Liquid phase analysis of methyldopa in the presence of tyrosine uses electrocatalytic effect of a catechol derivative at a surface of NiO nanoparticle modified carbon paste electrode

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Abstract

An electrocatalytic based sensor fabricated for square wave voltammetric determination of methyldopa in the presence of tyrosine. For this goal, carbon paste electrode modified with NiO nanoparticle (NiO/NPs) and 2-(3,4-dihydroxyphenethyl)isoindoline-1,3-dione (DHPID) (CPE/DHPID/NiO/NPs) suggested as a highly selective sensor. The CPE/DHPID/NiO/NPs showed an excellent character for electrocatalytic oxidization of methyldopa in aqueous solution. For the mixture containing methyldopa and tyrosine, the oxidation peaks potential well separated from each other with differential potential ~ 500 mV. Methyldopa peak current increased linearly with its concentration at the ranges of 0.08–500 μM . The CPE/DHPID/NiO/NPs was successfully used for the analysis of methyldopa in drug samples.

Keywords: Methyldopa, Tyrosine, Liquid phase determination, NiO nanoparticle, Electrocatalytic

1. Introduction

High blood pressure is one of the important problems for human healthy. A large number of people suffer from high blood pressure patients. Therefore, scientists suggested many drugs for resolving high blood pressure problem. In between, methyldopa is one of the most important and usable drug for treatment high blood pressure [1]. Methyldopa can be increased human heart rate and narrow body blood vessels [2]. On the other hand, high dose of methyldopa increase the risk of headache, drowsiness, and weakness. Coadministration of methyldopa and alcohol is not recommended due to increasing methyldopa side-effects, such as feeling sleepy or dizzy. Several different analytical methods have been suggested for the analysis of methyldopa that include spectrophotometry [3, 4], fluorometry [5], high performance liquid chromatography (HPLC) [6, 7], and electrochemical methods [8-10]. In between, electrochemical methods can be useful for fast and safe analysis of biological and pharmaceutical samples due to low time analysis and application of water as a usual solvent [11-24]. Also, tyrosine is an important amino acid in biological samples that can be interference for analysis of methyldopa in real samples. Determination of methyldopa in urine and blood sample in the presence of tyrosine isn't possible at a surface of bare electrodes using electrochemical methods. Application of modified electrodes as sensors can be help to trace analysis of electro-active compounds and resolve signal overlapping in simultaneous analysis [25-35].

In this work, we have used cyclic voltammetry, square wave voltammetry and chronoamperometry techniques at pH 7.0 to demonstrate the electro-catalytic behavior of methyldopa in the presence of tyrosine on the CPE/DHPID/NiO/NPs. For the first time, the CPE/DHPID/NiO/NPs has been used in the determination of methyldopa and tyrosine in

pharmaceutical and urine samples. The obtained data confirmed that the CPE/DHPID/NiO/NPs is highly selective in the determination of methyl dopa in the presence of tyrosine.

2. Experimental

2.1. Materials and apparatus

Tyrosine, methyl dopa, nickel nitrate, sodium hydroxide, phosphoric acid, graphite powder and paraffin oil were purchased from Sigma-Aldrich. Doubly distilled water was used for preparation of stock solution. All of the electrochemical investigations were performed with an Autolab PGSTAT system. Ag/AgCl/KCl, Pt wire and CPE/DHPID/NiO/NPs were used as reference, counter and working electrode, respectively. X-ray powder diffraction studies were carried out using a STOE diffractometer with Cu–K α radiation ($\lambda = 1.54 \text{ \AA}$).

2.2. Synthesis of NiO nanoparticle

NiO nanoparticles were synthesized by direct chemical precipitation method according to below procedure. 50 mL of sodium hydroxide 0.5 M drop wise to 50 mL of nickel nitrate 0.5 M at the temperature $\sim 50^\circ\text{C}$. The precipitated NiO nanoparticle was cleaned with deionized water then dry for 12 h at 100°C . Finally, the powder calcined at 400°C for 2.0 hours.

2.3. Fabrication of CPE/DHPID/NiO/NPs

50.0 mg of DEADEBD was hand-mixed with 850 mg of pure graphite powder and 100 mg of NiO nanoparticle in a mortar and pestle. The mixture homogenized by suitable amount of diethyl ether and after drying solvent, 15 drop of paraffin was added to the mixture powder for obtaining

a uniformly wetted paste. The obtained paste in previous part packed into a glass tube in the presence a copper wire.

2.4. Real sample preparation

The urine samples obtained from a safe man and centrifuged for 35 min at 3000 rpm. In continuous the urine sample was filtered using a 0.45 mm filter and then diluted 100 times with PBS (pH 7.0) for electrochemical analysis by standard addition method.

