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Full Paper

Fabrication of a Novel Electrochemical Nanosensor for Voltammetric Determination of Naproxen

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Abstract- A novel carbon paste electrode modified with NiO/CNTs nanocomposite and an ionic liquid (n-hexyl-3-methylimidazolium hexafluoro phosphate) was fabricated. The electrochemical study of the modified electrode, as well as its efficiency for voltammetric oxidation of naproxen, is described. The electrode was also employed to study the electrochemical oxidation of naproxen, using cyclic voltammetry, chronoamperometry and square wave voltammetry as diagnostic techniques. Square wave voltammetry exhibits a linear dynamic range from 7.5×10^{-7} to 8.0×10^{-4} M and a detection limit of 1.2×10^{-7} M for naproxen.

Keywords- Naproxen, NiO/CNTs nanocomposite, Drug analysis, Ionic liquids, Carbon paste electrode

1. INTRODUCTION

Naproxen is a proprionic acid derivative related to the arylacetic acid group of nonsteroidal anti-inflammatory drugs (NSAIDs). The chemical name for naproxen is 2-naphthaleneacetic acid (s) 6-methoxy-α-methyl [1]. It works by blocking the production of prostaglandins, substances in the body that play a role in pain and inflammation. It is used to

treat pain or inflammation caused by conditions such as rheumatoid arthritis, osteoarthritis, juvenile arthritis, ankylosing spondylitis, tendonitis and bursitis, and acute gout [2-4]. It is the preferred NSAID for long-term use in people with a high risk of cardiovascular (for example, heart attacks or strokes) complications, due to its relatively low risk of causing such complications. But it may cause ulcers and bleeding in your gastrointestinal (GI) tract. Ulcer and bleeding risk is higher if patients are elderly. In order to reduce the risk of stomach ulceration, it is often combined with a proton-pump inhibitor (a medication that reduces the production of stomach acid) during long-term treatment [5,6]. Thus, attention is focused on the development of a fast and sensitive method to determine naproxen for therapeutic application.

In this context, electrochemical sensors can offer the straight forward advantage of being able to distinguish one specific species in complex mixtures. Also, they are considered to have technical simplicity, good sensitivity and easy adaptability for in situ analysis with relatively cheap instrumental set-ups [7-12]. The use of voltammetric methods with solid electrodes was recommended for the determination of trace amounts of important species in real samples [13]. In recent years carbon paste electrode (CPE), which is made up of carbon particles and an organic liquid, is widely applied in the electroanalytical community due to its low cost, ease of fabrication, high sensitivity and selectivity for detection and renewable surface [14-16].

Over recent years increasing attention has been focused on the production of novel nanoscale materials [17]. Metal-oxide semiconductor nanomaterials are considered to be promising functional materials in biosensing area, because of their good biological compatibility, large surface area, special physical and chemical properties [18–25]. Of particular interest are the nanostructured metal oxide materials, such as ZnO, NiO, CuO, Co_3O_4, amongst others [26-29]. Specially, nickel oxide (NiO), a p-type semiconductor with a wide band gap of 3.7 eV and a high isoelectric point (IEP) of about 10.7, has been studied intensely because of its high chemical stability, electrocatalysis, electron transfer capability and good biological compatibility [30-32].

Room temperature ionic liquids (RTILs), which are compounds that consist only of ions, are liquids at around room temperature. Recently, RTILs have been developed and received much attention in many areas of chemistry and electrochemical industry [33-35]. The acknowledged advantages of these RTILs include good chemical and thermal stability, almost negligible vapor pressure, good ionic conductivity, wide electrochemical windows and low toxicity [36]. RTILs can be employed as not only supporting electrolyte but also modified materials. The RTIL modified carbon paste electrodes (CPEs) has shown higher electron rate transfer compared to that of bare CPE. Moreover, RTIL has been shown to be suitable media for supporting biocatalytic processing [37-39].

In the present work, we describe the preparation of a new carbon paste electrode modified with an ionic liquid and NiO/CNTs nanocomposite (ILNCNPE) and investigate its performance for the determination of naproxen in aqueous solutions.

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. A conventional three electrode cell was used at 25±1 °C. An Ag/AgCl/KCl (3.0 M) electrode, a platinum wire, and ILNCNPE were used as the reference, auxiliary and working electrodes, respectively. A Metrohm 710 pH meter was used for pH measurements.

Naproxen and all of the other reagents were of analytical grade and were obtained from Merck (Darmstadt, Germany). The buffer solutions were prepared from orthophosphoric acid and its salts in the pH range of 2.0-9.0. Ionic liquid (n-hexyl-3-methylimidazolium hexafluoro phosphate) was purchased from Sigma Aldrich Co. NiO/CNTs nanocomposite were synthesized in our laboratory according to the method described in literatures [40].

