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Full Paper

Sensitive Electrochemical Determination of Oxcarbazepine using MWCNT Modified Glassy Carbon Electrode

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Abstract- In this research project, an electrochemical sensor was developed to sensitively detect oxcarbazepine compound at a new level of glassy carbon using carbon nanotubes. The surface morphology of the resulting modified electrode was determined by field emission scanning electron microscopy technique (SEM). Under optimal conditions, a significant improvement in the electrochemical behavior of oxcarbazepine was observed at the surface of the modified electrode compared to the unmodified electrode. The results show that the electrocatalytic oxidation process of oxcarbazepine on the surface of the modified electrode is controlled by the diffusion process and the electrode process is controlled by surface adsorption. Modified Electrode by carbon nanotubes due to its high conductivity, good stability, ability to increase the electron transfer rate, and finally, the effective interaction of the analyte with the electrode surface increases the sensitivity in measuring oxcarbazepine compound and its electrocatalytic properties as an electrochemical sensor improved analyte drug measurement. Based on this study, the calibration plots to determine Oxcarbazepine concentrations were linear in the range of 2–40 µM (R^2= 00.9912), and the detection limits were found to be 1.9 µM. The results indicate that the proposed method is sensitive, selective, fast, and simple for the determination of Oxcarbazepine.

Keywords- Multi-walled carbon nanotubes; Modified-glassy carbon electrode; Determination of oxcarbazepine; Analyte drug; Sensor

1. INTRODUCTION

Oxcarbazepine (10,11-dihydro-10-oxo-5H-dibenz [b, f] azepine-5-carboxamide) (Figure 1) is one of the drugs used in the group of antiepileptic drugs. In this disease, seizures occur in most of the disturbed electrical current of cells in a part of the brain. Oxcarbazepine has been used as a voltage-dependent sodium channel blocker before and after synapse in the central nervous system for several years to treat generalized minor seizures, trigeminal neuralgia, and emotional disorders [1,2]. A seizure is a nerve attack caused by a disturbance in the electrical activity of the brain. Oxcarbazepine is used to transmit seizures by reducing abnormal electrical current in brain cells alone or in combination with other antiepileptic drugs [3,4].

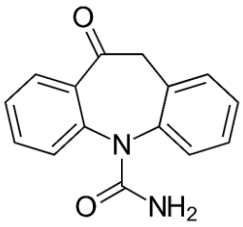


Figure 1. Chemical structure of oxcarbazepine

Voltammetry is widely used by a large number of chemists, physicists, and biochemists for the fundamental study of redox processes in various media [5,6], surface adsorption processes, and electron transfer mechanisms at the surface of chemically modified electrodes. In general, voltammetry involves a series of analytical methods in which information about compounds is obtained by following the current as a function of the applied potential. In voltammetry methods, the species react at the electrode level, and by plotting the intensity of the resulting current relative and quantitative and qualitative information about the species is obtained [7]. Cyclic voltammetry is more practical than any other method for obtaining information about the characteristics of electrode reactions. The value of this method is due to the considerable information that is rapidly related to the nature of electrode reaction (whether cathodic or anodic) that is, by the kinetics of non-uniform electron exchange reaction or chemical reactions, the electrode reactions and finally, the adsorption processes and their effect on the electrode processes are provided [8,9]. The study of the mechanism of electrode processes is shown using cyclic voltammetry and hanging mercury droplet electrodes. In the cyclic voltammetry method, the potentials applied to a working electrode in a stationary solution are changed according to a triangular program with respect to time [10]. However, in some cases, it is possible to repeat the change in the potential value of the electrode over several consecutive cycles. Then the current intensity changes are plotted according to the applied potential change. Carbon nanotubes were invented in 1991 by Sumio Iigima [11]. These compounds have received much attention due to their special electrical and mechanical properties. Recent studies show that carbon nanotubes have formed a new type of carbon material that has wider applications in

various fields such as energy conversion and strong [12], electrochemical actuators [13], chemical sensors [14], lithium storage [15], and hydrogen [16]. Nanotubes were divided into two categories: single-walled carbon nanotubes (SWCNT) and multi-walled carbon nanotubes (MWCNT). Carbon nanotubes, in addition to being very strong, also have good flexibility. One of its applications is composite. The most important property of nanotubes is their electrical conductivity, which varies depending on the order of the atoms. Carbon nanotubes themselves do not have any oxidative activity, but because of the properties mentioned above, they are very important for modifying the surface of the electrode.

