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Nano composite System based on ZnO-functionalized Graphene Oxide Nanosheets for Determination of Cabergoline

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ABSTRACT

In this paper we report an electrochemical sensor based on ZnO-functionalized graphene oxide nanocomposite (ZnO-GO) for the sensitive determination of the cabergoline. Cabergoline electrochemical behaviors were investigated by cyclic voltammetry (CV), chronoamperometry (CHA) and differential pulse voltammetry (DPV). The modified electrode shows electrocatalytic activity toward cabergoline oxidation in phosphate buffer solution (PBS) (pH 7.0) with a reduction of the overpotential of about 180 mV and an increase in peak current. The DPV data showed that the obtained anodic peak currents were linearly dependent on the cabergoline concentrations in the range of 1.0-200.0 μM, with the detection limit of 0.45 μM. The prepared electrode was successfully applied for the determination of cabergoline in real samples.

Keywords : Cabergoline, Voltammetry, ZnO-functionalized graphene oxide nanocomposite, Graphite screen printed electrode

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1. Introduction

Parkinson's disease was first medically described by James Parkinson in 1817 [1]. Parkinson's disease is a chronic neurodegenerative disease, which are the result of the loss of dopamine-producing brain cells. The lack of dopamine in brain causes symptoms such as tremors, muscle stiffness or rigidity, slowness of movement and poor balance [2-4]. Cabergoline (1-[(6-allelylergolin-8 beta-yl)carbonyl]-1-[3-(dimethylamino)propyl]-3-ethyl-urea), is an ergot alkaloid derivative and a potent dopamine receptor agonist on D2 receptors [5]. Cabergoline used in progressive phase treatment of Parkinson's disease with their longer half-life, are increasingly considered as a suitable option to provide continuous dopaminergic neurons stimulation in Parkinson's disease patients [6]. Therefore, to know the treatment and study of the mechanism of Parkinson's disease, determination of cabergoline in biological fluids can be of analytical interest [7]. The commonly employed techniques for the determination of cabergoline in pharmaceutical formulations and biological fluids are based on high performance liquid chromatography [8], mass spectrometry [9], capillary zone electrophoresis [10], spectroscopy [11], microbiological assays [12,13] and electrochemical methods [14]. These methods require advanced technical expertise and time consuming and are expensive and often need the pretreatment step [15]. But electrochemical techniques as alternative methods have also received much interest due to their higher selectivity, faster and simple operation, lower cost, quick response, and therefore, have become of considerable importance for determination of analytes [16].

The screen-printed electrodes (SPEs) have been designed especially for the miniaturization and development of disposable sensors to be used in electrochemical analytical systems [17,18]. They are highly-

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versatile, easy to use, cost-effective analytical tools, also suitable to miniaturization [19]. In order to improve their electrochemical performance, SPEs have been modified with nanosized materials [20-24]. Nanomaterials are particles with the shortest dimension <100 nm. These particles are characterized by very large surface-to-mass or surface-to-volume ratios [25].

Nanostructures modified electrodes have good electro-catalytic activity, sensitivity, and selectivity; they have also a low detection limit compared to unmodified electrodes [26-35]. These nanostructures include, for example, carbon nanomaterials and nanostructures metal oxides. Among metal oxides, ZnO nanostructures due to wide band gap (3.37 eV), large excitation binding energy (60 eV), non-toxicity, and high electron communication features is preferred for the fabrication of efficient sensors [36,37].

Graphene, as a novel one-atom thick planar sheet of sp^2 hybridized carbon atoms packed in a honeycomb lattice [38,39], has attracted considerable attention in recent years due to physicochemical properties such as large surface area, excellent conductivity and electrocatalytic activities, antifouling ability, high porosity, wide electrochemical window, strong mechanical strength, cheap production and biocompatibility [40-44]. Therefore, ZnO-functionalized graphene oxide nanocomposite is a great candidate for screen printed electrode surface modification.

According to the previous points, it is important to create suitable conditions for analysis of cabergoline in biological fluids. In this study, we describe application of ZnO-functionalized graphene oxide nanocomposite (ZnO-GO) as a nanostructure sensor for voltammetric determination of cabergoline. The proposed sensor showed good electrocatalytic effect on cabergoline. ZnO-GO/SPE shows advantages in terms of selectivity, reproducibility and sensitivity. Eventually, we evaluate the analytical performance of the suggested sensor for cabergoline determination in real samples.