2.2. Preparation of the electrode

ILNCNPEs were prepared by mixing 0.04 g of NiO/CNTs nanocomposite with 0.96 g graphite powder and approximately, ~0.8 mL of ionic liquids with a mortar and pestle. The paste was then packed into the end of a glass tube (ca. 3.4 mm i.d. and 15 cm long). A copper wire inserted into the carbon paste provided the electrical contact.

For comparison, ionic liquid / carbon paste electrode in the absence of NiO/CNTs nanocomposite (ILCPE), NiO/CNTs nanocomposite carbon paste electrode (NCNTPE) consistent of NiO/CNTs nanocomposite powder and paraffin oil, and bare carbon paste electrode (CPE) consisiting of graphite powder and paraffin oil were also prepared in the same way.

2.3. Preparation of real samples

Five naproxen tablets (labeled 250.0 mg per tablet) were grinding. Then, the tablet solution was prepared by dissolving 250.0 mg of the powder in 100 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 naproxen content was analyzed by the proposed method using the standard addition method.

Urine samples were stored in a refrigerator immediately after collection. Ten milliliters of the sample was centrifuged for 15 min at 2000 rpm. The supernatant was filtered out using a 0.45 µm filter. Then, different volume of the solution was transferred into a 25 mL volumetric flask and diluted to the mark with PBS (pH 7.0). The diluted urine sample was spiked with different amounts of naproxen.

3. RESULT AND DISCUSSION

3.1. Electrochemical behavior of naproxen at the surface of various electrodes

Fig. 1 displays cyclic voltammetric responses from the electrochemical oxidation of 100.0 µM naproxen at the surface of ILNCNPE (curve d), ILCPE (curve c), NCNTPE (curve b) and bare CPE (curve a). The results showed that the oxidation of naproxen is very weak at the surface of the bare CPE, but the presence of ILs in CPE could enhance the peak current and decrease the oxidation potential (decreasing the overpotential). A substantial negative shift of the currents starting from oxidation potential for naproxen and dramatic increase of the current indicates the highly ability of ILNCNPE (curve d) and ILCPE (curve c) to naproxen oxidation. The results showed that the combination of NiO/CNTs nanocomposite and the ionic liquid (curve d) definitely improved the characteristics of naproxen oxidation. However, ILNCNPE shows much higher anodic peak current for the oxidation of naproxen compared to ILCPE, indicating that the combination of NiO/CNTs nanocomposite and IL has significantly improved the performance of the electrode toward naproxen oxidation.

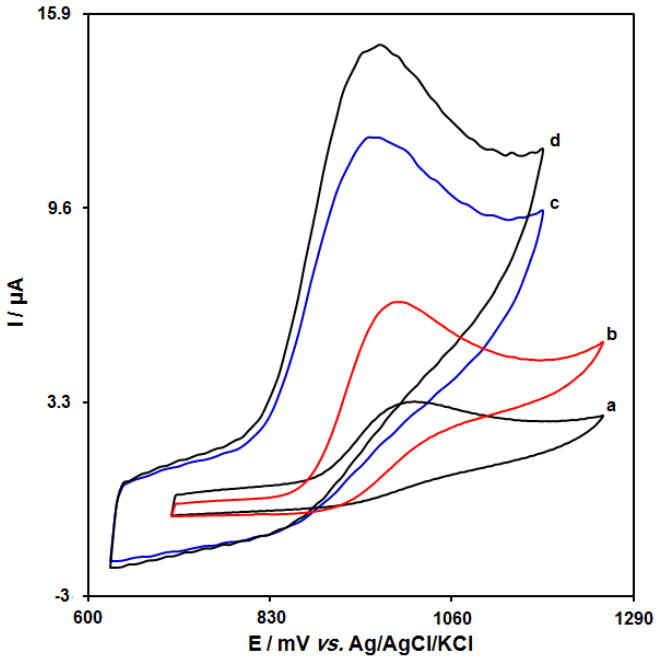

Fig. 1. CVs of a) CPE, b) NCNTPE, c) ILCPE and d) ILNCNPE in the presence of 100.0 µM naproxen at pH 7.0, respectively. In all cases the scan rate was 50 mV s^{-1}

3.2. Effect of scan rate

The effect of potential scan rates on the oxidation current of naproxen 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 50 to 700 mV s^{-1}.

