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Highly Sensitive Amperometric Detection of Propranolol using Graphite Screen Printed Electrode Modified with Zirconium Dioxide Nanoparticles

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Abstract- A graphite screen printed electrode modified with ZrO_2 nanoparticles (ZrO_2/SPE) was investigated for its ability to serve as a sensor towards propranolol. The ZrO_2/SPE was found to exhibit an electro-catalytic activity for the electrochemical oxidation of propranolol in 0.1 M phosphate buffer solution (pH 7.0). Cyclic voltammetry and differential pulse voltammetry were employed to study the electrochemical properties of the modified electrode. The electrochemical oxidation of propranolol occurs at +0.95 V with a limit of detection (3σ) found to be 1.5 μM and with linear range of 10.0 μM to 200.0 μM. The present study widens the scope of applications of ZrO_2 nanoparticles for on-site monitoring of propranolol.

Keywords- Propranolol, ZrO_2 nanoparticles, Graphite screen printed electrode, Voltammetry

1. INTRODUCTION

Propranolol, 1-[isopropylamino-3-[1-naphthyloxy]2-propanol], is a β-adrenoceptor antagonist (β-blocker), which is widely used in the treatment of several diseases such as cardiac arrhythmia, angina pectoris, sinus tachycardia, thyrotoxicosis, hypertrophic subaortic stenosis and hypertension [1]. Propranolol is commercially employed in the form of

hydrochloride and has also been suggested for use in a number of other conditions including dysfunctional labor and anxiety [2]. Because it is also used in low activity sports as doping agent, which acts reducing cardiac frequency and contraction force, the International Olympic Committee included it in the list of forbidden substances. In addition it is well-demonstrated that propranolol has in vitro anticancer, antiproliferative and antiangiogenesis properties against malignancies [3,4]. Preclinical studies on ovarian and breast cancer models demonstrated that specifically through anti-angiogenic and immunostimulatory mechanisms, propranolol harnesses tumor-related stress and metastasis. Thus, determination of propranolol is very important for pharmaceutical and biological Investigation [5]. Different techniques have been used to determine propranolol in pharmaceutical formulations and biological samples, including methods based on flow injection-chemiluminescence, titrimetry, spectrofluorimetry, ion selective electrodes, chromatography, kinetics-colorimetry and electrophoresis [6-10]. When used for analyzing complex biological matrices, all of these methods demand tedious preliminary steps such as pre-concentration in an organic solvent or proteins precipitation [11-14]. In particular, electrochemical techniques are useful alternative methods, having important advantages including simplicity, reliability, sensitivity and selectivity. These techniques are more often used in pharmaceutical preparations and biomedical analysis [15-19].

Screen-printed electrodes (SPEs) have attracted considerable attention in recent years because they generally offer beneficial attributes over the traditional electrodes, such as they are portable, field-based size and cost-effective sensors which offer true potential for application in-the-field [20]. SPEs are inexpensive to manufacture which allows them to be disposable. This aspect is clearly important when testing biological samples and thus avoids surface fouling complications [21]. In addition SPEs are reliable, simple to operate with high sensitivity, selectivity and are highly reproducible [22-25].

Therefore the oxidation of propranolol represents a serious problem which arises from the high over- potential in the direct oxidation of propranolol at most unmodified electrode surfaces. In this respect, many researchers have attempted to diminish the over-potentials by using different modified electrodes [26-32]. Recently, many studies have been focused on the application of nano-materials in fabrication and modification of different conventional electrodes to improve their sensitivity and selectivity [33-39]. Compared with single component, the nanoparticles have certain synergistic effects such as good signal-to-noise ratio, fast electron transport and larger surface area [40-47]. Previous studies showed that metal nanoparticles could act as modifier for electrochemical sensors [48-53].

In the current study we have chosen Zirconium dioxide nanoparticles (ZrO_2-NPs) because of its stability, non-toxicity, high strength and fracture toughness, high melting point, low thermal conductivity and high corrosion resistance [54]. Due to these unique properties ZrO_2

exhibited interesting applications in different research fields such as in gas-sensing, catalyst or catalyst support, photocatalysis and in wastewater treatment [55-57].

