A Simple And Rapid Electrochemical Determination Of Tramadol In Biological Fluids And Pharmaceutical Preparations Utilizing A Nanoparticles Decorated Carbon Paste Electrode

Rasha A. Ahmed 1,2

1 Chemistry Department, Faculty of Science, Taif University, Saudi Arabia
2 Forensic Chemistry Laboratories, Medical Legal Department, Ministry of Justice, Cairo, Egypt.

Abstract

Tramadol is a narcotic-like pain reliever, like morphine. Tramadol can still be addictive in a unique way to other drugs [1]. In addition, its overdose can cause dizziness, vomiting, and nausea since it is considered as a toxic material in nature. Therefore, developing sensitive and selective method for its determination in biological samples is highly desirable in clinical contexts and diagnostic research. Several analytical techniques have been reported for the determination of TRA in biological and environmental samples such as high-performance liquid chromatographic (HPLC) [2,3], mass spectrometry [4], fluorescence detection [5], gas chromatography (GC) [6]. It is necessary to note that therapeutic level of tramadol in plasma samples is within the range of 100–300 ng/mL and its concentration in urine depends on the prescribed dosage [1]. This concentration range is below the detection limit of most analytical instruments. Besides, direct analysis of biological samples is not possible due to the presence of interfering compounds along with the desired molecule. However all these techniques are associated with problems like higher time consumption for sample preparation, use of harmful and costly chemicals and pricey instrumentation. Furthermore, matrix effect, and low sample concentration can retard Tramadol determination. Voltammetric analysis inherits numerous advantages in comparison to above mentioned methods on account of its instrumental simplicity, ease of sample preparation, lower cost and higher sensitivity [7]. Among voltammetric methods, DPV is considered as the most sensitive and rapid technique for trace analysis of pharmaceuticals. Moreover the exploitation of nanomaterials in the field of electroanalysis has revolutionized the sensing capability of traditional electrodes. Owing to small size (1–100 nm) metal oxides nanoparticles exhibit unique physical, chemical and electronic properties that can be exploited into sensors with remarkable sensitivity [8]. In the present work, a novel strategy was introduced to promote the electroanalysis technique by mixing TiO2 and ZnO2 nanoparticles to carbon paste electrode for TRA determination in urine and pharmaceutical formulations.

Introduction

Tramadol is a narcotic-like pain reliever, like morphine. Tramadol can still be addictive in a unique way to other drugs [1]. In addition, its overdose can cause dizziness, vomiting, and nausea since it is considered as a toxic material in nature. Therefore, developing sensitive and selective method for its determination in biological samples is highly desirable in clinical contexts and diagnostic research. Several analytical techniques have been reported for the determination of TRA in biological and environmental samples such as high-performance liquid chromatographic (HPLC) [2,3], mass spectrometry [4], fluorescence detection [5], gas chromatography (GC) [6]. It is necessary to note that therapeutic level of tramadol in plasma samples is within the range of 100–300 ng/mL and its concentration in urine depends on the prescribed dosage [1]. This concentration range is below the detection limit of most analytical instruments. Besides, direct analysis of biological samples is not possible due to the presence of interfering compounds along with the desired molecule. However all these techniques are associated with problems like higher time consumption for sample preparation, use of harmful and costly chemicals and pricey instrumentation. Furthermore, matrix effect, and low sample concentration can retard Tramadol determination. Voltammetric analysis inherits numerous advantages in comparison to above mentioned methods on account of its instrumental simplicity, ease of sample preparation, lower cost and higher sensitivity [7]. Among voltammetric methods, DPV is considered as the most sensitive and rapid technique for trace analysis of pharmaceuticals. Moreover the exploitation of nanomaterials in the field of electroanalysis has revolutionized the sensing capability of traditional electrodes. Owing to small size (1–100 nm) metal oxides nanoparticles exhibit unique physical, chemical and electronic properties that can be exploited into sensors with remarkable sensitivity [8]. In the present work, a novel strategy was introduced to promote the electroanalysis technique by mixing TiO2 and ZnO2 nanoparticles to carbon paste electrode for TRA determination in urine and pharmaceutical formulations.