. In recent years, chemically modified electrodes have attracted much attention. In chemically modified electrodes, a specific chemical compound called a modifier, is fixed on the surface of the electrode. This chemical participates as an intermediary in the electron exchange reaction. Electrochemists have found that placing different compounds as modifiers on a conductive or semiconductor substrate strongly affects the behavior of the electrodes so the electrochemical properties of some electroactive materials on the surface of such electrodes are quite different from unmodified electrodes. In studies, electrochemists have found that if the nature of the surface layer of an electrode can be changed in an appropriate way, a variety of electrochemical properties can be expected for a compound on the surface of that electrode. Modified electrodes also increase the selectivity of electrochemical reactions and eliminate the interference of the surface adsorption of different species on the electrode surface [17-20].

Therefore, the aim of the present work is to study the electrode reaction of Oxcarbazepine at a glassy carbon electrode (GCE) by using CV and differential pulse voltammetric techniques (DPV). The electrode process dynamic parameters were also investigated by cyclic voltammetry. The optimum experimental conditions for the determination of Oxcarbazepine were also investigated. As a result, a sensitive, fully validated, rapid, Linear dynamic range, and selective voltammetric method was developed for the simple and direct determination of Oxcarbazepine in pharmaceutical formulations levels in human plasma samples using a DPV technique, which is one of the advantages of this research compared to similar works [21-23].

2. EXPERIMENTAL SECTION

2.1. reagents and materials

Oxcarbazepine, dimethyl form amide (DMF), and methanol were of analytical grade supplied by Merck. Multi-walled carbon nanotubes (OD=10^{-30} nm, ID=5^{-10}nm, length=0.5^{-500} μm, 95%) were purchased from Aldrich. Deionized water was used for the preparation of all solutions. Phosphate buffer solutions were prepared with 0.1 mol L^{-1} NaH_2PO_4-Na_2HPO_4 and by adjusting the pH with 0.1 mol L^{-1} H_3PO_4 and 0.1 mol L^{-1} NaOH. The pH of the solutions was adjusted to 7 with phosphate buffer. All aqueous solutions were prepared in twice-distilled de-ionized water and used analytical-grade chemicals. Argon gas (purity 99%) was used to remove oxygen in the experimental solutions.

2.2. Apparatus

Electrochemical measurements were performed with an Autolab potentiostat/galvanostat model PGSTAT 30 (Metrohm, Utrecht, Netherlands), and a system was run on a PC using GPES 4.9 software. A three-electrode cell, consisting of a GCE, modified with MWCNT as a working electrode. A platinum wire was employed as a counter electrode, and a saturated Ag/AgCl (saturated KCl) served as the reference electrode, and all potentials in the text refer to it. The pH measurements were made with a Metrohm 632 pH meter using a combined glass electrode. A personal computer was used for data storage and processing. The morphology of GCE modified with MWCNTs surface was observed using a scanning electron microscope (SEM) from SERON technology AIS-2100. All electrochemical experiments were performed at room temperature (25±0.5) °C.

2.3. preparation of MWCNT (multi-walled carbon nanotubes)- modified GGE

Preparation of carbon nanotube suspension pour 1mg of multi-walled carbon nanotube powder into mL of DMF solvent (dimethyl form amide) and expose to sound waves in an ultrasonic device for 60 minutes to obtain a uniform solution. Before electrochemical modification, the surface bare GCE was polished with alumina powder (Al_2O_3) and washed first with acetone, then it was rinsed. The electrode was then placed in 10 mL of 1 mM hexacyanoferrate solution, and by applying one cycle in the potential range of -0.2 to 0.8 V, the surface of the electrode was ensured to be clean. In the next step, the electrode was placed in a fixed position, and 10 µL of carbon nanotube solution was injected into it by the sampler (Figure 2).