Fig. 2B shows the Tafel plot for the sharp rising part of the voltammogram at the scan rate of 50 mV s^{-1}. If deprotonation of naproxen is a sufficiently fast step, the Tafel plot can be used to estimate the number of electrons involved in the rate determining step. A Tafel slope of 0.2011 V was obtained which agrees well with the involvement of one electron in the rate determining step of the electrode process [41], assuming a charge transfer coefficient, α of 0.7.

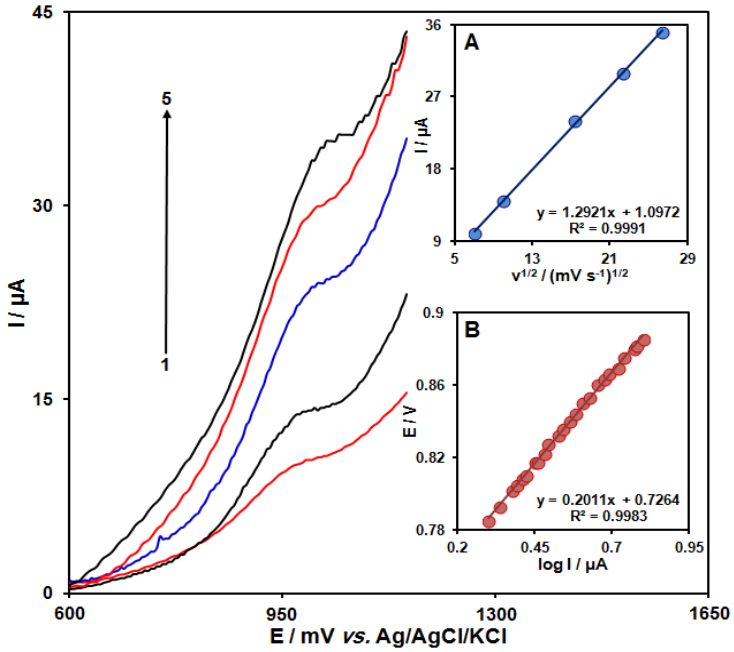

Fig. 2. CVs of ILNCNPE in 0.1 M PBS (pH 7.0) containing 100.0 µM naproxen at various scan rates; numbers 1-5 correspond to 50, 100, 300, 500 and 700 mV s^{-1}, respectively. Insets: (A) Variation of anodic peak current *vs*. square root of scan rate, (B) Tafel plot derived from the LSV at the scan rate of 50 mV s^{-1}

3.3. Chronoamperometric measurements

Chronoamperometric measurements of naproxen at ILNCNPE were carried out by setting the working electrode potential at 1.1 V *vs*. Ag/AgCl/KCl (3.0 M) for the various concentrations of naproxen in PBS (pH 7.0) (Fig. 3). For an electroactive material (naproxen

in this case) with a diffusion coefficient of D, the current observed for the electrochemical reaction at the mass transport limited condition is described by the Cottrell equation [41].

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

Where D and C_b are the diffusion coefficient ($cm^2\ s^{-1}$) and the bulk concentration (mol cm^{-3}), respectively. Experimental plots of I *vs.* $t^{-1/2}$ were employed, with the best fits for different concentrations of naproxen (Fig. 3A). The slopes of the resulting straight lines were then plotted *vs.* naproxen concentration (Fig. 3B). From the resulting slope and Cottrell equation the mean value of the D was found to be 1.42×10^{-5} cm^2/s.

