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Application of modified carbon paste electrode with multiwall carbon nanotube as a simple and an effective catalyst for determination of cefixime in real samples

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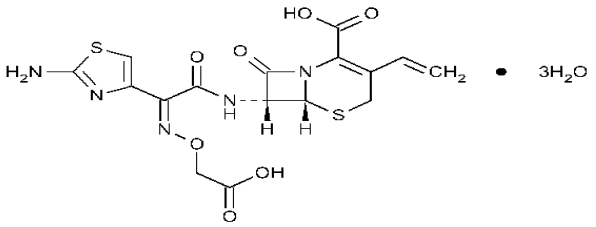
In this research, a modified electrode has been produced by mixing of graphite and multiwall carbon nanotube (MWCNT-CPE). This modified electrode has a very good activity toward the cefixime electrooxidation in a phosphate buffer solution (pH=5). Under optimal experimental conditions, the peak current response increased linearly with cefixime concentration over the range of 3-12×10^3μM. The detection limit (3δ) of the method was 2.5μM. Therefore, this modified electrode was a simple, rapid and effective electrode to determine cefixime in pharmaceutical preparations.

Keywords: Cefixime, modified electrode, electrooxidation, real sample.

INTRODUCTION

Cefixime [6R-[6a,7b(Z)]]-7-[[(2-amino-4-thiazoyl) [(carboxymethoxy) imino]acetyl]amino] 3-ethenyl -8-oxo -5- thia-1-azabicyclo[4.2.0]oct-2-ne-2-carboxylic acid (Scheme 1)is a third generation cephalosporin. It is a useful antibiotic for the treatment of a number of bacterial infections such asotitis, sinusitis, tonsillitis and bronchitis. It is also used to treat typhoid fever. It is also a primary candidate for switch therapy owing to its very good efficacy and safety profile [1].



Scheme 1. Chemical structure of cefixime

Up to now, several analytical methods have been reported for the determination of cefixime including High-performance liquid chromatography (HPLC) [2,3], high-performance capillary electrophoresis [4], high-performance thin-layer chromatography (TLC) [5],liquid chromatography (LC)–tandem mass spectrometric [6] and various spectrophotometry methods [7]. In most of the reported methods, the selectivity and sensivity have been improved, but they are time-consuming, involving a large number of complicated pretreatment steps for analysis, and they require sophisticated and expensive instrumentation. In comparison with above methods, using of voltammetric methods has advantages such as simplicity, cheapness and increasing in sensitivity and selectivity by modifying electrodes.

On the other hand, carbon nanotubes (CNTs) are considered as a novel nanosized material playing a main role in the field of nanotechnology. They are widely used in materials sciences, physical and electronic fields for various applications [8-12]. Several unique properties of CNTs such as good electrical conductivity, extremely high mechanical strength and high chemical stability [13, 14] have been caused numerous investigations were focused on the studies of their properties and applications. In addition, the subtle electronic behavior of CNTs reveals that they have the ability to promote electron transfer reaction and have a high electrocatalytic effect when used as electrode materials [15, 16]. All these fa scinating properties make CNTs as a suitable candidate for the modification of electrodes [17, 18].

The goal of this study was to development of new, fully validated and rapid for the simple and direct determination of cefixime in drug dosage forms without any time-consuming extraction or separation steps prior to drug assay.

Our literature survey indicates that, there is no report about using of modified carbon paste electrode with MWCNT-CPE for determination of cefixime. In this work, we decided to use of this modified electrode for the aim of electrocatalytic oxidation of cefixime. Also, the study aimed at examining the applicability of this modified electrode to determine cefixime in some real samples.

EXPERIMENTAL

Reagents and materials

The solvent used in this work was twice distilled water. The electrolyte solutions were 0.1 M

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phosphate buffer in pHs of 2, 5, 7, 9,11and 13 respectively. Cefixime was prepared from Sari Pharmaceutical (Sari, Iran) and used without further purification. High viscosity paraffin (density = 0.88 g cm^{-3}) from Fluka (Sydney, Australia) was used as the pasting liquid for CPE. Graphite powder (particle diameter = 0.10 mm) from Merck and MWCNT (New Jersey, US) (with purity >95%, outer diameter 5-20 nm, inner diameter 2-6 nm, length 1-10 mm, number of walls 3-15, apparent density 0.15-0.35 g cm^{-3} from Nanostar Tech. Co., Tehran, Iran) were used as the working electrode substrates. To activate MWCNTs and remove any residual metals in the nano-structure, 0.5 g of MWCNTs plus 20 mL of concentrated acids (H_2SO_4/HNO_3: 3/1) were mixed in a 25-mL flux and then the mixture was refluxed for 8 h. Then, the MWCNTs were separated from the mixture and washed with 50 mL doubly distilled water, centrifuged (3500 rpm) and dried at room temperature. All other reagents were analytical grade.

