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Voltammetric determination of zolpidem by using glassy carbon electrode modified with Ag/ZnO nanoplates

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Abstract

Zolpidem is an imidazopyridine derivative, non-benzodiazepine and sedative-hypnotic medicine. It is a widely prescribed medication in adults used for the short-term treatment of a sleep problem called insomnia and frequent awakenings. In this work, the zolpidem was determined using Ag/ZnO nanoplates modified glassy carbon electrode (Ag-ZnO/GCE). Electrochemical behavior of the zolpidem was investigated by differential pulse voltammetry (DPV), chronoamperometry (CHA), and cyclic voltammetry (CV) using the Ag-ZnO/GCE. The results revealed that, the current responses of the zolpidem improved significantly due to the high catalytic activity and electron transfer reaction of nanoplates. The linear range of zolpidem was found to be from 0.1 µM to 500.0 µM with the detection limit of 0.03 µM. In addition, this original sensor showed numerous benefits such as reproducibility, high stability, and rapid response (20 s).

Keywords: Zolpidem; voltammetric determination; glassy carbon electrode; Ag/ZnO nanoplates.

Introduction

Zolpidem is an imidazopyridine derivative and non-benzodiazepine sedative-hypnotic drug [1]. Zolpidem is structurally different from the benzodiazepines; however, they both have the same pharmacological effect. Zolpidem has a rapid onset of action. It has short half-life and anticonvulsant effects, and used for treatment of anxiety and sleep disorders [2]. Zolpidem has a highly selective interaction with omega-1 receptor subtype belonging to the γ-aminobutyric acid (GABA)ergic system, which is mostly associated with sleep [3-5]. Zolpidem has been quantified in various biological samples using common analytical techniques including,

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high performance liquid chromatography [6], GC/MS [7], chemiluminescence [8], spectrophotometry [9], radioimmunoassay [10], gas chromatography [11], and electrochemical methods [12,13].

Majority of the approaches are time consuming and have entail inadequate sensitivity, made them complicated experiment procedures. Compared to other approaches, the electrochemical approaches exhibited some advantages such as enhanced sensitivity and selectivity. Thus, there is substantial focus on developing a straightforward, expeditious, cost-efficient, and sensitive electrochemical approach to detect analytes [14-25]. Due to the exceptional characteristics of the nanoparticles, they have been used in various industries. Several factors may impact nanoparticles structure including the adopted approach and temperature [26-42].

New platforms should meet some factors such as low detection limits, good stability, simplicity, low cost, and high speed. Moreover, prompt response is vital in most situations such as illness diagnostics which will entail faster treatment. Some of the techniques should be integrated under such new lenses. Electrochemical detection was found to be suitable to be combined with the paper based analytical device, as such combination may enhance analyte quantification, resulting in increased sensitivity and reduced detection limits as well as characteristics such as low costs, simplicity, portability, and miniaturization [47,48].

To the best of our knowledge, no study has been reported so far on the determination of zolpidem by using Ag-ZnO/GCE. In this research study, we report the preparation and application of Ag-ZnO/GCE for the determination of zolpidem without any additional modification such as addition of electron transfer mediator or specific reagents for the first time. The main objectives of this Ag-ZnO/GCE for determination of zolpidem are: wide linear dynamic range, short time of the procedure and no use of electron transfer mediator.

Experimental

Chemicals and apparatus

An Autolab potentiostat/galvanostat (PGSTAT 302N, Eco Chemie, the Netherlands) was utilized to conduct electrochemical measurements. The General Purpose Electrochemical System (GPES) software was used to control the defined experimental settings. A glassy carbon electrode (Azar Electrode, Urmia, Iran with 2 mm diameter) modified with Ag/ZnO nanoplates as working electrode, an Ag/AgCl/KCl (3.0 M) reference electrode (Azar Electrode, Urmia, Iran) and a platinum wire counter electrode (Azar Electrode, Urmia, Iran) are the parts that form the electrochemical cell. To measure the pH, a 710 pH meter metrohm was used.

Analytical grade zolpidem was used along with all other analytical grade reagents which were obtained from Merck, Darmstadt, Germany. Orthophosphoric acid was used to prepare buffer solution. The relevant salts were above 2.0-9.0 pH range. Ag/ZnO nanoplates were synthesized as the procedure reported previously [49].