According to the previous points, it is important to create suitable conditions for analysis of propranolol in biological fluids. In this study, we describe application of novel ZrO_2 nanoparticles as a nanostructure sensor for voltammetric determination of propranolol. The proposed sensor showed good electrocatalytic effect on propranolol. The modified electrode shows advantages in terms of selectivity, reproducibility and sensitivity. Eventually, we evaluate the analytical performance of the suggestion sensor for propranolol determination in real samples.

2. EXPERIMENTAL

2.1. Apparatus and chemicals

The electrochemical measurements were performed with an Autolab potentiostat/galvanostat (PGSTAT 302N, Eco Chemie, the Netherlands). The experimental conditions were controlled with 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.

All solutions were freshly prepared with double distilled water. Propranolol and all other reagents were of analytical grade and were obtained from Merck chemical company (Darmstadt, Germany). The buffer solutions were prepared from orthophosphoric acid and its salts in the pH range of 2.0-9.0. The ZrO_2 nanoparticles (surface area=65 m^2g^{-1} and particle size=21.0 nm) was purchased from Sigma Aldrich.

2.2. Preparation of modified electrode

The bare graphite screen printed electrode was coated with ZrO_2 nanoparticles as follows. A stock solution of ZrO_2 in 1 mL aqueous solution was prepared by dispersing 1 mg ZrO_2 with ultrasonication for 1 h, and a 5 µl aliquot of the ZrO_2/H_2O suspension solution was casted on the carbon working electrodes, and waiting until the solvent was evaporated in room temperature.

3. RESULTS AND DISCUSSION

3.1. Electrocatalytic oxidation of propranolol at a ZrO_2/SPE

The electrochemical behavior of propranolol is dependent on the pH value of the aqueous solution. Therefore, pH optimization of the solution seems to be necessary in order to obtain the electrocatalytic oxidation of propranolol. Thus the electrochemical behavior of

propranolol was studied in 0.1 M PBS in different pH values (2.0< pH<9.0) at the surface of ZrO_2/SPE by CV. It was found that the electrocatalytic oxidation of propranolol at the surface of ZrO_2/SPE was more favored under neutral conditions than in acidic or basic medium. Thus, the pH 7.0 was chosen as the optimum pH for electrocatalysis of propranolol oxidation at the surface of ZrO_2/SPE.

Fig. 1 depict the cyclic voltammetric responses for the electrochemical oxidation of 100.0 µM propranolol at ZrO_2/SPE (curve a) and bare SPE (curve b). The anodic peak potential for the oxidation of propranolol at ZrO_2/SPE (curve a) is about 950.0 mV compared with 1150.0 mV for that on the bare SPE (curve b). Similarly, when the oxidation of propranolol at the ZrO_2/SPE (curve a) and bare SPE (curve b) are compared, an extensive enhancement of the anodic peak current at ZrO_2/SPE relative to the value obtained at the bare SPE (curve b) is observed. In other words, the results clearly indicate that the ZrO_2 nanoparticles improve the propranolol oxidation signal.

The effect of potential scan rates on the oxidation current of propranolol has been studied (Fig. 2). The results showed that increasing in the potential scan rate induced an increase in the peak current. In addition, the oxidation process is diffusion controlled as deduced from the linear dependence of the anodic peak current (I_p) on the square root of the potential scan rate ($v^{1/2}$) over a wide range from 10 to 600 mV s^{-1}.

Fig. 3 show a Tafel plot that was drawn from points of the Tafel region of the LSV. The Tafel slope of 0.1539 V obtained in this case agrees well with the involvement of one electron in the rate determining step of the electrode process, assuming a charge transfer coefficient of α=0.62 [58].

