_1 increased with increase in pH in the range of 2.1–7 at TiO_2-CPE. This revealed that the pH of the supporting electrolyte exerted a significant influence on electrooxidation of BZP at TiO_2-CPE. Above pH 7, the peak a_1 became broader, ill-defined and undetectable while c_1 peak disappeared. This indicated that the oxidation of a_1 became irreversible above pH 7. The best results with respect to enhancement, shape and reproducibility of the peak current were obtained in BR buffer solution of pH 7. For this reason, we have considered BR buffer of pH 7 for analytical applications.

3.3. Effect of scan rate

Scan rate plays an important role in electrochemical investigation as it influences the rate of adsorption of species on the electrode. The effect of scan rate on voltammogram of BZP at TiO_2-CPE was investigated in BR buffer of pH 7 (Fig. 3).

With increase in scan rate, the electrooxidation of peak current of BZP increased with positive shift in peak potential, suggesting a kinetic limitation in the reaction [16]. The plot of $\log i_p$ *versus* $\log \upsilon$ in the scan rate range of 10–200 mV s^{-1} yielded a straight line with a slope of 0.55. This value was observed to be close to the theoretical value of 0.5, which is expected for an ideal reaction condition for a diffusion-controlled electrode process [17].