Apparatus

Electrochemical experiments were performed with potentiostat/galvanostat μ-Auto lab type system (Eco Chemie BV, Netherlands), general purpose electrochemical system (GPES). The voltammetric measurements were performed in a three-electrode cell using the modified CPE as working electrode, a Ag | AgCl | KCl (3 M) from Azar electrode (Urmia, Iran) as reference electrode and a platinum rod from Azar electrode (Urmia, Iran) as counter-electrode. All experiments were carried out at room temperature. No action was taken to remove oxygen from solutions.

The electrode modification

A mixture of graphite powder (0.99 g) plus MWCNT (0.01 g) were blended by hand mixing with a mortar and pestle. Using a syringe, the amount of paraffin was added to the mixture and mixed well until a uniformly wetted paste was obtained. The resulting paste was then inserted in thebottom of a glass tube (internal radius: 1.7 mm). The electrical connection was implemented by a copper wire lead fitted into the glass tube. A fresh electrode surface was generated rapidly by extruding a small plug of the paste out of the tube and smoothing the resulting surface on white paper until a smooth shiny surface was observed.

RESULTS AND DISCUSSION

Oxidation of cefixime at MWCNT-CPE

Preliminary experiments were carried out to compare electrochemical behavior of cefixime in phosphate buffer of pH=5 at CPE and MWCNT-CPE by cyclic voltammetry. Fig. 1 shows cyclic voltammograms recorded at CPE and MWCNT-CPE in the absence and the present of cefixime. No cathodic and anodic peaks were observed in the investigated potential range (0.2 to +1.2 V) on CPE but at the surface of MWCNT-CPE, only an anodic peak was observed at about 0.82 V (more than 380 mV negative shift compared to the observed solvent oxidation wall at CPE).As it is obvious, the cefixime signal is sensitive and occurs at a much lower over potential than on CPE. These results show that MWCNT-CPE reduces the over potential of cefixime oxidation and in fact imparts electrocatalytic activity for cefixime determination.

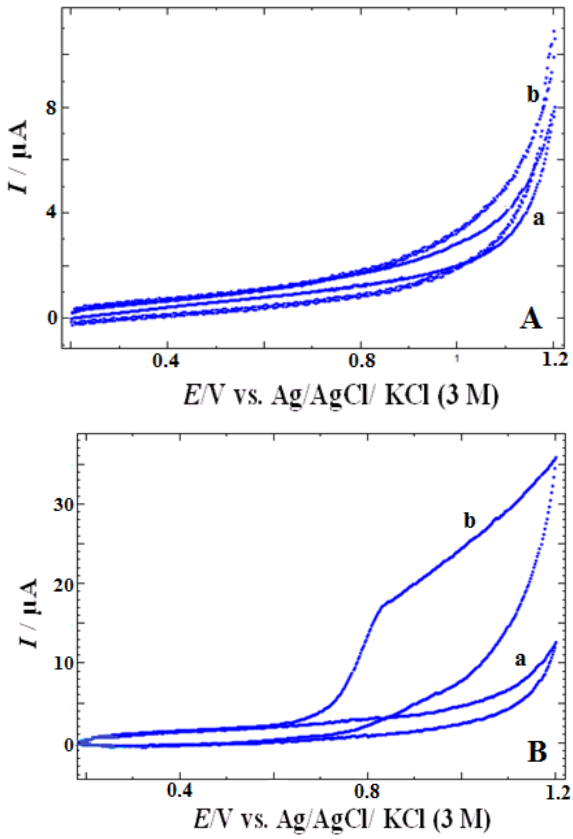

Fig. 1. Cyclic voltammograms of (A) CPE and (B) MWCNT-CPE in 0.1 M phosphate buffer solution (pH=5), in the absence (*a*) and presence of 1 mM cefixime (*b*), Scan rate = 20 mV s^{-1}.

Optimization of electrode variables for efficient performance of MWCNT-CPE towards cefixime oxidation

Effect of different percents of MWCNT to graphite

Figure 2 shows the effect of the paste composition on the resulting voltammetric response. MWCNT-CPE with different percents of MWCNT to graphite (0.5, 1, 5, 10, 15 and 25%) was studied in the absence and the presence of cefixime. There is an increase in the oxidation current peak density with increasing of percents of MWCNT to graphite through a maximum at 1%. Based on Figure 2, as the amount of MWCNT is increased more than 1%, the current value decreases. However, large surface areas can cause increments in background current, which might decrease the resulting current values as in the case of our work in agreement with previous works [19-21]. As a result, further studies were conducted using a 1% MWCNT to graphite.