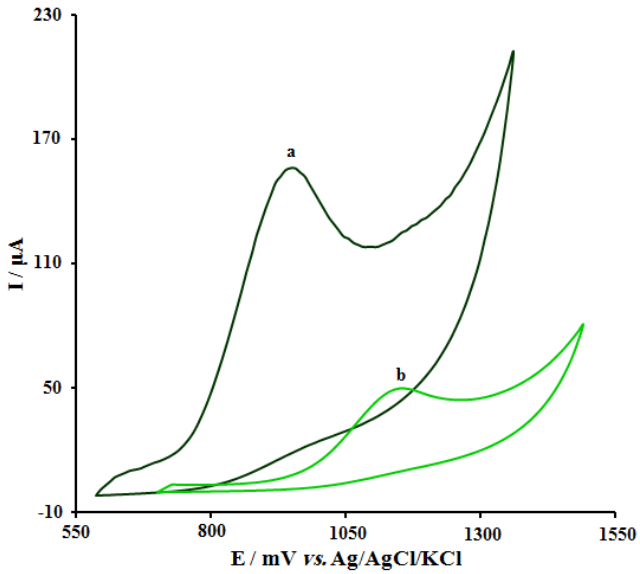

Fig. 1. Cyclic voltammograms of (a) ZrO_2/SPE and (b) bare SPE in 0.1 M PBS (pH 7.0) in the presence of 100.0 µM propranolol at the scan rate 50 mVs^{-1}

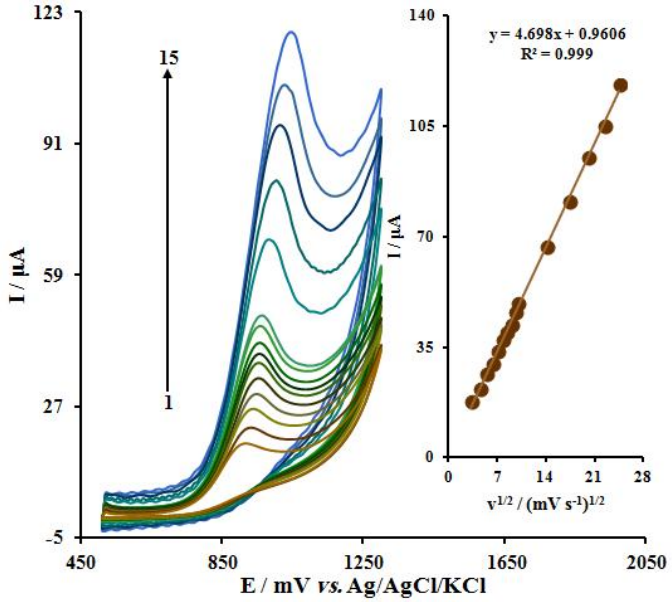

Fig. 2. Cyclic voltammograms of ZrO_2/SPE in 0.1 M PBS (pH 7.0) containing 200.0 µM propranolol at various scan rates; numbers 1-15 correspond to 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, and 600 mV s^{-1}, respectively. Inset: variation of anodic peak current *vs*. $v^{1/2}$

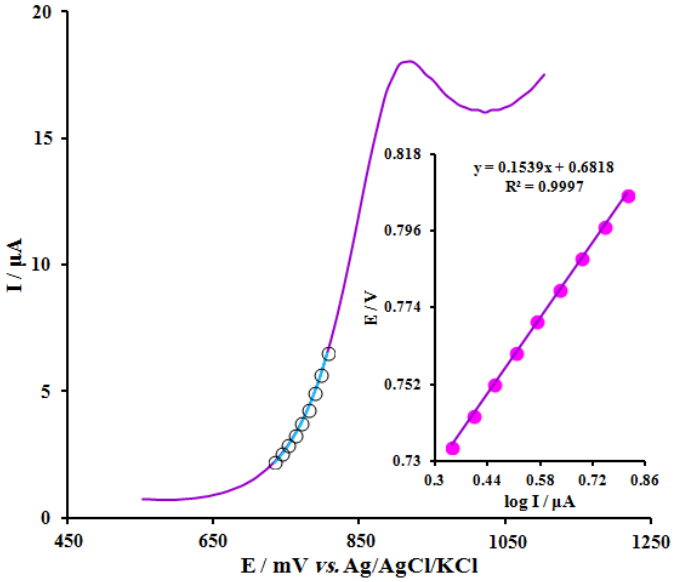

Fig. 3. LSV (at 10 mV s^{-1}) of electrode in 0.1 M PBS (pH 7.0) containing 200.0 µM propranolol. The points are the data used in the Tafel plot. The inset shows the Tafel plot derived from the LSV

