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Electrochemical monitoring of piroxicam in different pharmaceutical forms with multi-walled carbon nanotubes paste electrode

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Abstract

The electrochemical behavior of piroxicam on a multi-walled carbon nanotubes electrode for the first time was investigated. A highly sensitive and fast responding sensor for determination of piroxicam was simply and conveniently fabricated. The constructed electrode exhibits efficiently catalytic activity for the electrooxidation of piroxicam at a reduced over potential with high sensitivity, stability, and long lifetime in the wide concentration rang of piroxicam. The oxidation process was found to be dependent on the pH of the supporting electrolyte. The behavior is further exploited as a sensitive detection method for piroxicam determination by differential pulse voltammetry. Under the optimized conditions the calibration plots are linear in the concentration range of 0.15–5 $\mu g\,ml^{-1}$. Application of the method for the determination of the drug in the dosage form (Feledene capsules and tablets and also piroxicam gel), without any interference, from the excipients, resulted in acceptable deviation from the stated concentrations. Recoveries were obtained in the range 96.35–104.16%. The detection limit of 0.1 $\mu g\,ml^{-1}$ was obtained for piroxicam determination.

Keywords: Multi-walled carbon nanotubes; Determination; Piroxicam; Pharmaceutical; Carbon paste; Voltammetry

1. Introduction

Non-steroidal anti-inflammatory drugs (NSAIDs) are a well-known class of drugs that are antipyretic, analgesic and anti-inflammatory agents. They are used to reduce pain in different arthritis and other post-operative conditions [1]. Recently several other functions of this group of drugs have been identified which include chemoprevention [2,3], chemosuppression [4,5], UV-sensitization [6–8], UV-protection [9], etc. These drugs are also found to be very good anti-oxidants [10]. Piroxicam is of great pharmacological and therapeutic interest, being a long-lasting non-steroidal anti-inflammatory drug (NSAID) with limited gastric mucosal side effects. The drug is quite efficient in the treatment of rheumatoid arthritis, osteoarthrosis, ankylosing spondylitis and acute pain in muscular, skeletal disorders and acute gout and has a long half-life [11]. Side effects can occur with all medications. The most important side effect that has been reported with piroxicam is gastrointestinal. Other side effects such as headache, dizziness, skin rashes, palpitations, edema, and tinnitus are less important and infrequent [12,13]. Several methods have been proposed involving either spectroscopic or chromatographic techniques for the determination of piroxicam in pharmaceuticals and biological fluids [14–18]. However, most of those methods presented insufficient sensitivity owing to the use of large biological fluid volumes or chromatographic interferences. So there is a considerable interest in developing a simple and sensitive method for piroxicam detection.

Voltammetric techniques have found widespread use in pharmaceutical analysis, since the procedures usually involve a simple dilution step, and most of the excipients used do not interfere in the subsequent with the determination step. However, with respect to electrochemical behavior of this molecule, only few studies were found in the literature [19–25]. According to Kauffmann et al.'s work [19], piroxicam is polarographically reducible and give a well-defined wave. These authors gave an excellent explanation of its reduction process by using electrochemical and optical observations. Electrochemical behavior related to the reduction of piroxicam at mercury pool electrode was also studied [20]; in this work, the authors gave

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the electrode reaction mechanism. The identification of reduction products was carried out on a mercury pool in acidic and alkaline media. According to these authors, the process takes place by the irreversible reduction of the double bond of the enol function over the entire pH range studied. In another paper, these authors completed the aspects of the electrode reactions using different pH media and gave a brief discussion of electrooxidation of this compound identifying only the oxidation site [21]. They confirmed that piroxicam is also electrochemically oxidizable on several carbon electrodes. Recently Torriero et al. [25] presented a paper on electrochemical oxidation behavior of the piroxicam at the glassy carbon electrode in 10% ACN + 90% 0.2 M Britton–Robinson buffer. In this work they applied cyclic voltammetry (CV) and controlled potential electrolysis in combination with UV–vis, GC–MS and NMR analysis to identify the complex mixture of products formed during the electrooxidation of piroxicam, this study permits a better knowledge of the piroxicam electrochemical behavior. However, in this work there is no report on determination of piroxicam.

Recent studies demonstrated that CNT's can impart strong electrocatalytic activity; and the excellent electrocatalytic activity of carbon nanotubes in redox behavior of different compounds has been reported. The unique electronic properties of these materials have been effectively exploited in electrochemistry as a means of promoting the electron transfer reaction of wide biological compounds [26–28]. The ability of CNT's-modified electrodes to promote electron-transfer reactions of important biomolecules has been investigated. Glassy carbon, Pt, and Au electrode modified with CNT's has been shown excellent electro catalytic activity toward many compounds [29–33].