For drug analysis, some tablets of methyldopa (labeled 250 mg per tablet) completely grinding and were dissolved in 100 mL water by ultrasonication.

3. Results

3.1. NiO nanopowder characterization

XRD pattern of NiO nanoparticles are shown in Figure 1A. As can be seen, the presence of miller indexes (111), (200), (220), (311) and (222) confirm synthesized of NiO nanoparticles (JCPDS NO. 47-1049) with FCC structure. TEM image of NiO nanopowder confirm spherical shape for synthesized nanoparticle (Fig. 1B). **“Here Figure 1”**

3.2. Electrocatalytic investigation

For the electrocatalytic activity investigation of methyldopa at a surface of CPE/DHPID/NiO/NPs, cyclic voltammetric responses of 600 μ M methyldopa recorded at pH 7.0 (see Fig. 2). CPE/DHPID/NiO/NPs showed a pair of well-defined redox peaks relative of DHPID oxidation/reduction in the absence of methyldopa (curve a). After addition of 600 μ M methyldopa, a drastic enhancement on the anodic peak current occurred and cathodic peak

current removed from the reverse scan (Fig. 2, curve c). This phenomenon confirms a good electrocatalytic effect [36-38]. On the other hand and in the presence of 600 μM methyl dopa, the electro-oxidation of methyl dopa at CPE/NiO/NPs and CPE shows an irreversible signal at more positive potentials (Fig. 2, curve d and e). The electro-catalytic peak potential is found to be ~ 330 mV, whereas that of the uncatalyzed peak is ~ 563 mV. According to the obtained data, the overvoltage for oxidation of methyl dopa decreases ~ 233 mV with the CPE/DHPID/NiO/NPs. Also, at a surface of CPE/DHPID (curve b) methyl dopa has a less current than in compared to CPE/DHPID/NiO/NPs that show the effect of NiO nanoparticle to improve electrical conductivity of carbon paste electrode. **“Here Figure 2”**

The relation between sweep rate (v) and peak current of 200.0 μM methyl dopa in $\text{pH}=7.0$ was studied in the range of 3–20 mV/s at CPE/DHPID/NiO/NPs (Fig. 3, inset). As can be seen, a linear relationship between the oxidation current and $v^{1/2}$ confirms the diffusion controlled [39-44] process for the electro-oxidation of methyl dopa on the surface of CPE/DHPID/NiO/NPs (Fig. 3). **“Here Figure 3”**

Tafel investigation was used for obtaining information about the rate-determining step (Fig. 4). The slope of the Tafel plot was equal to $2.3RT/n(1-\alpha)F$, which came up to 0.2121 and 0.2592 V decade⁻¹ for scan rates 5 and 20 mV/s, respectively. Therefore, we obtained the mean value of α equal to 0.74. **“Here Figure 4”**

Chronoamperometric investigation was used to determine the diffusion coefficient of methyl dopa (Not shown). We have determined the diffusion coefficient, D , of methyl dopa using the cottrell equation ($I = nFAD^{1/2}C/(\pi \times t)^{1/2}$). According to the above equation, we calculated a diffusion coefficient of 7.43×10^{-5} cm²/s for methyl dopa. The rate constant for the chemical reaction between methyl dopa and the redox sites in CPE/DHPID/NiO/NPs, k_h , can be evaluated

using chronoamperometry according to the Galus method [45]. Based on the slope of the I_C/I_L versus $t^{1/2}$ plot, k_h can be obtained for a given methyldopa concentration (not shown). From the value of the slope, the value of k_h was found to be $k_h = 9.24 \times 10^2 \text{ mol}^{-1} \text{ L s}^{-1}$.

Dynamic range and limit of detection are two major analytical factors for a novel electrochemical sensor [46-50]. The SW voltammograms clearly show that the plot of peak current vs. methyldopa concentration is linear for 0.08–550 μM of methyldopa with sensitivity 0.0995 $\mu\text{A}/\mu\text{M}$. The detection limit was 0.03 μM methyldopa according to the definition of $Y_{\text{LOD}} = Y_B + 3\sigma$. The determination of methyldopa in the presence of tyrosine is main object of the presence work using CPE/DHPID/NiO/NPs. This was performed by simultaneously changing the concentrations of methyldopa and tyrosine, and recording the SWVs. The voltammetric results showed well defined anodic peaks at potentials of 170 and 670 mV, corresponding to the oxidation of methyldopa and tyrosine, respectively. This is indicating that simultaneous determination of these compounds is feasible at CPE/DHPID/NiO/NPs as shown in Fig. 5. The sensitivity of the CPE/DHPID/NiO/NPs towards the oxidation of methyldopa in the presence of tyrosine was found to be 0.0967 $\mu\text{A}/\mu\text{M}$ (Fig. 5 insert). This is very close to the value obtained in the absence of tyrosine (0.0995 $\mu\text{A}/\mu\text{M}$) indicating that the oxidation processes of methyldopa and tyrosine at the CPE/DHPID/NiO/NPs are independent. **“Here Figure 5”**