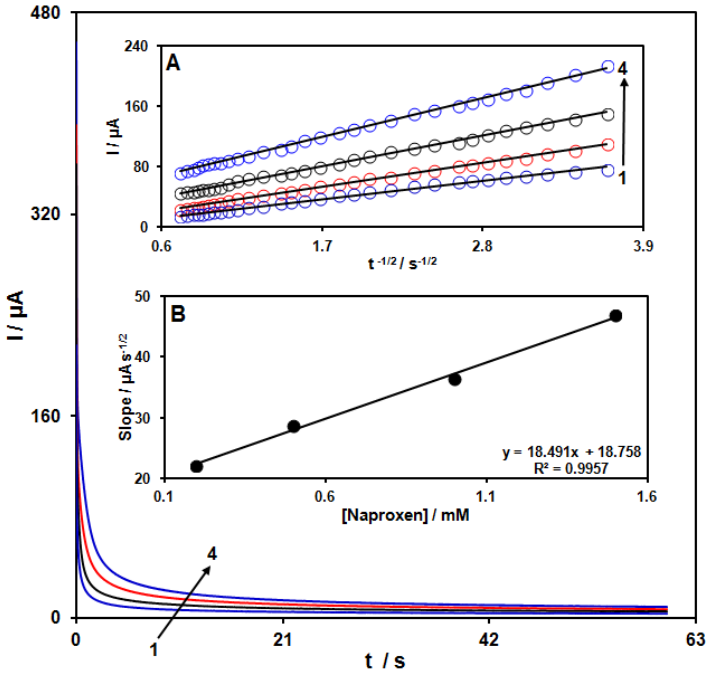

Fig. 3. Chronoamperograms obtained at ILNCNPE in 0.1 M PBS (pH 7.0) for different concentrations of naproxen. The numbers 1–4 correspond to 0.2, 0.5, 1.0 and 1.5 mM of naproxen. Insets: (A) Plots of I *vs.* $t^{-1/2}$ obtained from chronoamperograms 1–4. (B) Plot of the slope of the straight lines against naproxen concentrations

3.4. Calibration plot and limit of detection

The peak current of naproxen oxidation at the surface of the modified electrode can be used for determination of naproxen in solution. Therefore, square wave voltammetry (SWV) experiments were done for different concentrations of naproxen (Fig. 4). The oxidation peak currents of naproxen at the surface of modified electrode were proportional to the concentration of the naproxen within the ranges 7.5×10^{-7} to 8.0×10^{-4} M with detection limit (3σ) of 1.2×10^{-7} M.

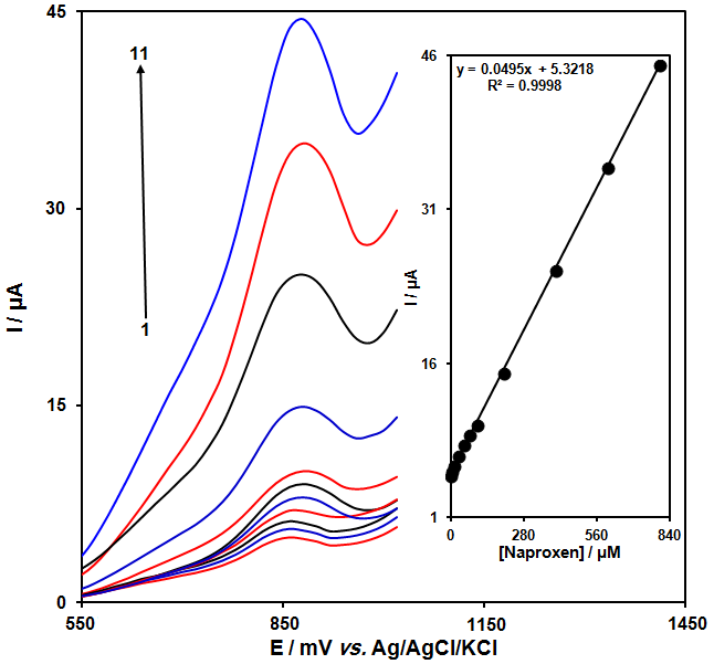

Fig. 4. SWVs of ILNCNPE in 0.1 M PBS (pH 7.0) containing different concentrations of naproxen. Numbers 1-11 correspond to 0.75, 2.5, 10.0, 30.0, 50.0, 70.0, 100.0, 200.0, 400.0, 600.0 and 800.0 µM of naproxen. Inset shows the plots of the peak current as a function of naproxen concentration in the range of 0.75-800.0 µM

Table 1. Determination of naproxen in naproxen tablet and urine samples. All the concentrations are in µM (n=5)

Sample	Spiked	Found	Recovery (%)	R.S.D. (%)
Naproxen tablet	0	8/0	-	3/3
	2/5	10/8	102/8	1/9
	7/5	15/4	99/3	2/2
	10/0	18/2	101/1	2/9
	12/5	19/9	97/1	3/1
Urine	0	-	-	-
	10/0	10/3	103/0	2/8
	15/0	15/1	100/7	3/3
	20/0	19/5	97/5	2/1
	25/0	24/8	99/2	1/7

3.5. Real sample analysis

In order to evaluate the analytical applicability of the proposed method, also it was applied to the determination of naproxen tablets and urine samples. The results for determination of the three species in real samples are given in Table 1. Satisfactory recovery

of the experimental results was found for naproxen. The reproducibility of the method was demonstrated by the mean relative standard deviation (R.S.D.).

4. CONCLUSION

In the present study, a modified paste electrode is constructed. The modified electrode was applied for determination of naproxen. Excellent features, like a wide linear range, low detection limit, high reproducibility and repeatability and longtime stability proved the successful application of this sensor for the determinations of naproxen

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