Palleschi and Rivas have reported on the advantages of carbon nanotubes paste electrodes on the electrochemical behavior of some biological compounds [34,35]. Some researchers characterized the new kind of CNT's paste-based modified electrodes. They described the use of CNT's paste electrode prepared by dispersion of carbon nanotubes within mineral oil for studying the adsorption and electrooxidation of nucleic acids, dopamine, ascorbic acid, hydrogen peroxide and some other biological and pharmaceutical compounds [36–39]. The new composite electrode had very good ability to promote the adsorption and electron-transfer reactions with the attractive remarks of composite materials. In electrochemical investigations, CNT's paste electrodes have showed a very stable electrochemical behavior so they can use to study electrochemistry of a wide range of molecules for promising sensor applications.

This work is the first report on the electrooxidation and determination of piroxicam at multi-walled carbon nanotubes paste electrodes (MWCNT's paste elecrode). In present work, owing to the presence of potentially oxidizable amide and enol functionalities in piroxicam molecular structure, it was decided to investigate the voltammetric behavior of this compound at MWCNT's paste electrodes, in order to develop a sensitive method for its determination. We found this electrode can be used for determination of piroxicam in a good sensitivity without any need of the modifier, This electrode present advantages over previous mentioned electrodes as it can be used in a mild pH medium, in previous works researchers have used surfactant or non aqueous solvent such as acetonitrile in acidic media for piroxicam assay but in the following work, we will demonstrate the accelerated oxidation of piroxicam at multi-walled carbon nanotubes paste electrodes and the resulting electrode showed good activity determination of this drug.

2. Experimental

2.1. Reagents and solutions

Paraffin oil, graphite powder, potassium chloride, sodium chloride, sodium nitrate, sodium hydroxide, hydrochloric acid, and acetic acid are from Fluka or Merck companies and were used as purchased, without further purifications. Multi-walled carbon nanotubes with a 95% purity o.d. = 10–30 nm, i.d. = 5–10 nm and 0.5–500 μm length were obtained from Aldrich. Piroxicam in analytical grade was provided from Sigma. Since piroxicam generally has a low solubility in water, a stock solution of piroxicam (50 $\mu g\,ml^{-1}$) was prepared by dissolving appropriate amount of it in analytical pure grade methanol and then diluted with distilled water (water–methanol 1:1) and stored at 5 °C in the dark. The dilute solutions were prepared daily with solutions composed of methanol–water aqueous solutions (supporting electrolyte and 0.1 M buffer acetate). Pharmaceutical formulations of piroxicam (Feldene tablets and Feldene capsules, Pfizer, NY, USA, 0.5% piroxicam gel, Razi Co., Tehran, Iran) were purchased from the local market. Doubly distilled deionized water was used throughout the work.

2.2. Instrumentation and software

Voltammetric experiments were performed using a Metrohm electroanalyzer (model 757 VA Computrace) connected to a 633 MHz Pentium II computer. The system was operated and measurements recorded using VA Computrace version 2 (Metrohm) that run under windows XP. The three electrodes system consists of the CNT's paste and carbon paste electrodes as working electrode, Ag|AgCl| 3 M KCl as a reference electrode and a platinum wire as an auxiliary electrode. The body of working electrode was a PTFE cylinder that tightly packed with carbon paste. A copper wire inserted into the carbon paste provided the electrical contact. The measurements of pH were made with a Metrohm 780 pH meter (Metrohm Ltd., CH-9100-Hesau, Switzerland) using a combined glass electrode.

2.3. Pretreatment of carbon nanotubes material

In order to remove graphite nano particles, amorphous carbon, and catalyst impurities the MWCNT's were first purified as reported previously [29,34]. Briefly, 100 mg of it were oxidized at 400 °C for 30 min to remove amorphous carbon particles and to eliminate metal oxide catalyst. Further purification was accomplished by stirring the CNT's in 2 M of nitric acid at 25 °C for 24 h and then the residue washed until the pH of the solution was neutral, then dried.

2.4. Electrode preparation

The MWCNT's paste electrodes were prepared by hand mixing of multi-walled carbon nanotubes powder and mineral oil. Electrodes prepared with different ratios of multi-walled carbon nanotubes powder and mineral oil was constructed (30/70, 35/65, 40/60, 50/50, 65/35, 70/30% (w/w)), the electrodes with the ratio of 65/35 and 70/30% (w/w) produced paste with good consistency and also had approximately the same background. However, the electrode prepared with a 70.0% (w/w) carbon nanotubes powder and 30.0% (w/w) mineral oil, offered the lowest resistance.

The ohmic resistance was directly measured by connecting the electrode surface and copper wire to an ohmmeter. It is interesting to note that the untreated and treated CNT's electrodes showed resistance (10 Ω and 15 Ω) values of a little smaller than that of CP (25 Ω) electrode.