The repeatability and stability of CPE/DHPID/NiO/NPs were investigated by SWV determination of 20.0 μM methyldopa. The relative standard deviation (RSD) for ten successive assays was 1.8 %. When four different CPE/DHPID/NiO/NPs were used, the RSD for seven measurements was 2.2 %. When the CPE/DHPID/NiO/NPs is stored in the laboratory, the CPE/DHPID/NiO/NPs retains 96 % of its initial response after 12 days and 90 % after 35 days. These results indicate that CPE/DHPID/NiO/NPs has good stability and reproducibility.

The influence of vitamins, biological and some other interference compounds on the determination of 20.0 μM methyldopa was studied with acceptance error 5%. The results are given in Table 1, which shows the peak current of methyldopa is not affected by all conventional vitamins, cations, anions, and organic substances. **“Here Table 1”**

To evaluate the applicability of the CPE/DHPID/NiO/NPs for the analysis of methyldopa in real samples, its utility was tested by determining methyldopa in drug and urine samples by standard addition method. The results are listed in Table 2 and confirmed ability of CPE/DHPID/NiO/NPs for determination of methyldopa in real samples. **“Here Table 2”**

4. Conclusion

This paper explained construction of CPE/DHPID/NiO/NPs for the determination of methyldopa in the presence of tyrosine in aqueous solution. A potential difference of 500 mV between methyldopa and tyrosine was detected, which was large enough to determine methyldopa and tyrosine individually and/or simultaneously. The plot of peak current vs. methyldopa concentration is linear for 0.08–550 μM with sensitivity 0.0995 $\mu\text{A}/\mu\text{M}$ and detection limit 0.03 μM . Finally, CPE/DHPID/NiO/NPs were used for the determination of methyldopa in real samples with satisfactory results.

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Figure and Scheme Captions:

Figure 1. A) XRD patterns of as-synthesized NiO nanoparticles. B) TEM patterns of as-synthesized NiO nanoparticles

Figure 2. Cyclic voltammograms of (a) CPE/DHPID/NiO/NPs in the buffer solution pH=7.0, (b) CPE/DHPID in the presence of 600 μM methyl dopa, (c) CPE/DHPID/NiO/NPs in the presence of 600 μM methyl dopa, (d) CPE/NiO/NPs in the presence of 600 μM methyl dopa, and (e) CPE in the presence of 600 μM methyl dopa.

Figure 3. Variation of anodic peak current *vs.* $\nu^{1/2}$. Insert: Cyclic voltammograms of CPE/DHPID/NiO/NPs (pH 7.0) containing 200 μM methyl dopa at various scan rates; numbers a-f correspond to 3.0, 5.0, 9.0, 14.0, 17.0 and 20.0 mV s^{-1} , respectively.

Figure 4. Tafel plot for CPE/DHPID/NiO/NPs in 0.1 M PBS (pH 7.0) with scan rates of 5 and 20 mV/s in the presence of 200.0 μM methyl dopa.

Figure 5. Square wave voltammograms of CPE/DHPID/NiO/NPs in 0.1 M PBS (pH 7.0) containing different concentrations of methyl dopa and tyrosine (from inner to outer) mixed solutions of a) 14.0+50.0, b) 45.0+100.0, c) 70.0+150.0, d) 100.0+200.0, e) 150.0+250.0, f) and 200.0+300.0 μM methyl dopa and tyrosine, respectively. Plot of the peak currents as a function of methyl dopa concentration.

Figure 1

Figure 2

Figure 3

Figure 4

Figure 5

Table 1 Interference study for the determination of 20.0 μM methyldopa under the optimized conditions.

Species	Tolerance limits (W/W)
Glucose , Fructose, Lactose , Sucrose, Alanine, Phenyl alanine,	1000
Histidine, Threonine, Glycine, Na^+ , F^- , K^+ , Cl^- , Br^- , Tryptophan	600
Starch	Saturation
Urea	100

Table 2: Determination of methyldopa in drug and urine samples (n=5).

Sample	Added (μM)	Expected (μM)	Founded (μM)	Recovery %
Urine	---	---	<Limit of detection	---
	10.00	10.00	10.45 $\pm$ 0.56	104.5
	30.00	30.00	30.78 $\pm$ 0.89	102.9
Tablet	---	5.00	4.87 $\pm$ 0.47	96.8
	10.00	15.00	15.33 $\pm$ 0.57	102.2

Graphical Abstract

This is first voltammetric report sensor for analysis of methyldopa in the presence of tyrosine using modified electrochemical sensors.