Formation of electrode

Ag-ZnO nanoplates was applied as coating on the bare glassy carbon electrode. Dispersion of 1 mg of Ag-ZnO nanoplates with ultrasonication for 1 h was used to prepare a stock solution of Ag-ZnO nanoplates in 1 mL of the aqueous solution, whereas 5 µL of aliquots of the Ag-ZnO nanoplates/H_2O suspension solution was cast on the glassy carbon electrode. Then, it

remained up to the time of evaporation of the solvent in room temperature.

Real specimen preparation

Five tablets of zolpidem were grinding. By dissolving 100 mg of the powder in 25 mL water using ultrasonication, the solution of tablet was prepared. Various amounts of this solution was transferred into cell and diluted with buffer solution. The amount of the drug in tablet was obtained using the standard addition method. Upon collecting urine samples, they were promptly kept in a refrigerator for 15 min at 2000 rpm centrifugation was implemented for 10 mL of the samples. A 0.45 µm filter was used to filter the supernatant. Then, various solution volumes were put into a 25 mL volumetric flask prior to being diluted with PBS of pH 7.0 to the mark. Various volumes of zolpidem were used to spike the diluted urine samples. The proposed method was used to analyse the zolpidem contents using the standard addition method.

Results and discussion

Zolpidem electrochemical profile on Ag-ZnO/GCE

The electrochemical behaviour of zolpidem is dependent on the pH value of the aqueous solution (Figure 1). Thus, optimizing the solution pH would apparently be crucial for achieving zolpidem electro-catalytic oxidation. Therefore, CV was used to explore the zolpidem electrochemical behaviour in 0.1 M PBS in diverse pH-values (2.0<pH <9.0) on Ag-ZnO/GCE surface (Figure 2). Outputs revealed that, the zolpidem electro-catalytic oxidation at the Ag-ZnO/GCE surface has been very desirable under the neutral conditions compared to in the basic or acidic media. Therefore, such a condition would appear as the progressive development in the anodic peak current in the CVs equal to zolpidem. Finally, pH of 7.0 was targeted as an optimized pH for electrocatalyzing zolpidem oxidation at Ag-ZnO /GCE surface.