The classical carbon (graphite) paste electrode (CPE) was prepared in a similar way by mixing graphite powder with mineral oil as our previous work [40]. The paste surface was smoothed and rinsed with water before each measurement. The composition of 70/30% for both CNT's paste and CP electrodes was chosen because it furnished rate constant reasonably independent of composition. A portion of the resulting paste was packed firmly into the cavity of a Teflon tube. The body of working electrode was a PTFE cylinder (1.9 mm i.d.) that tightly packed with carbon paste. A copper wire inserted into the carbon paste provided the electrical contact.

2.5. Procedure for calibration

The freshly polished CNT's paste electrodes were pretreated by performing several times cyclic voltammetric scan from 0.0 to 1.0 V, until a low and steady background was obtained (about 10 cycles).

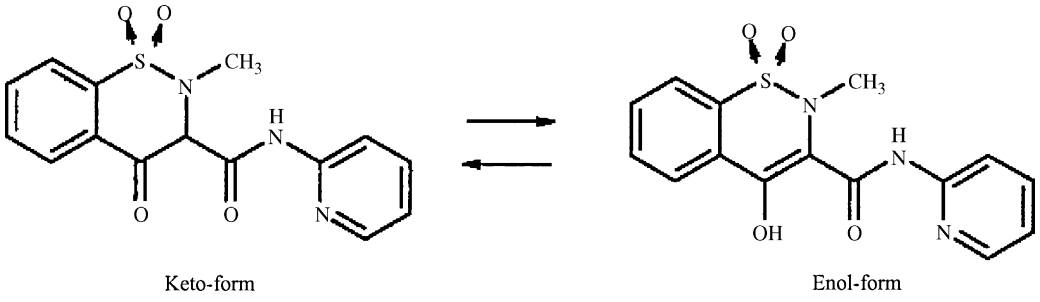
Cyclic voltammetric experiments were carried out by scanning at a rate of 50 mV s^{-1} over a range of 0–0.80 V versus Ag/AgCl in solutions containing 0.25 M KNO_3 as supporting electrolyte and 0.1 M buffer acetate (pH 6.0). Hydrodynamic voltammograms were recorded by scanning the potential over the range of 0.3–0.65 V versus Ag/AgCl at a scan rate of 50 mV s^{-1} and at various rotation speeds of a rotating disk electrode (RDE). Differential pulse voltammetric experiments were performed using, the pulse amplitude of 0.05 V; pulse duration time of 0.04 s; step time of 0.4 s and a scan rate of 50 mV s^{-1} over the potential range of 0.3–0.65 V versus Ag/AgCl. All the solutions were free of oxygen by bubbling nitrogen gas for 10 min, and all experiments were carried out under a nitrogen atmosphere.

2.6. Procedure for pharmaceutical analysis

The contents of 20 tablets or capsules of piroxicam (Feledene) were individually weighed, in order to find the average mass of each tablet, then powdered or evacuated. An accurately weighed portion of the powder was transferred into 100 ml calibrated flasks and diluted to volume with solvent (as in standard solution, water–methanol 1:1); shaken well for 15 min and the solutions were filtered through 0.45 μm membrane filter. Then, 1 ml aliquots were transferred from each flask to 25 ml volumetric flasks and completed to volume with water–methanol as working solution. For determination of piroxicam in gel form about 1.0 g gel 0.5% of piroxicam (Razi Co., Tehran, Iran) was accurately weighted and dissolved in 10 ml 0.25 M NaOH solution and 10 ml methanol, this mixture sonicated for 15 min, then the solution filtered and diluted in a 50 ml volumetric flask to the mark (as in standard solution, water–methanol 1:1); appropriate aliquots from the working solutions were taken for the determination of piroxicam, and diluted to obtain final concentrations in the range of calibration graph. Then solutions assayed as described under optimized proposed procedure.

3. Results and discussion

Piroxicam is an enolic acid and exhibits a weakly acidic 4-hydroxy proton and weakly basic pyridyl nitrogen. It has the following structural formula and tautomeric forms (Scheme 1) [11], piroxicam can be ionized as a zwitterions that has two pKa values ($pK_{a_1} = 1.86$ and $pK_{a_2} = 5.46$). The presence of potentially oxidizable functional groups such as amide and enol suggested us to carry out study on electrooxidation of this drug on the surface of MWCNT's paste electrode for the electrochemical study and also in order to develop a method for its determination. To the best of our knowledge there is no any report about determination of this drug in pharmaceutical preparations using MWCNT's paste electrodes.



Scheme 1. Tautomeric forms of piroxicam.