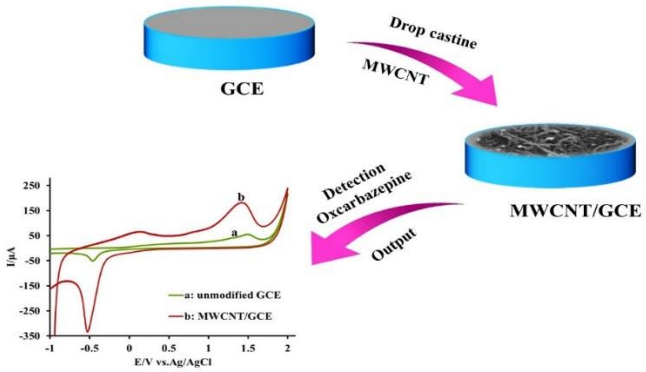


Figure 2. Schematic of modified electrode preparation

2.4. Determination of oxcarbazepine in blood serum

According to the results of differential pulse voltammograms in the measurement of oxcarbazepine in this part to check the efficiency of the modified electrode, its measurement was done in the blood serum sample as a real sample of blood serum was kept in the refrigerator

for one day and night before use to form a clot. Then, 1.5 mL of blood serum sample, and 2 mL of methanol were added in order to the proteins in the blood and it was placed on a stirrer for 5 minutes and then centrifuged for 10 minutes to separate the phases. Centrifuge the supernatant solution, the clear solution obtained with 0.1 mol L^{-1} phosphate buffer, pH = 7, about 10 mL was reached and then it was transferred to the electrochemical cell for analysis and using the measurements voltammogram was recorded by differential pulse method.

3. RESULTS AND DISCUSSION

3.1. The electrochemical response of oxcarbazepine at modified GCE

Figure 3 shows CV curves of 2.0×10^{-5} mol L^{-1} oxcarbazepine at bare GCE (a) and modified GCE (b) in 0.1 mol L^{-1} PBS (pH 7.0), respectively

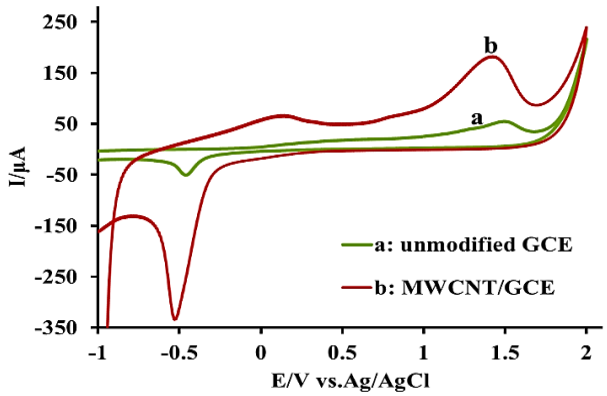


Figure 3. Cyclic voltammograms of 2.0×10^{-4} mol L^{-1} oxcarbazepine (a) bare GCE and ;(b) MWCNT modified GCE in 0.1 mol L^{-1} phosphate buffer solutions. Scan rate: 100 mVs^{-1}; supporting electrolyte

The electrochemical properties of the MWCNT-modified carbon glassy electrode were studied using cyclic voltammetry. Figure 3 cyclic voltammograms show the electrochemical behavior of oxcarbazepine on the surface of GGE modified with MWCNT and bare GCE. The signification increase in anodic current is due to the presence of carbon nanotubes. Also, the peak potential in the modified electrode is equal to 1.53 V, and in the modified electrode is 1.44 V. This indicates a reduction in the oxidation potential of oxcarbazepine at the modified electrode surface. Given that differential pulse voltammetry has a better sensitivity than cyclic voltammetry oxcarbazepine. DPV method is used to measure oxcarbazepine on the surface of a carbon glass electrode modified with carbon nanotubes. Figure 4 shows differential pulse voltammograms obtained on the unmodified surface in the buffer pH=7, 0.1 mol L^{-1} phosphate. As shown in Figure 4, by modifying the electrode in addition, as the current increases, the

overvoltage also decreases. Therefore, the above electrode was introduced as a new sensor and was used to measure oxcarbazepine.