2. Experimental

2.1 Chemicals and Apparatus

The measurements were performed on an Autolab potentiostat/galvanostat (PGSTAT 302 N, Eco Chemie, the Netherlands), while controlling the experimental parameters using General Purpose Electrochemical System (GPES) software. The screen-printed electrode (DropSens, DRP-110, Spain) consists of three main parts which are a graphite counter electrode, a silver pseudo-reference electrode and a graphite working electrode. A Metrohm 710 pH meter was used for pH measurements.

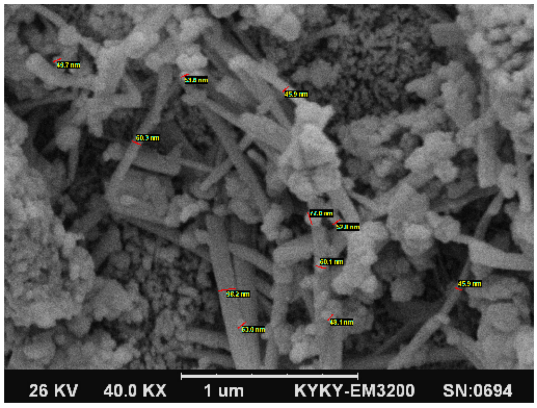


Fig. 1. SEM image of ZnO nanorods/graphene oxide nanocomposite.

Cabergoline and all other reagents were analytical grade, and were obtained from Merck (Darmstadt, Germany), and the orthophosphoric acid and its salts were used to prepare buffers in the pH range of 2.0-11.0.

2.2 Synthesis of ZnO nanorods/graphene oxide nanocomposite

Graphene oxide nanosheets were synthesized from natural graphite flakes based on the modified Hummers and Offemans method. The reduced graphene oxide (0.096 g) was dispersed in 40 ml water and the solution was kept in ultrasonic bath for 1 h. The prepared solution was added to 40 ml of $ZnCl_2$ (0.04 M) solution. Final solution pH was set 11.7 by ammonia solution. The solution was kept at 95°C for 4 h. The precipitate was gathered at 15000 rpm centrifugation for 15 min. Then it was washed by distilled water three times. Finally it was dried in oven at 45°C for 4 h. Fig. 1 shows typical SEM for synthesized ZnO nanorods/graphene oxide nanocomposite.

2.3 Preparation of the electrode

The bare screen-printed electrode was coated with ZnO-functionalized graphene oxide nanocomposite as follows. A stock solution of ZnO-GO in 1 mL aqueous solution was prepared by dispersing 1 mg

ZnO-GO with ultrasonication for 1 h, and a 5 µl aliquot of the ZnO-GO/H_2O suspension solution was casted on the carbon working electrodes, and waiting until the solvent was evaporated in room temperature.

2.4 Preparation of real samples

Five cabergoline tablets (labeled 0.5 mg per tablet) were grinding. Then, the tablet solution was prepared by dissolving 2.5 mg of the powder in 25 mL water by ultrasonication. Then, different volume of the diluted solution was transferred into a 25 mL volumetric flask and diluted to the mark with PBS (pH 7.0). The cabergoline content was analyzed by the proposed method using the standard addition method.

The urine specimens were kept in a refrigerator after sampling. To prepare the test samples 10 millilitres of these were taken or centrifuged at 2000 rpm for 15 min. After filtering the supernatant with a 0.45 µm filter, different volumes of it were diluted in 25 mL volumetric flasks using PBS (pH=7.0). The diluted urine sample was spiked with different amounts of cabergoline.

3. Results and Discussion

3.1 Electrochemical profile of cabergoline on the ZnO-GO/SPE

Due to the fact that the electrochemical behavior of cabergoline is pH-dependent optimizing the pH of the solution is necessary for obtaining the best results. Hence, the evaluations were performed in different pH values ranging from 4.0-9.0, and the results showed that the best results during the electro-oxidation of cabergoline at the surface of the modified electrodes could be obtained at pH=7 (Fig. 2).

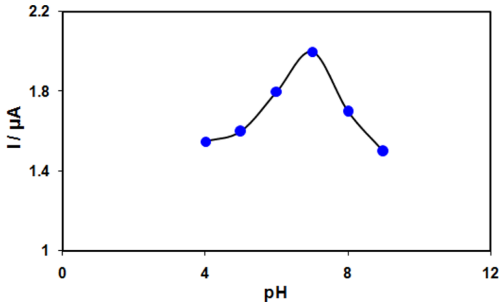


Fig. 2. Plot of I_p vs. pH for ZnO-GO/SPE in 0.1 M PBS (pH 7.0) in the presence of 200.0 µM cabergoline.