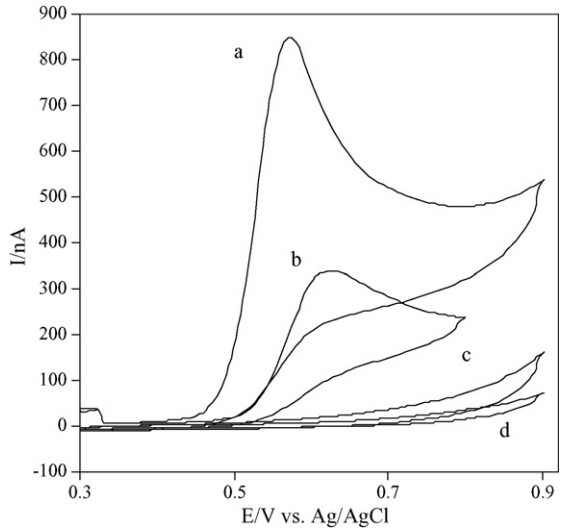


Fig. 1. Cyclic voltammograms 5 μg ml^{-1} piroxicam in 0.25 M KNO_3 as supporting electrolyte and 0.1 M buffer acetate (pH 6.0) at the surface of (a) MWCNT's paste electrode, (b) carbon paste electrode, (c) background current for MWCNT's paste electrode, (d) background current for carbon paste electrode; scan rate: 100 mV s^{-1}.

3.1. Electrochemical behavior of piroxicam at the MWCNT's paste electrode and CPE

The cyclic voltammetric responses of a 5 μg ml^{-1} piroxicam at a MWCNT's paste and carbon paste electrode in 0.25 M KNO_3 as supporting electrolyte and 0.1 M buffer acetate (pH 6.0) and scan rate of 100 mV s^{-1} were recorded. Fig. 1 shows the representative cyclic voltammograms.

At both electrodes, an anodic current by the oxidation of piroxicam is observed, on the reverse scan, no distinct reduction wave was observed, indicating that the drug is irreversibly oxidized at the electrodes; however, no cathodic peak is found which indicate an irreversible heterogeneous charge transfer reaction in this system. This behavior is agreed with those of the previous report for piroxicam oxidation [24,25].

The anodic peak potential for oxidation of piroxicam at a bare CPE is about 630 mV (curve b) while, piroxicam starts to oxidize at about 460 mV (curve a) at a MWCNT's paste electrode under identical conditions and its peak potential is about 560 mV so, a decrease in over potential is observed, and in comparison with the CPE the peak current was increased significantly at MWCNT's. On the other hand, the use of multi-walled carbon nanotubes paste electrode to mediate the piroxicam oxidation is evident from the reduction of over potential and, 2.45-fold increases in current compared with that of the conventional carbon paste electrode. These values indicate electrocatalytic oxidation of piroxicam at the MWCNT's paste electrode.

3.2. Optimizing of some experiment conditions

3.2.1. Effect of the supporting electrolyte

To optimize the determination condition of piroxicam the effects of various supporting electrolytes such as KCl, NaCl, $NaNO_3$, KNO_3, K_2SO_4, NH_4NO_3 and KBr, on catalytic ability of MWCNT's paste electrode were examined. The subsequent studies showed that, the best electrocatalytic effect could be obtained in a solution containing 0.25 M of KNO_3. It is found that the peak current becomes the highest in solution containing KNO_3 and the voltammogram shape is well defined. The oxidation peak potential is shifted more negatively in the presence of this supporting electrolyte, so from the results it can be found, this solution (0.25 M of KNO_3) is the most suitable electrolyte for the electrochemical oxidation of piroxicam and it was chosen as the supporting electrolyte in this experiment to investigate the electrochemical behavior of this drug in detail.

3.2.2. Influences of accumulation potential and time

Accumulation step is usually a simple and effective way to enhance the determining sensitivity. Accumulation potential and time are two crucial parameters for the accumulation step. The oxidation peak current of 2 μg ml^{-1} of piroxicam was compared, at different potential between 0.00 and 0.45 V by cyclic voltammetry. The peak current almost does not vary with shifting the accumulation potential, revealing that the accumulation potential has no influence on the oxidation peak current of piroxicam at the MWCNT's paste electrode thus, the accumulation of piroxicam was carried out under open-circuit conditions. Unlike accumulation potential, the accumulation time influences the oxidation peak current responses. The accumulation times were examined in the range of 0–20 min. The peak heights was increased with increasing accumulation time up to 5 min and then leveled off, it could be concluded that the adsorption of piroxicam on MWCNT's paste electrode became saturated. Thus, the accumulation step in this study was accumulation time, and the experiments were performed under open-circuit for 5 min.