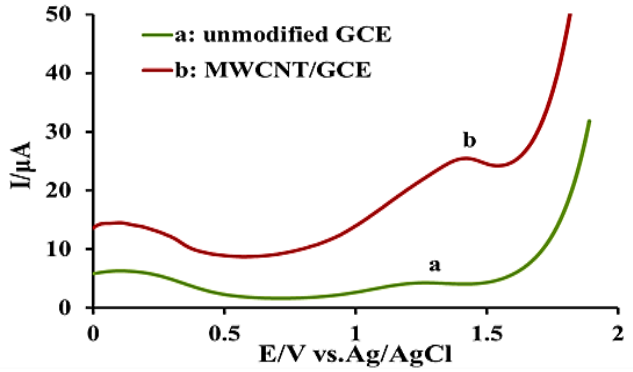


Figure 4. Differential pulse voltammograms of unmodified GCE; (a) GCE modified with MWCNT; (b) in the presence of oxcarbazepine 15 µmol L^{-1} in phosphate buffer solution 0.1 mol L^{-1}, pH=7

3.2. Effect of potential scanning rate on oxidation of oxcarbazepine

In electrochemical studies using cyclic voltammetry methods, one of the variables affecting the behavior of electrochemical modifying of electrodes is the scanning rate potential of the working electrode. To investigate the effect of potential scanning rate on the electrochemical behavior of oxcarbazepine, cyclic voltammograms of 2.0×10^{-5} mol L^{-1} oxcarbazepine were obtained at different scanning rates from 10-100 mV s^{-1}.

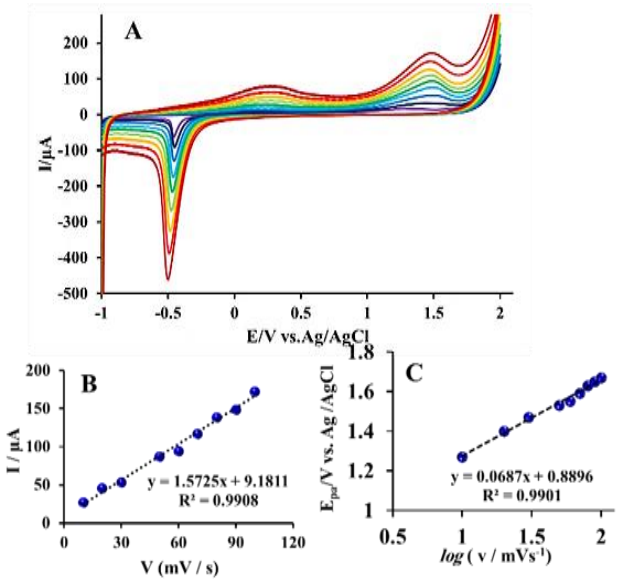


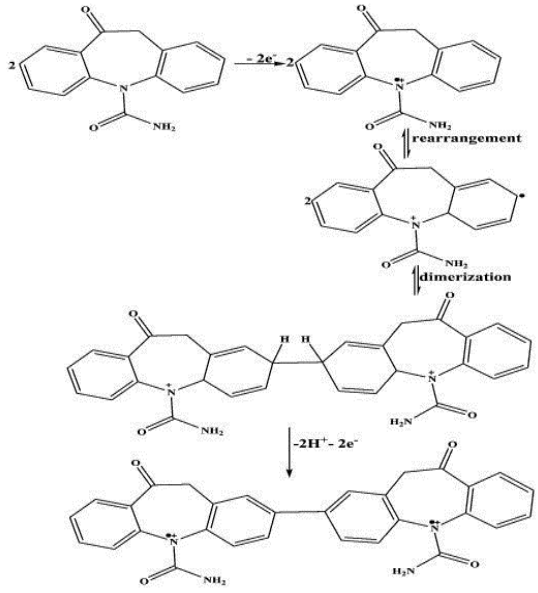
Figure 5. A). CV voltammograms of 2.0×10^{-5} mol L^{-1} oxcarbazepine at modified GCE with MWCNT; scan rate 10-100 mV s^{-1}; B) plot of change current anodic peak relative scan rate; C) diagram of potential changes according to the logarithm of the potential scan rate

As shown in Figure 5, gradually the peak oxidation potential of oxcarbazepine shifts to a more positive potential; this indicates a kinetic constraint on the oxidation process it is oxcarbazepine, which means that the above potential is required to perform the electrode process increases. In the case of a modified electrode with a fixed surface coating of a modifier, the peak height of the cyclic voltammogram increases as the potential scan rate increases. A good linear relationship between the square root of the scan rate and peak current was obtained between the range of 10-100 mV s^{-1} (Figure 5).