3.2. Calibration plot and limit of detection

The peak current of propranolol oxidation at the surface of the modified electrode can be used for determination of propranolol in solution. Therefore, differential pulse voltammetry (DPV) experiments were done for different concentrations of propranolol (Fig. 4). The oxidation peak currents of propranolol at the surface of a modified electrode were proportional to the concentration of the propranolol within the ranges 10.0 to 200.0 µM. The detection limit (3σ) of propranolol was found to be 1.5×10^{-6} M.

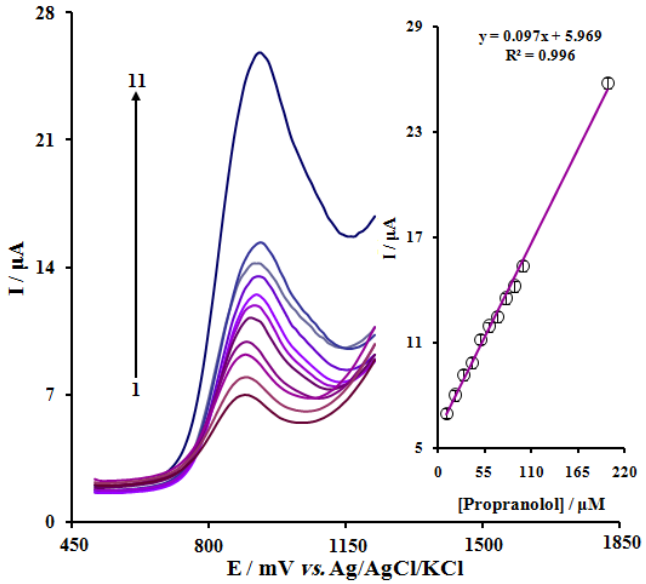

Fig. 4. DPVs of ZrO_2/SPE in 0.1 M (pH 7.0) containing different concentrations of propranolol. Numbers 1–11 correspond to 10.0, 20.0, 30.0, 40.0, 50.0, 60.0, 70.0, 80.0, 90.0, 100.0 and 200.0 µM of propranolol. Inset: Plot of the electrocatalytic peak current as a function of propranolol concentration in the range of 10.0-200.0 µM

3.5. Real sample analysis

In order to evaluate the analytical applicability of the proposed method, also it was applied to the determination of propranolol in propranolol tablet and urine samples. The results for determination of propranolol in real samples are given in Table 1. Satisfactory recovery of the experimental results was found for propranolol. The reproducibility of the method was demonstrated by the mean relative standard deviation (R.S.D.).

Table 1. The application of ZrO_2/SPE for determination of propranolol in propranolol tablet and urine samples (n=5). All concentrations are in µM

Sample	**Spiked**	**Found**	**Recovery (%)**	**R.S.D. (%)**
	Propranolol	Propranolol	Propranolol	Propranolol
Propranolol tablet	0	10.0	-	2.5
	2.0	12.2	101.7	1.7
	4.0	13.6	97.1	3.1
Urine	0	0	-	-
	12.5	12.9	103.2	2.9
	22.5	22.2	98.7	3.2

4. CONCLUSIONS

In summary, a ZrO_2/SPE was developed for the electrochemical determination of propranolol in various real samples. The ZrO_2 nanoparticles have a large electroactive surface area and good electrical conductivity. The ZrO_2/SPE shows a good electrochemical response for determination of propranolol with the wide linear range between 10.0 to 200.0 µM and the limit of detection was calculated to be 1.5 µM. Moreover, ZrO_2/SPE operates well in the determination of propranolol in urine and propranolol tablet samples with good accuracy and precision.

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