Results

The surface morphology of carbon paste electrode CPE and the modified TiO2-ZnO2-CPE was investigated by scanning electron microscopy (SEM) as shown in Figure 1. TiO2-ZnO2 NPs were uniformly monodispersed at the carbon paste (Figure 1B). They appeared as spherical nanoparticles of diameters in the range of 10–30 nm. Bi-oxides nanoparticles work on increasing the surface area responsible for drug adsorption. Differential pulsed voltammetry was utilized to investigate the electrochemical behavior of 1 mM TRA in phosphate buffer solution (pH 7.0) (Figure 2) at (a) a bare CPE, (b) modified ZnO2/CPE, (c) TiO2/CPE, and (d) bi-oxide TiO2-ZnO2/CPE. The Differential pulsed voltammogram of TRA showed a weak oxidation behavior at the bare CPE. On the TiO2-ZnO2/CPE, TRA oxidation peak was enhanced, showing the electrocatalytic effect of the bi-oxides nanoparticles on the CPE, due to the high surface area of the nanoparticles which facilitates the TRA adsorption.

Figure 3. Uric acid (UA) and Ascorbic acid (AA) co-exist in the extracellular fluid of the central nervous system and serum. DPV mode was used for the oxidation of a solution containing equimolar concentrations of 1.0 mM of TRA, AA and UA. The oxidation peak potentials of TRA, UA and AA are well-resolved at TiO2/ZnO2-CPE. The large separation of the peak potentials allows for the first time selective and simultaneous determination of TRA, AA and UA in their mixture.

Methods

This schematic diagram illustrates the stepwise mixing of ZnO2 with TiO2 with carbon and addition of paraffin oil to form a paste, then an empty electrode will be filled with this paste. The modified electrode is connected to a three electrode cell with reference and auxiliary electrode and connected to the Autolab. The test solution is Tramadol and buffer solution.

Figures and Tables

Figure 1. SEM for (A) CPE and (B) modified CPE for TiO2/ZnO2/CPE. The red arrows shows the value of the enhanced current in presence of bi-oxide nanoparticles.

Table 1. Recoveries in spiked human urine samples

| | | | | | |
|---|---|---|---|---|
| | | | | |
| 1 | 0.00 | 3.00 | 94.3 | 2.4 |
| 2 | 0.00 | 10.14 | 104.2 | 3.3 |
| 2 | 12.95 | 10.15 | 106.2 | 3.9 |

Figure 2. Differential puls voltammetry of 1 mM TRA in phosphate buffer solution (pH 7.0) at (a) a bare CPE, (b) modified ZnO2/CPE, (c) TiO2/CPE, and (d) bi-oxide TiO2-ZnO2/CPE. The red arrows shows the value of the enhanced current in presence of bi-oxide nanoparticles.

Table 2. Tablet results and recoveries obtained for four determinations of TRA in spiked tramadol tablets

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean % recovery (n=4)</th>
<th>RSD %</th>
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<td>1</td>
<td>101.4</td>
<td>3.0</td>
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<tr>
<td>2</td>
<td>99.3</td>
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<td>3</td>
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<td>96.2</td>
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Conclusions

Employing ZnO2 and TiO2 nanoparticles as modifiers for carbon paste electrode, a novel sensor has been developed for determination of TRA concentration using the voltammetry technique. The obtained results are the basis for the optimization of Tramadol determination by simple, instant and sensitive method, without sample pretreatment and no matrix interference. Furthermore, determination of Tramadol is carried out without using HPLC or GC/MS, which are expensive instruments. The increase of the electroactive surface area and the synergistic electrocatalytic activity that were achieved by combining bi-oxides nanoparticles with CPE are responsible for the improved performance of the modified electrode.

This method has demonstrated that it is easy to discriminate TRA from AA and UA that are common interferences in biological fluids. This electrode can detect TRA in its pure form and pharmaceutical formulation and in human urine without pretreatment for the samples. On the basis of the obtained results it can be stated that nanoparticles/carbon paste electrode can be applied in clinics and hospital for Tramadol determination even if it is in nano concentration range.

References


Bibliography

Rasha Afif is working as Assi. Prof. of physical chemistry and material science in Taif University, KSA since (2012). She is an Expert in toxicology and Narcotic drugs, Ministry of Justice, Egypt (2004). She did her Ph.D. in Cairo University (2011). Her research interests includes the usage of different nanomaterials, and conducting polymers to develop new electrochemical sensor and/or biosensor for the determination of narcotic and neurotransmitter drugs in urine and pharmaceutical formulations. Email: rashaafif@yahoo.com