As shown in Figures 5 (B, C); it can be concluded that the linearity of peak current change diagrams is higher in terms of scanning rate. Therefore, we conclude that the electrode process is controlled by surface adsorption. Because the process is controlled by adsorption, the electrode reaction is based on absorption. According to Lauren's theory, for a completely irreversible absorption reaction and in the absence of any ohmic drop, the relationship between the logarithm of the scan rate and the potential of the peak is described by the following equation:

$$E_p = b \log v + \text{constant} \quad (1)$$

where Ep is peak potential, b is TOEFL slope, and V is the potential scan rate. The slope obtained for this line (TOEFL slope) equals 68.9 mV. By placing nα equal to 2, the anode transfer coefficient aα is calculated to be 0.43 mV. The oxidation mechanism of oxcarbazepine is shown in Scheme 1.



Scheme 1. Oxidation mechanism of oxcarbazepine

3.3. Effect of oxcarbazepine concentration

One of the suitable and ideal properties of the electrode for use in the oxidation of the desired material is its linear response in exchange for increasing certain amounts of analyte. As

this linear range increases, the efficiency of the electrode increases. To investigate the effect of oxcarbazepine concentration on anodic current from its oxidation under optimized conditions and to draw a measurement curve was carried out using the cyclic voltammetry method. Figure 6 cyclic voltammogram, the GCE shows the modified flow of the nostrils relative to the concentration of oxcarbazepine during increasing different concentrations of oxcarbazepine, and Figure 6 shows the changes in peak current relative to the concentration of oxcarbazepine. Increasing the concentration of oxcarbazepine from this limit has little effect on the resulting current. This can be attributed to the saturation of active electrocatalyst sites. The current diagram in terms of concentration shows a good linear relationship between current and concentration. From the slope of the linear region (20-350 µmol L^{-1}), the detection limit of 17.09 µ mol L^{-1} was obtained.

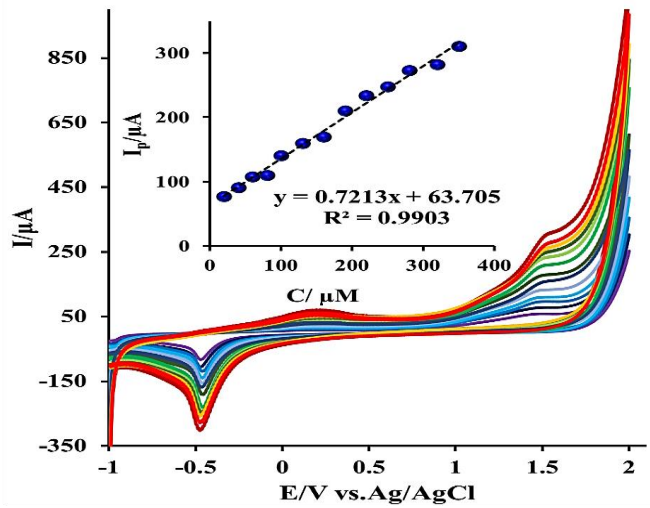


Figure 6. Plot of concentration versus current for oxcarbazepine

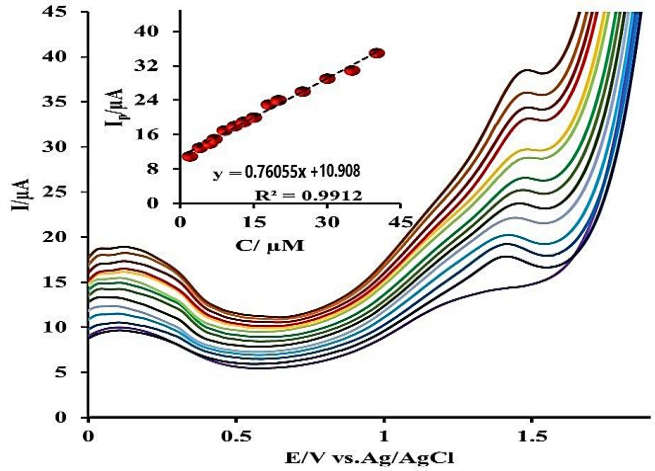


Figure 7. DPV voltammograms of oxcarbazepine at modified GCE with MWCNT in the range 2×10^{-5}-23×10^{-5} mol L^{-1} for 0.1 mol L^{-1} PBS supporting electrolyte

3.4. investigation of the effect of oxcarbazepine concentration on peak current using differential pulse voltammetry (DPV)

The determination of oxcarbazepine concentration at modified GCE with MWCNT was performed with differential pulse voltammetry (DPV). Under the optimum analytical conditions, the determination of oxcarbazepine at different concentrations was performed. A linear calibration curve (Figure 7) was obtained for oxcarbazepine in the range of 2×10^{-5}-23×10^{-5} mol L^{-1} for 0.1 mol L^{-1} PBS supporting electrolyte (Figure 7).