3.2.3. Effect of the solution pH

The electrooxidation of piroxicam was studied over pH range of 1.5–8.5. Cyclic voltammograms of 4 μg ml^{-1} piroxicam at different pH in this range were recorded at the surface of a multi-walled carbon nanotubes paste electrode. The results showed the oxidation peak is pH dependent. Piroxicam has potentially oxidizable amide and enol functionalities in its molecular structure; it bears a weakly basic pyridyl group and an enolic function. The presence of the basic pyridyl function enhances the acidity of the enolic group and, consequently, influences its lipophilicity [25].

The effect of pH on the peak currents for the oxidation of piroxicam is shown in Fig. 2a. As the pH is increased, the enolate form increases in solution and the peak current slightly began to decrease. From these results it may be inferred that the primary oxidation site is the amide function, followed by the oxidation of the enol function.

To obtain more insight about the mechanism of electrooxidation of piroxicam, an analysis of the dependence of E_p versus pH was performed. In water the proton transfer from or toward organic molecules is usually considered fast [25], meaning that H^+ are in equilibrium in solution near the electrode. This type of situation should prevail in acidic or not excessively basic media, especially when the site of protonation is an oxygen atom. The

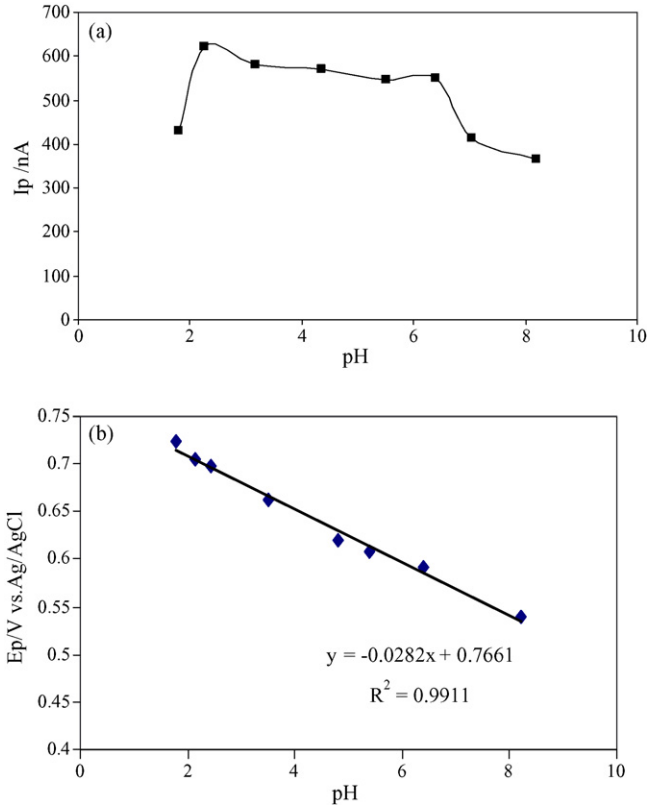


Fig. 2. (a) Peak current for oxidation of 4 μg ml^{-1} piroxicam in 0.25 M KNO_3 electrolyte at a MWCNT's paste electrode at different pH, scan rate: 50 mV s^{-1}. (b) Plots of peak potential of piroxicam oxidation at a MWCNT's paste electrode vs. pH, for 4 μg ml^{-1} piroxicam in 0.25 M KNO_3 electrolyte, scan rate: 50 mV s^{-1}.

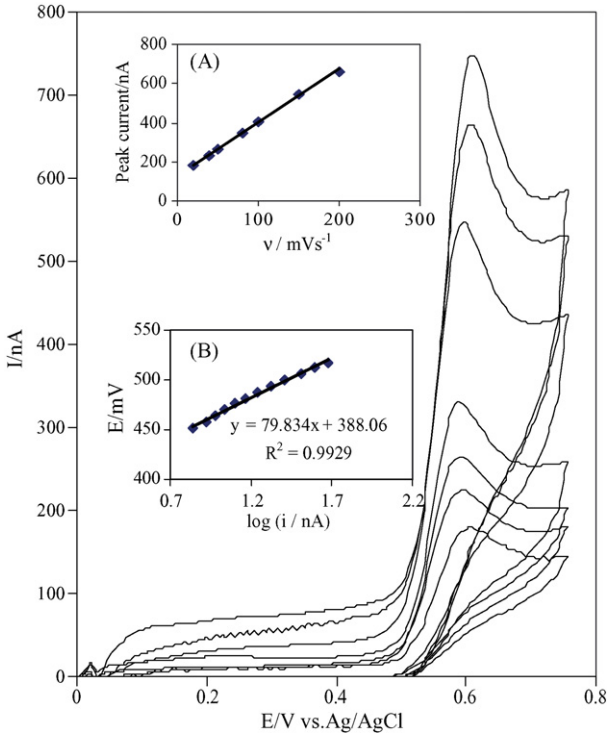


Fig. 3. Dependence of the cyclic voltammetric response at a MWCNT's paste for 2 μg ml^{-1} of piroxicam in 0.25 M KNO_3 and pH 6.0 on sweep rate: 10, 30, 50, 80,100, 150, 200 mV s^{-1}. (Inset A) Plot of anodic peak current vs. scan rate mV s^{-1}. (Inset B) Tafel plot from the rising part of the current voltage curve at a scan rate of 10 mV s^{-1}.

dependence of the peak potential to the pH suggests an overall electrode process, which is determined by a proton transfer.