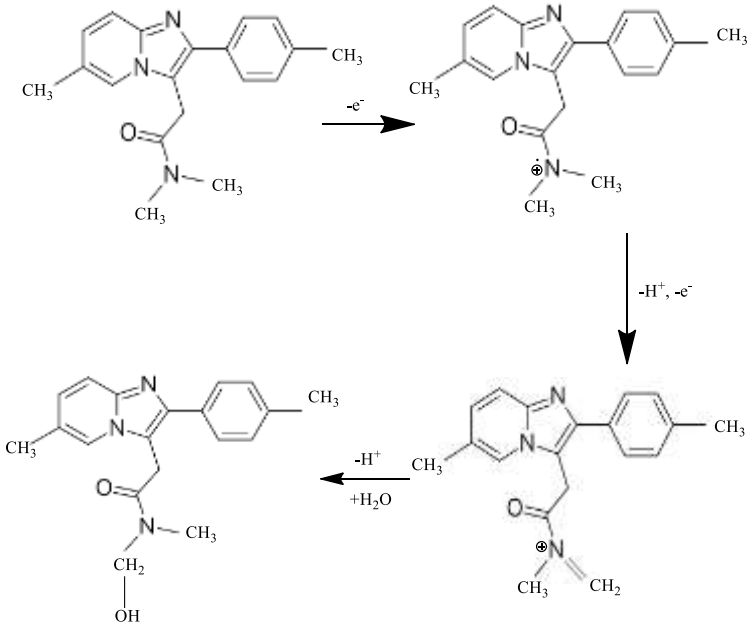

Figure 1. Electrochemical mechanism for oxidation of zolpidem

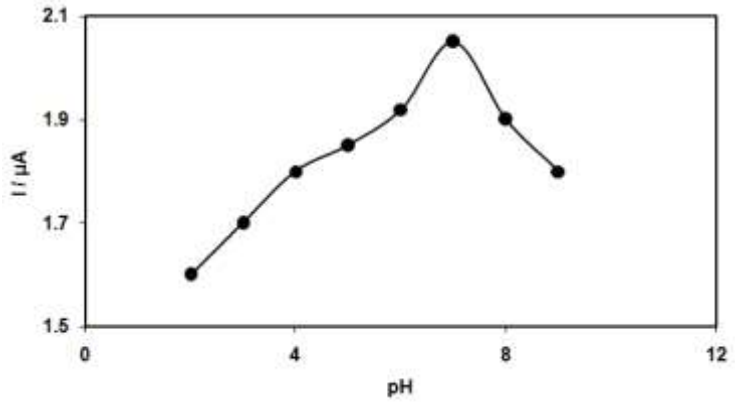

Figure 2. Plot of I_p vs. pHs of buffer solution (2.0, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0 and 9.0) in the presence of 200.0 µM zolpidem

Figure 3 depicts the 100.0 µM of zolpidem cyclic voltammograms acquired by applying the unadjusted GCE (Curve a) and Ag-ZnO/GCE (Curve b). Regarding the zolpidem oxidation at the adjusted electrode surface, the peak potential was at 900 mV. This value is 200 mV more negative compared to that of the unadjusted GCEs. This showed a significant improvement of the electrode performance toward zolpidem oxidation by changing the constant GCE with Ag/Zno nanoplates. Curve c shows the Ag-ZnO/GCE in 0.1 M PBS (pH 7.0) in the absence of zolpidem.

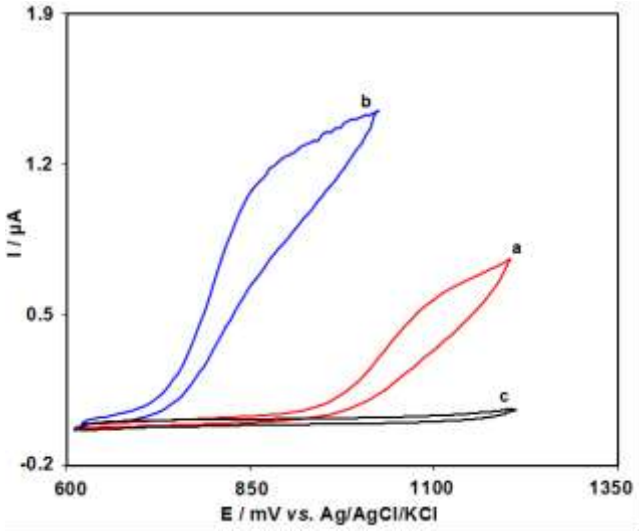

Figure 3. Cyclic voltammograms of (a) bare GCE and (b) Ag-ZnO/GCE in 0.1 M PBS (pH 7.0) in the presence of 100.0 µM zolpidem at the scan rate 50 mVs^{-1}. Also curve c shows Ag-ZnO/GCE in 0.1 M PBS (pH 7.0) in the absence of zolpidem

Effect of scan rate

Figure 4 depicts the impacts of possible scan rates on zolpidem oxidation currents, showing that by enhancing the scan rate, the peak currents enhanced. Moreover, due to the linear Ip plot against the potential scan rate square root ($\nu^{1/2}$) for the zolpidem, it was proven that oxidation procedure was diffusion regulated [50].

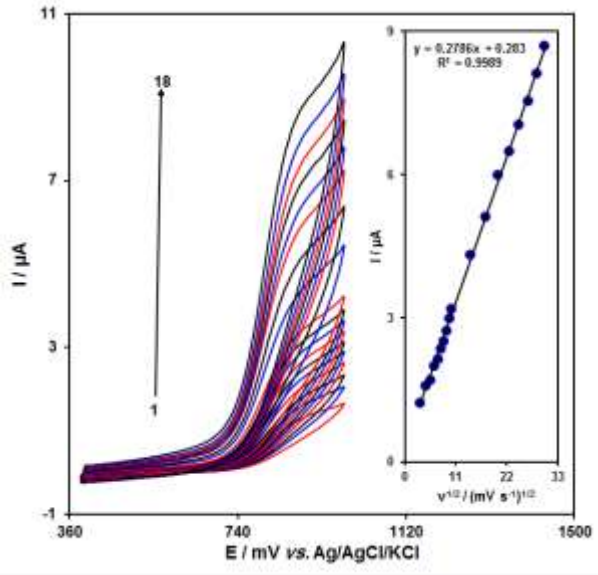

Figure 4. Cyclic voltammograms of Ag-ZnO/GCE in 0.1 M PBS (pH 7.0) containing 200.0 µM zolpidem at various scan rates; numbers 1-18 correspond to 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800 and 900 mV s^{-1}, respectively. Inset: variation of anodic peak current vs. $v^{1/2}$.