As can be seen, with increasing analyte concentration, the peak current increases, and the peak potential shifts to more positive values. The oxidative current is linearly dependent on the concentration of oxcarbazepine. The peak current diagram for the concentration of oxcarbazepine in Figure 6 has a liner region with the following equation:

$$I_p=0.6055\ C + 10.908\ (R^2=0.9912) \qquad (2)$$

The detection limit of 1.9 µmol L^{-1} was obtained from the slope of the liner region using the $k.S_b.m^{-1}$ relation.

3.5. Chronoamperometric studies

The electrocatalytic oxidation of oxcarbazepine at MWCNT-modified carbon glassy electrode was studied by chronoamperometry. Chronoamperometry is commonly used to measure the diffusion coefficient of electroactive species (Figure 8). In this method, a stationary electrode with a specified area floats in a solution containing an electroactive compound with concentration; it is certain that such a potential is applied that the potential of the working electrode is placed on the propagation platform of the electroactive species. The dependence of the current on time is followed. Concentration gradient change near the electrode surface with a curve current-time is related, and as time progresses, the emission layer becomes wider and prevents the electroactive composition from reaching the surface of the electrode reduced, and as a result, the slope of the concentration profile decreases with the progress of time [24].

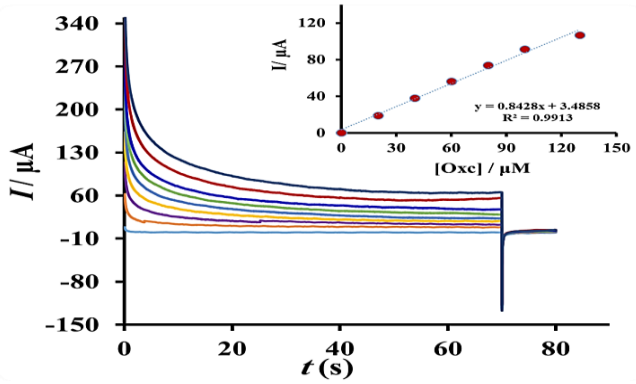


Figure 8. Chronoamperometric response of at MWCNT modified GCE in 0.1 mol L^{-1} phosphate buffer solution (pH 7.0)

So that the electrode is modified in solutions of oxcarbazepine with concentrations differently placed in phosphate buffer solution (pH=7), and the reciprocal phase potentials were kept constant at 1.40 and 0.0 V relative to the reference electrode, respectively, and Chronoamperograms were recorded. Therefore, the current intensity in a planar electrode decreases with time. The result of the electrochemical reaction of an electroactive species follows the following equation:

$$I=n\ \mathrm{FAD}^{1/2}\mathrm{C}/\pi^{1/2}\ t^{1/2} \qquad (3)$$

where D is the diffusion coefficient (cm^2s^{-1}) and c is the bulk concentration (mol cm^{-3}). The plot of I versus $t^{-1/2}$ will be linear, and from the slope, the value of D can be obtained. (Figure 9 B), inset shows the experimental plots of the resulting straight line were then plotted versus the concentration of oxcarbazepine (Figure 9 A), from which we calculated a diffusion coefficient of D=5.64×10^{-6} cm^2s^{-1} for oxcarbazepine.

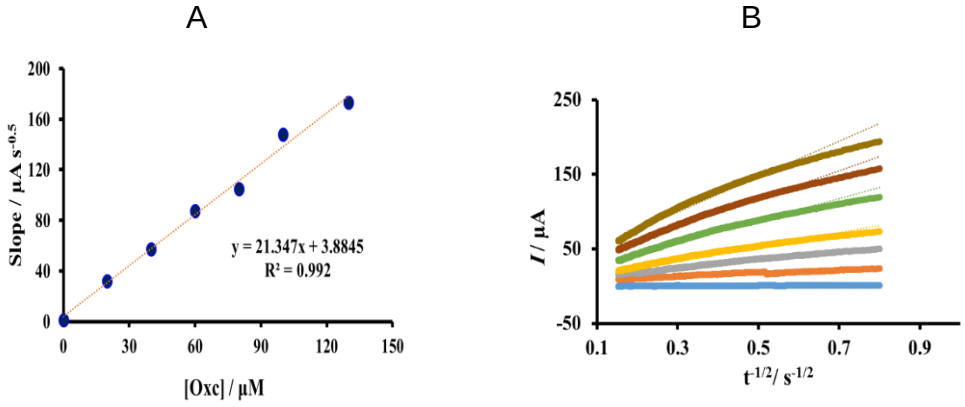


Figure 9. (A) Plot of the slope of linear segments against the oxcarbazepine concentration; (B) current diagram in the terms of t -0.5 for chronoamperograms (Figure 8)