Fig. 3 illustrates the cyclic voltammograms of a 200.0 µM cabergoline obtained using the (a) bare SPE (765 mV) (b) ZnO/SPE (680 mV), (c) GO/SPE (640 mV) and (d) ZnO-GO/SPE (570 mV). As it can be easily noticed the maximum oxidation of cabergoline occurs at 570 mV in the case of ZnO-GO/SPE that is around 180 mV more negative than that observed in the case of the unmodified SPE. Based on these results, we propose an electrochemical mechanism, shown in Fig. 4, to describe the electrochemical oxidation of cabergoline at ZnO-GO/SPE.

3.2 Effect of scan rate on the results

Fig. 5 illustrates the effects of potential scan rates on the oxidation currents of cabergoline, indicating that increasing the scan rate increased the peak currents. Also based on the fact that the plots of Ip

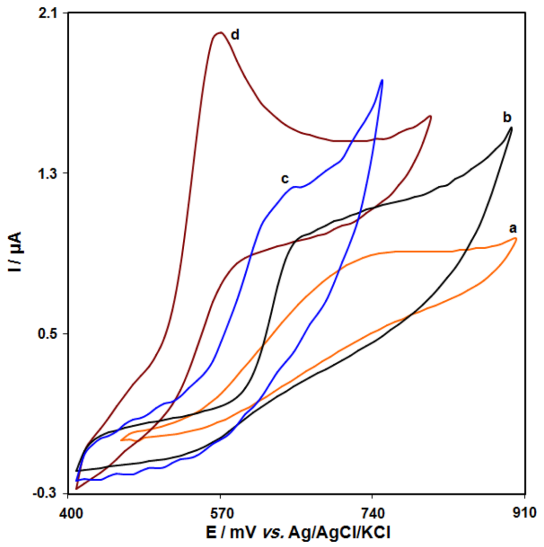


Fig. 3. CVs of (a) bare SPE (b) ZnO/SPE, (c) GO/SPE and (d) ZnO-GO/SPE in 0.1 M PBS (pH 7.0) in the presence of 200.0 µM cabergoline at the scan rate 50 mVs^{-1}.

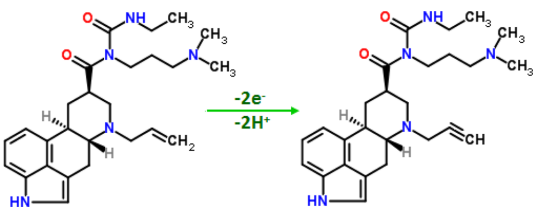


Fig. 4. Electro-oxidation mechanism of cabergoline at ZnO-GO/SPE.

against the square root of the potential scan rate ($\nu^{1/2}$) was linear, it was concluded that the oxidation process is diffusion controlled.

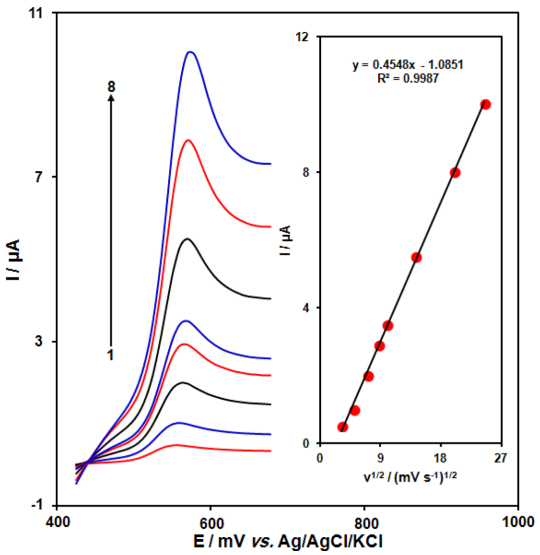


Fig. 5. LSVs of ZnO-GO/SPE in 0.1 M PBS (pH 7.0) containing 200.0 µM cabergoline at various scan rates; numbers 1-8 correspond to 10, 25, 50, 75, 100, 200, 400 and 600 mV s^{-1}, respectively. Inset: variation of anodic peak current vs. $\nu^{1/2}$.