Between pH 1.50 and 8.50, the oxidation peak potential (E_p) is shifted to more negative values with increasing pH. This is a consequence of the deprotonation in the oxidation process that is facilitated at higher pH. The electrode shows better oxidation activity between the pH ranges of 5.0–6.50 values.

It can be concluded that the catalytic oxidation is more favored at this range of pH, so pH 6 was selected for detection, because in this pH MWCNT's paste electrode possesses good electrode activity for oxidation of piroxicam.

A plot of E_p versus pH is shown in Fig. 2b. A linear portion was observed in the range of pH from 1.50 to 8.50, with a slope of 0.0282 V/pH. Following equation displays correlation between peak potential and pH:

$$E_p\,(\text{pH}\ \ 1.50\text{–}8.50) = 0.766 - 0.0282\text{pH}, \quad R^2 = 0.9911$$

The slope is close to that expected for a two electronic electrode reaction, which is 0.0296 V/pH at 25 °C [23]. The possibility is that the number of proton transfers is 1. That is 0.0592(h/n) V/pH, where h and n are the number of protons and electrons involved in the electrode process. The oxidation process of the amide function involves two electrons and one proton. This agrees with the mechanism proposed for the anodic oxidation of amides in aqueous solutions [23]. It starts by one electron oxidation to form the cation radical at the nitrogen. This followed by a rapid loss of a second electron and proton to give the iminium ion, to which the water is subsequently added.

3.2.4. Scan rate effect studies

Effect of scan rates on the electrooxidation of piroxicam at the MWCNT's paste electrode was investigated by cyclic voltammetery. Fig. 3 shows the cyclic voltammograms corresponding to the response of a MWCNT's paste electrode in the presence of 2 μg ml^{-1} piroxicam at different scan rates. The anodic peak currents are linearly proportional to the scan rate over this range with a correlation coefficient of 0.998 as shown in the inset (A) of Fig. 3; under these conditions the currents were adsorption controlled. Considering the structure and porosity of carbon nanotubes, it is reasonable to expect adsorption on it. In addition, with increasing scan rate, oxidation peak potential (E_p) shifts to more positive values, this positive shift in the peak potential also confirm the irreversibility of the process.

A Tafel plot from the rising part of the current voltage curve at a scan rate of 10 mV s^{-1} is illustrated in inset (B) of Fig. 3. The Tafel slope having the value of $2.3RT/(1-\alpha)$ nF for an oxidation reaction [41], a slope of 79.83 mV decade^{-1} is obtained and based on this slope, the value of $n(1-\alpha)$ is calculated to be 0.738.

There is a linear correlation between the peak potential and the logarithm of scan rate, log ν. The evaluated slope of E_p versus log ν is 40.22 and $R^2 = 0.9904$. From this slope, Tafel slope, b,

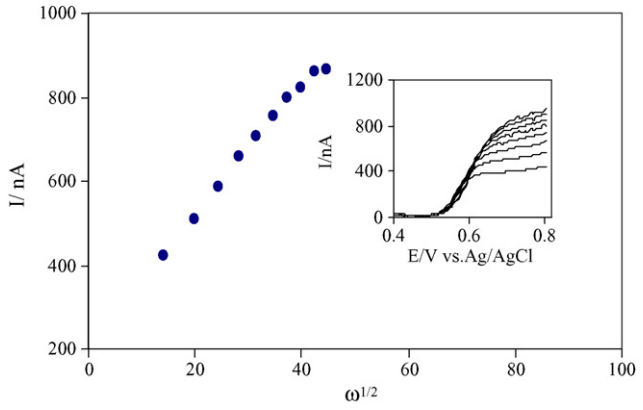


Fig. 4. Levich plot derived from rotating disk electrode voltammograms of a MWCNT's paste electrode for 2 μg ml^{-1} of piroxicam in 0.25 M KNO_3 as supporting electrolyte and pH 6.0 at rotation rates from 200 to 1600 from bottom to top, respectively. Scan rate: 50 mV s^{-1}. (Inset) Corresponding voltammograms.

can be obtained using the following equation [42]:

$$E_p = \left[\frac{b}{2}(\log\ \nu)\right] + \text{constant}$$

where $b = 80.44$. By considering a two-electron mechanism, it can be demonstrated that the transfer coefficient, α, is equal to 0.632.