Chronoamperometric analysis

The zolpidem specimen' chronoamperometric analysis via the Ag-ZnO/GCE was conducted at 950 mV and the outcomes for various zolpidem specimens in PBS, pH=7.0 are depicted in Figure 5. For electroactive materials' chronoamperometric analysis at transfer restricted circumstances, the Cottrell equation is as following (Equation 1).

$$I = nFAD^{1/2}C_b\pi^{-1/2}t^{-1/2} \quad (1)$$

Where D is the diffusion coefficient (cm^2 s^{-1}), and C_b is the bulk concentration (mol cm^{-3}). Optimal I vs. $t^{-1/2}$ plots on the basis of the experiment was depicted for the various zolpidem specimens and the straight line slope was plotted against the zolpidem concentrations. D was obtained 3.3×10^{-6} cm^2/s for the zolpidem.

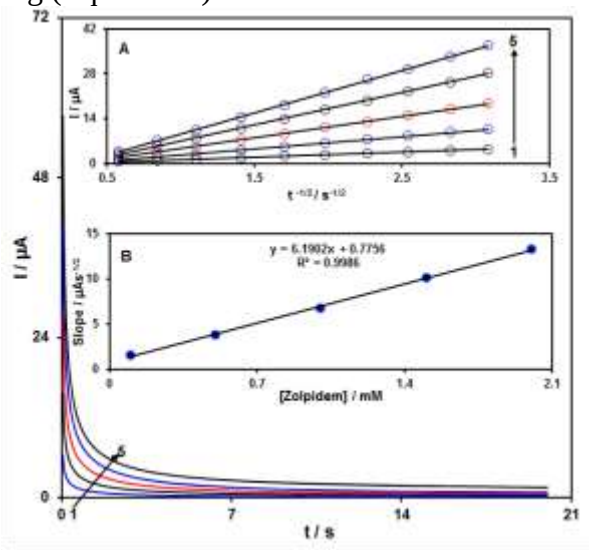

Figure 5. Chronoamperograms obtained at Ag-ZnO/GCE in 0.1 M PBS (pH 7.0) for different concentration of zolpidem. The numbers 1–5 correspond to 0.1, 0.5, 1.0, 1.5 and 2.0 mM of zolpidem. Insets: (A) Plots of I vs. $t^{-1/2}$ obtained from chronoamperograms 1–5. (B) Plot of the slope of the straight lines against zolpidem concentration.

Calibration curve

The zolpidem peak currents *via* the Ag-ZnO/GCE were applied to quantitatively analyse the zolpidem within water solutions. Due to the differential pulse voltammetry advantages concerning enhanced sensitivity and improved investigative utilization properties. The adjusted electrode was applied as a working electrode in DPV analysis within the zolpidem range solution in 0.1 M PBS (Step potential=0.01 V and pulse amplitude=0.025 V). In regard to DPV of zolpidem via Ag-ZnO/GCE, linear activity was evident within the 0.1 -500.0 µM range and correlation coefficient of 0.9994 (Figure 6). The relevant detection limit was 0.03 µM. Table 1 depicts a comparison of analytical properties for the detection of zolpidem at the prepared electrode in this work.