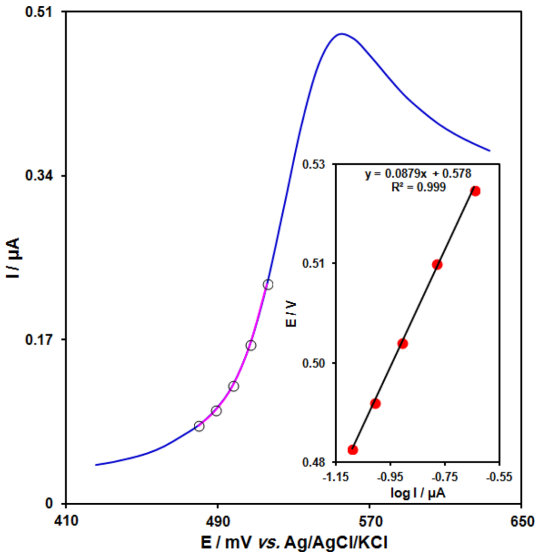


Fig. 6. LSV (at 10 mV s^{-1}) of electrode in 0.1 M PBS (pH 7.0) containing 200.0 µM cabergoline. The points are the data used in the Tafel plot. The inset shows the Tafel plot derived from the LSV.

Further Tafel curve of cabergoline was plotted using the data from the rising section (i.e. the Tafel regions) of the current-voltage curve obtained at 10 mVs^{-1} using lineae sweep voltammetry (LSV) (Fig. 6). The Tafel regions of the current potential curve is influenced by the electron transfer kinetic of the electrode reactions. The results showed Tafel slope of 0.0879 V $decade^{-1}$, for the electrode process [45] for charge transfer coefficient (α) of 0.33 (Fig. 6).

3.3 Calibration curve

The peak currents obtained for cabergoline using the ZnO-GO/SPE were used for the quantitative analysis of the cabergoline in aqueous solutions. Given the advantage of DPV in terms of improved sensitivity and better characteristics for analytical applications, the modified electrode was used as the working electrode in DPV analyses in a range of cabergoline solutions in 0.1 M PBS and the results (Fig. 7), show that there is a linear relation between the peak currents and concentrations of cabergoline over the concentration range of 1.0-200.0 µM (with a correlation coefficient of 0.9989) and a detection limit (3σ) of 0.45 µM was obtained. These values are comparable

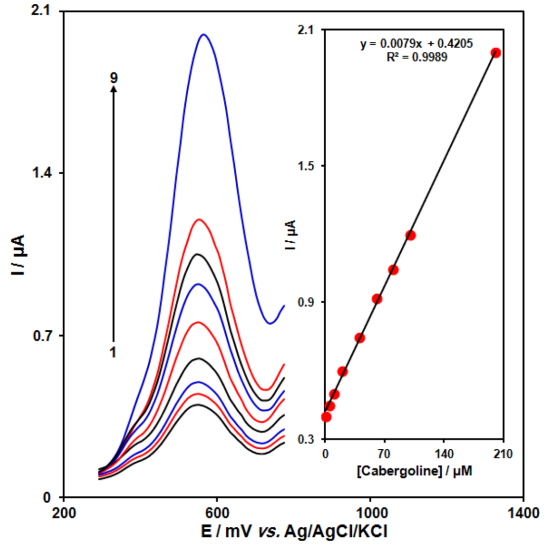


Fig. 7. DPVs of ZnO-GO/SPE in 0.1 M (pH 7.0) containing different concentrations of cabergoline. Numbers 1-9 correspond to 1.0, 5.0, 10.0, 20.0, 40.0, 60.0, 80.0, 100.0 and 200.0 µM of cabergoline. Inset: Plot of the electrocatalytic peak current as a function of cabergoline concentration in the range of 1.0-200.0 µM.

Table 1. Comparison of the efficiency of some modified electrodes used in detection of cabergoline.

Method	Modifier	Sensitivity	LOD	LDR	Ref.
Voltammetry	Graphene	0.2930 μA. μg mL^{-1}	5.441 ng mL^{-1}	0.2-5.2 μg mL^{-1}	[5]
Voltammetry	Nickel nanoparticles	0.5618 μA. μM^{-1}	2.0 μM	5.0-2700.0 μM	[6]
Voltammetry	Maghemite (γ-Fe_2O_3) nanoparticles	0.5516 μA. μM^{-1}	0.03 μM	0.1-0.35 μM	[46]
Voltammetry	Graphene oxide/ZnO nanocomposite	0.0079 μA. μM^{-1}	0.45 μM	1.0-200.0 μM	This work

with values reported by other research groups for determination of cabergoline at the surface of chemically modified electrodes (see Table 1).