3.2.5. Rotating disk electrode study

The hydrodynamic voltammograms of 2 μg ml^{-1} concentration of piroxicam on surface of the MWCNT's paste were recorded at different rotation rates over a range of 200–2000 rpm. Using these hydrodynamic voltamograms, limiting current versus square root of rotation rate was plotted as shown in Fig. 4. From Levich equation, it would be expected that this plot should be linear as this figure shows, for diffusion limited process Levich equation predicts a linear relationship between i_L and $\omega^{1/2}$. However, under these conditions a small deviation can be observed from linearity above rotation rate 1600 and this suggests that the process of electrode reaction is not completely controlled by diffusion of piroxicam.

3.3. Differential pulse voltammetery detection of piroxicam at MWCNT's paste electrod

3.3.1. Calibration graph and limit of detection

The calibration curve for piroxicam was characterized by differential pulse voltammetry, the differential pulse voltammograms obtained for a series of piroxicam solutions with various concentrations are illustrated in Fig. 5. As mentioned before the best parameters on the MWCNT's paste electrode for detection of piroxicam is accumulation time (5 min). The pulse amplitude of 0.05 V; pulse duration time of 0.04 s; step time of 0.4 s and at a scan rate of 50 mV s^{-1} over the potential range of 0.3–0.65 V versus Ag/AgCl. As inset in Fig. 5 shows there is a linear relationship in the plot of i_p versus piroxicam concentration between 0.15 and 5 μg ml^{-1}. That relationship can be described with the following linear regression equation in the mentioned concentration range: i_p (nA) = 83.57C + 110.87, where C is concentration

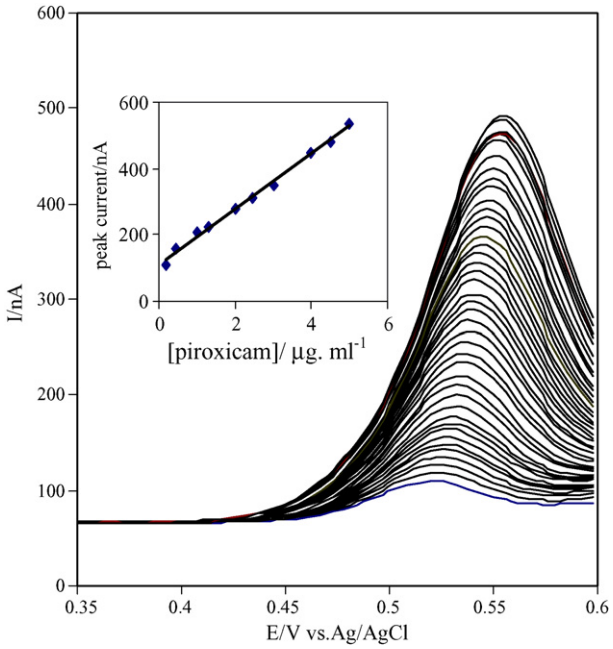


Fig. 5. Differential pulse voltammogams for piroxicam at a MWCNT's paste electrode in the presence of various concentration of piroxicam inset: calibration curve for piroxicam at a MWCNT's paste electrode in 0.25 M KNO_3 as supporting electrolyte and 0.1 M buffer acetate (pH 6.0) and accumulation time 5 min.

of piroxicam in μg ml^{-1}, with a correlation coefficient of 0.9972. By using $3s_b$ in the calibration equation; we calculated the detection limit concentration [43]. The detection limit of 0.1 μg ml^{-1} was estimated.

3.4. Stability and reproducibility of MWCNT's paste electrode

The stability of MWCNT's paste electrode and its effect on oxidation of piroxicam was investigated by recording the cyclic voltammograms of MWCNT's paste electrode response. The time stability of CNT's paste electrode in air condition is shown in Fig. 6 where the peak current versus time plot of

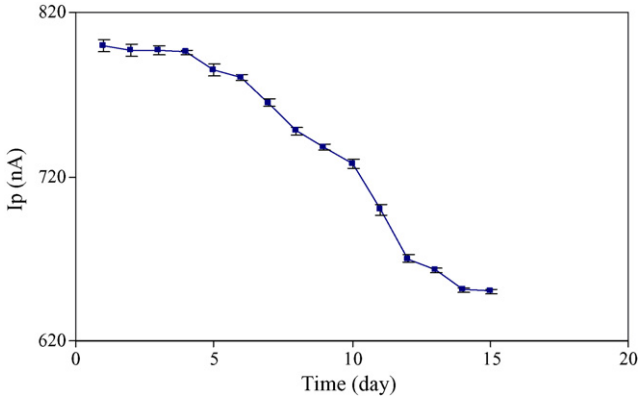


Fig. 6. Investigation of stability of a MWCNT's paste electrode for 4 μg ml^{-1} of piroxicam in 0.25 M KNO_3 as supporting electrolyte and pH 6.0 and accumulation time 5 min. Scan rate: 100 mV s^{-1}. Error bars show standard deviation for five replicates.