No observation of cathode current in the reversal potential range indicates that the electrochemical behavior of oxcarbazepine on the case electrode the comment is irreversible. The resulting line graphs show the electrocatalytic oxidation of oxcarbazepine is controlled at the modified electrode surface by the diffusion process.

In determining oxcarbazepine levels in blood serum (real sample), Initially, due to the absence of oxcarbazepine-related waves, it can be concluded that this compound is not present in the primary blood sample. Therefore, to evaluate analytical application the electrode in the blood serum sample was performed using the method of increasing the standard of sample recovery tests. In this method, a known concentration of oxcarbazepine was injected into the test cell and voltammograms were recorded with increasing each time, the height of the anodic wave increased from the standard solution. Table 1 shows the recovery values of oxcarbazepine in human blood serum samples by the standard increase method. The results listed in Table 1

show that this sensor is successful in effectively measuring this drug in the human blood serum sample and determines about 100% of this drug.

Table 1. Analytical data of oxcarbazepine recovery in blood serum sample

No.	Added ($\mu mol\ L^{-1}$)	Found ($\mu mol\ L^{-1}$)	Recovery (%)
1	0	Not detected	-
2	2	1.99	99.50
3	4	3.94	98.67
4	6	6.02	100.42
5	8	7.95	99.45

One of the common methods for studying the structure and size of such electrocatalysts is the use of scanning electron microscopy. Therefore, SEM analysis has been used to study the morphology of electrode surface particles. Figure 10 A shows an image of the unmodified (bare) glassy carbon electrode. As can be seen, the surface of the glassy carbon electrode is smooth and uniform and no pores can be seen. In Figure 10 B, the surface of the electrode covered with carbon nanotubes was seen and the size of the particles was also determined. According to the SEM images of the electrode surface, the smaller the modifier particles are on the electrode surface and the more porous the surface, the contact surface required for catalysis and analyte oxidation increases and the overvoltage required for analyte oxidation decreases.

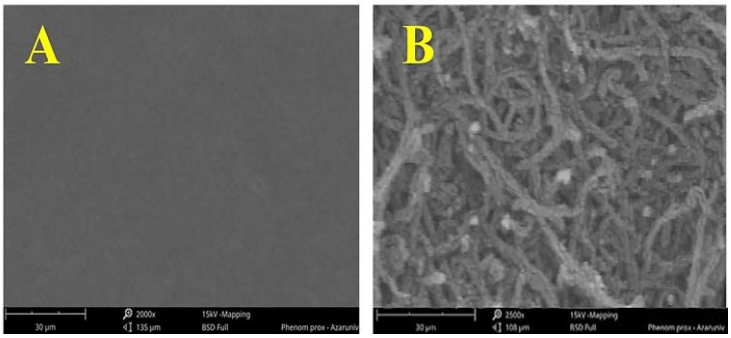


Figure 10. (A) Scanning electron image of unmodified glassy carbon electrode; (B) Electrode surface covered with carbon nanotubes

4. CONCLUSION

This study presented a new sensor to investigate the electrochemical behavior of oxcarbazepine with carbon glass electrodes coated with carbon nanotubes. Examination of cyclic voltammograms of oxcarbazepine on a modified electrode with carbon nanotube powder shows that the current is due to absorption oxidation. Some kinetic and thermodynamic parameters related to oxcarbazepine oxidation, such as load transfer coefficient, and number of

electrons involved in the velocity determination step can be evaluated by cyclic voltammetry methods. The advantages of the mentioned electrode can be a detection limit of 1.9 µmol L^{-1}, surface stability, and high sensitivity; he pointed out that the correction steps were not time-consuming. A sensor prepared to measure oxcarbazepine in a serum sample was successfully used.

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Declarations of interest

The authors declare no conflict of interest in this reported work.

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