3.4 The repeatability and stability of ZnO-GO/SPE

The longterm stability of the ZnO-GO/SPE was tested over a 2-week period. When CVs were recorded after the modified electrode was stored in atmosphere at room temperature, the peak potential for cabergoline oxidation was unchanged and the current signals showed less than 2.4% decrease relative to the initial response. The antifouling properties of the modified electrode toward cabergoline oxidation and its oxidation products was investigated by recording the CVs of the modified electrode before and after use in the presence of cabergoline. CVs were recorded in the presence of cabergoline 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 2.5%. Therefore, at the surface of ZnO-GO/SPE, not only the sensitivity increase, but the fouling effect of the analyte and its oxidation product also decreases.

3.5 Interference study

The influences of various foreign species on the determination of cabergoline were investigated. The tolerance limit was taken as the maximum concentration of the foreign substances which caused an approximately ±5% relative error in the determination. Based on the obtained results uric acid, ascorbic acid, dopamine, epinephrine, norepinephrine, methyldopa, carbidopa, isoproterenol, caffeine and glucose did not show interference in the determination of cabergoline.

3.6 Analysis of real samples

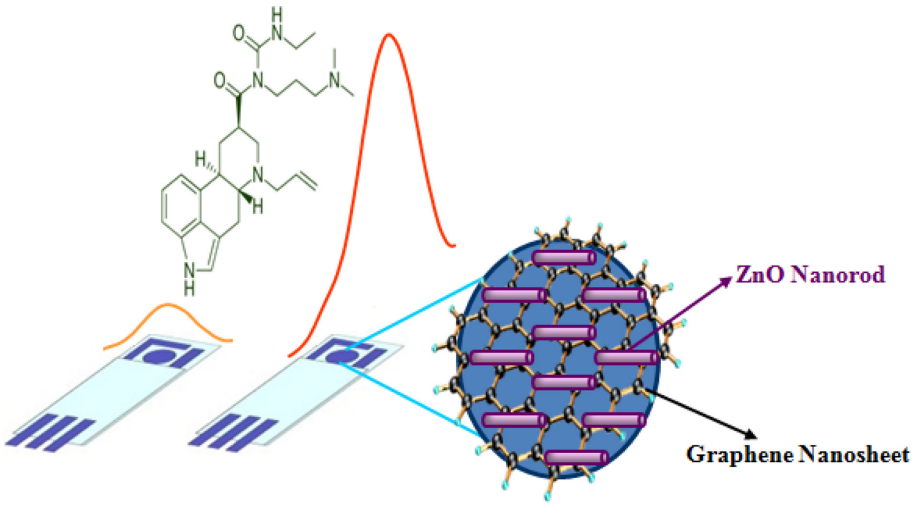
To assess the applicability of the application of the modified electrode for the determination of cabergoline in real samples, the described method was applied to the determination of cabergoline in cabergoline tablets and urine samples. For the purpose of this analysis the standard addition method was used and the results are given in Table 2. The observed recoveries of cabergoline were satisfactory and the reproducibility of the results was demonstrated based on the mean relative standard deviation (R.S.D.).

Table 2. The application of ZnO-GO/SPE for determination of cabergoline in cabergoline tablet and urine samples (n=5). All concentrations are in μM.

Sample	Spiked	Found	Recovery (%)	R.S.D. (%)
Cabergoline tablet	0	2.5	-	3.2
	2.5	4.9	98.0	1.7
	7.5	10.1	101.0	2.8
	12.5	15.5	103.3	2.4
	17.5	19.8	99.0	2.3
Urine	0	-	-	-
	5.0	5.1	102.0	2.9
	10.0	9.7	97.0	3.3
	15.0	14.9	99.3	1.8
	20.0	20.2	101.0	2.5

4. Conclusions

A graphite screen printed electrode was modified with ZnO-functionalized graphene oxide nanocomposite (ZnO-GO/SPE). The ZnO-GO/SPE exhibits highly electrocatalytic activity for oxidation of cabergoline. The peak potential of cabergoline is shifted by 180 mV at the surface of the ZnO-GO/SPE. The DPV currents of cabergoline at ZnO-GO/SPE increased linearly with the cabergoline concentration in the range from 1.0 to 200.0 μM with a detection limit of 0.45 μM. Also, ZnO-GO/SPE was used for determination of cabergoline in some real samples.



Graphical Abstract. A novel Nano cabergoline electrochemical nanosensor is constructed.

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