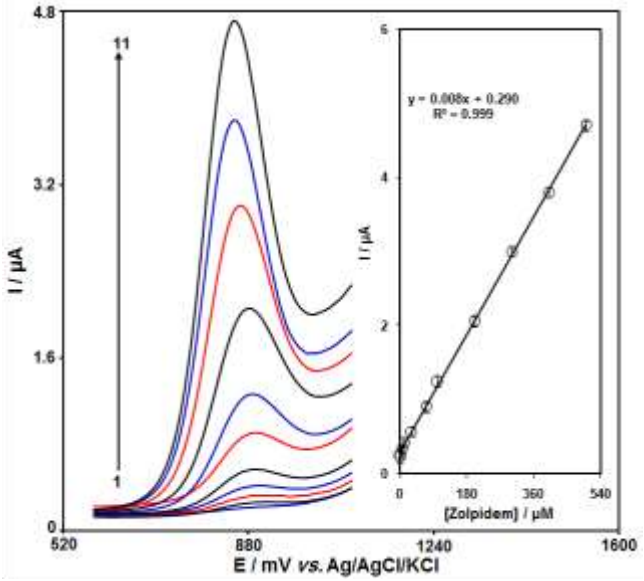

Figure 6. DPVs of Ag-ZnO/GCE in 0.1 M (pH 7.0) containing different concentrations of zolpidem. Numbers 1–11 correspond to 0.1, 1.0, 5.0, 10.0, 30.0, 70.0, 100.0, 200.0, 300.0, 400.0 and 500.0 µM of zolpidem. Inset: plot of the peak current as a function of zolpidem concentration in the range of 0.1-500.0 µM.

Table 1. A comparison of the efficiency of various modified electrodes reported for the detection of zolpidem.

Electrode	Modifier	LOD (µM)	LDR (µM)	Ref.
Pencil Graphite Electrode	-	1.0	10-30	12
Glassy Carbon Electrode	-	0.2	0.5–10	13
Glassy Carbon Electrode	Ag/ZnO nanoplates	0.03	0.1-500.0	This work

Interference studies

This study examined the effects of diverse materials as the compounds with a potential interference with zolpidem detection under the optimized conditions with 50.0 µM zolpidem at pH=7.0. It should be noted that, the potentially interfering materials have been selected from a group of materials that are usually observed with zolpidem in the biological fluids. Moreover, the limit of tolerance was described as the highest concentration of the interfering material with the standard deviation of ±5%. As shown by the outputs, glucose, NADH, acetaminophen, uric acid, dopamine, epinephrine, norepinephrine, isoproterenol, lactose, saccarose,

fructose, benzoic acid, methanol, ethanol, urea, caffeine, Ca^{2+}, Mg^{2+}, Al^{3+}, NH_4^+, Fe^{+2}, Fe^{+3}, F^-, SO_4^{2-} and S^{2-} had no interference with the zolpidem detection.

Repeatability and stability of Ag-ZnO/GCE

Long-term stability of the Ag-ZnO/GCE was assessed over a 3-week period. The CVs were recorded after the modified electrode was stored in atmosphere at room temperature. The peak potential for zolpidem oxidation was found to be unchanged and the current signals revealed less than 2.3% decrease relative to the initial response. The antifouling properties of the modified electrode toward zolpidem oxidation and its oxidation products were investigated by recording the CVs of the modified electrode prior and after being used at the presence of the zolpidem. The CVs were recorded at the presence of the zolpidem after having cycled the potential 15 times at a scan rate of 50 $mV.s^{-1}$. The peak potentials were unchanged and the currents decreased by less than 2.2%. Therefore, the sensitivity of the Ag-ZnO/GCE increased, and the fouling effect of the analyte and its oxidation decreased.

Analysis of real samples

To evaluate the zolpidem within the real specimens, the presented approach was implemented to determine zolpidem in the form of tablet sample and urine. Thus, the standard addition method was implemented for this analysis and the outcomes are presented in Table 2. The acquired zolpidem recoveries were found to be adequate and the reproducibility of the results was on the basis of the mean relative standard deviation (RSD).

Table 2. The application of Ag-ZnO/GCE for determination of zolpidem in real samples (n=5). All concentrations are in µM.

Sample	Spiked	Found	Recovery (%)	R.S.D. (%)
Tablet	0	5.0	-	3.2
	2.5	7.6	101.3	2.2
	5.0	9.7	97.0	2.4
	7.5	12.4	99.2	1.7
	10.0	15.5	103.3	2.9
Urine	0	-	-	-
	5.0	4.9	98.0	2.7
	10.0	10.3	103.0	1.8
	15.0	15.2	101.3	3.4
	20.0	19.5	97.5	2.3

Conclusion

In this study, Ag/ZnO nanoplates were synthesized. An original sensing layer was fabricated by incorporating the assembled Ag/ZnO nanoplates within a glassy carbon electrode to determination of zolpidem. When the peak currents were plotted against the analyte concentrations within the 0.1 µM to 500.0 µM range, the linear calibration curve was acquired. The zolpidem detection limit was 0.03 µM. The resulting electrode displayed favorable results when used to determine the zolpidem within the real samples.

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