Table 1
Reproducibility of CNT paste electrode on freshly prepared electrodes tested with 4 μg ml^{-1} piroxicam

Day	i_p (nA)	E_p (mV)
1	798[a]	547[a]
2	797	562
3	801	565
4	800	570
5	802	578
6	786	568
Average	797	565
R.S.D. (%)	0.73	1.83

[a] Average for five replicate.

Table 2
A comparison of observed and reported piroxicam concentration in different pharmaceutical forms

Sample	Preparation label claim (mg per tablet or capsule or % gel)	Found[a]: mg ± R.S.D. (%)
Feldene		
Tablet 1	20	19.56 ± 0.67
Tablet 2	10	10.56 ± 1.98
Capsule1	20	19.09 ± 1.67
Capsule2	10	11.56 ± 2.31
Piroxicam gel	0.5	0.55 ± 0.65

[a] Average of five determinations.

4 μg ml^{-1} of piroxicam are presented. As it can be seen after 15 days the CNT's paste electrode maintained about 80% of the initial current response, which shows MWCNT's paste electrode has a good long-time stability for the determination of piroxicam.

Reproducibility of MWCNT's paste electrode was investigated by using cyclic voltammetry. Six freshly packed electrodes were prepared on six consecutive days and the peak current and peak potential values of a solution containing 4 μg ml^{-1} of piroxicam was measured for each electrode. The results are presented in Table 1. As it can be seen, a relative standard deviation R.S.D. of cyclic voltammogarm's currents for five replicate was less than 0.73% and that of peak potential was 1.83%.

4. Analytical application

4.1. Analysis of commercial tablets

Because of its important anti-inflammatory activity, piroxicam is commercialized in several types of pharmaceutical preparations, such as tablets, capsules, suppositories, gel, oral drops and injectables, commercially available dosage forms of this drug were analyzed by the proposed method. The application of the proposed method to the assay of dosage forms was examined by analyzing tablets and capsules and gel. Stock solutions of pharmaceutical compound obtained as mentioned in procedure section and were subsequently diluted so that piroxicam concentration falls in the range of calibration plot. Differential pulse voltammograms were then recorded under exactly identical conditions that were employed for plotting calibration plot. The values of experimentally determined piroxicam and reported in various dosage forms are tabulated in Table 2. As can be seen, the data are in good agreement with labeled amounts in all cases.

4.2. Mean recovery test and effect of excipients

In order to assess the possible analytical applications of the proposed method, the effects of some substances that often accompany piroxicam in various pharmaceutical formulations were studied by adding different amounts of these substances into the pure solution of the drug in the buffer pH 6.0. It was observed that fructose, glucose, dextrose, magnesium stearate, lactose, and starch did not interfere in the determination of piroxicam at levels far in excess of their normal occurrence in pharmaceutical preparations.

Table 3
Recovery study of piroxicam solution in the presense of some excipients

Drug	Concentration		Recovery (%)	R.S.D. (%)[a]
	Taken (μg ml^{-1})	Found (μg ml^{-1})		
Piroxicam solution[b]				
1	0.25	0.24	96.00	3.0
2	1.00	0.98	98.00	2.28
3	1.85	1.79	96.75	0.98
4	2.65	2.68	101.13	1.61
5	4.78	4.98	104.18	1.23

[a] The number of replicates = 5.
[b] Synthetic solutions of piroxicam containing: glucose, lactose and fructose: 10%, and magnesium stearate: 50 μg ml^{-1}.

Moreover recovery studies were carried out, in order to check the accuracy of the proposed method. Mean recovery values ranged between 96.35 and 104.16% in all cases. Results are summarized in Table 3. The small value of relative standard deviation; indicate that the proposed method is highly accurate, precise and reproducible.

5. Conclusion

In summery, the result presented in this study confirm that MWCNT's paste electrode enable, very fast and stable voltammetric measurement of piroxicam in a good sensitivity. This electrode present advantages over previous mentioned electrodes. Constructed MWCNT's paste electrode offers a marked decrease on overvoltage for piroxicam oxidation without need any modifier as well as better sensitivity to those observed at a conventional CPE. The procedure to fabricate of this electrode is simpler than those used for other piroxicam sensors. This electrode exhibits excellent electrocatalytic behavior toward piroxicam oxidation in a mild aqueous media, with overpotential of about 90 mV less than that at a CP electrode. The resulting electrode showed sensitive, stable and fast electrochemical behavior and possesses good electrode activity for oxidation and determination of piroxicam.

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