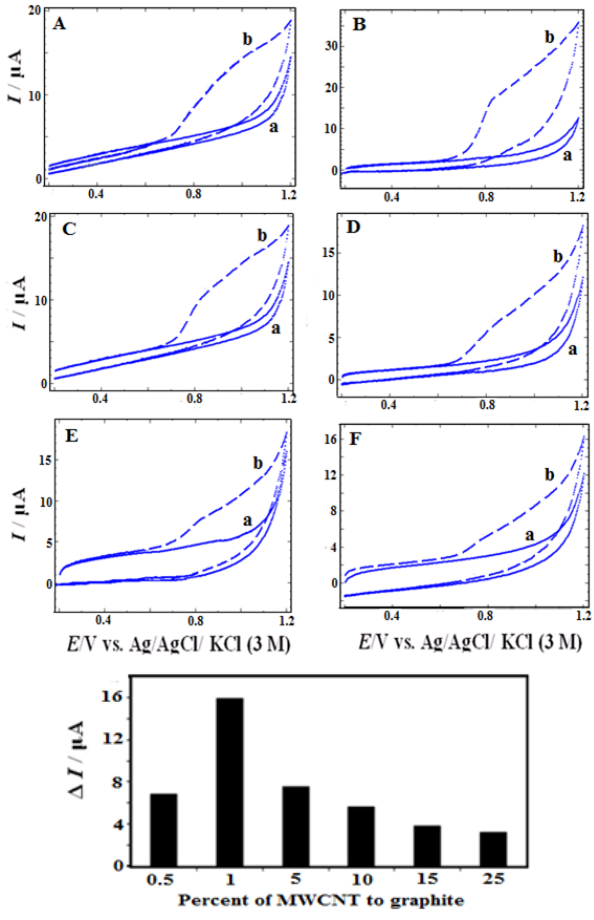

Fig. 2. Cyclic voltammograms of different percents of MWCNT to graphite (A) 0.5%, (B) 1%, (C) 5%, (D) 10%, (E) 15% and (F) 25% at the MWCNT-CPE in (a) absence and (b) in presence of 1 mM cefixime and in 0.1 M phosphate buffer solution (pH=5) at a scan of 20 mV s^{-1}, Inset: Comparison of electrocatalytic currents for the oxidation of cefixime observed on MWCNT-CPE.

Effect of pH

We have tested the electrocatalytic activity of MWCNT deposited on CPE against cefixime electrooxidation in the buffered solutions with various pHs in the range of 2–13 (Fig. 3).For all of them, the modified electrode shows electrocatalytic activity. However, higher electrocatalysis peak currents are observed at pH=5 (the value of ΔI is the most of others).Based on such investigations, a buffered solution of pH=5 was chosen as an optimum condition in order to obtain the best sensitivity in all voltammetric measurements.

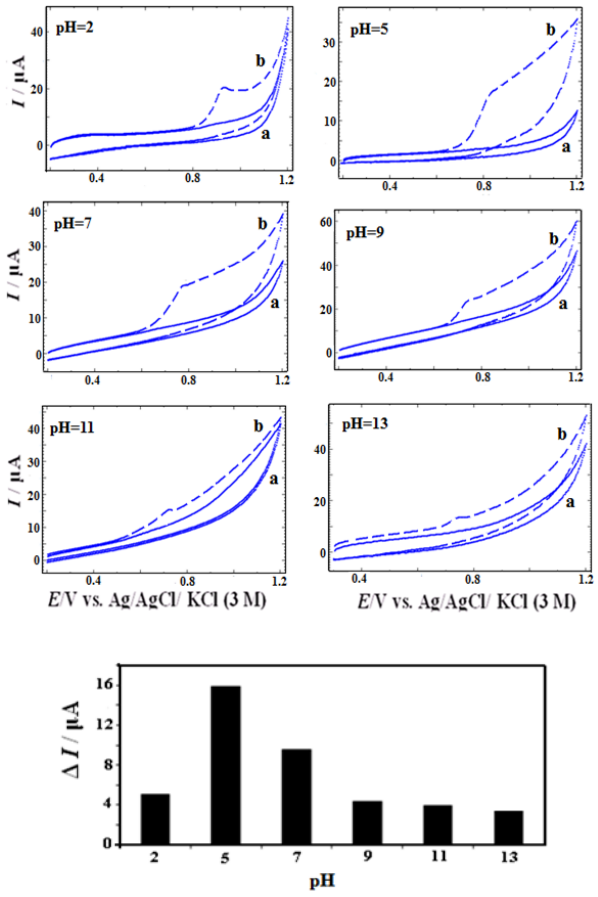

Fig. 3. Cyclic voltammograms of MWCNT-CPE in different pH solutions, in the absence (a) and the presence of 1 mM of cefixime (b) at scan rate of 20 mVs^{-1}.

Effect of cefixime Concentration

Figure 4 shows the effect of cefixime concentration on the cyclic voltammograms of the MWCNT-CPE. As can be seen from this figure, the height of the anodic peak increases with increasing in cefixime concentration. The characteristic shape of CV in this potential region indicates that the signal is due to the oxidation of cefixime. The catalytic peak current is proportional to the concentration of cefixime in the range of 0.003 to 12mM. The linear regression equation is I (µA) = 5.939C_{cefixime} (mM) + 11.68 (R^2 = 0.99). The detection limit calculated

from the calibration graph was 0.0025mM when the signal to noise ratio was 3.

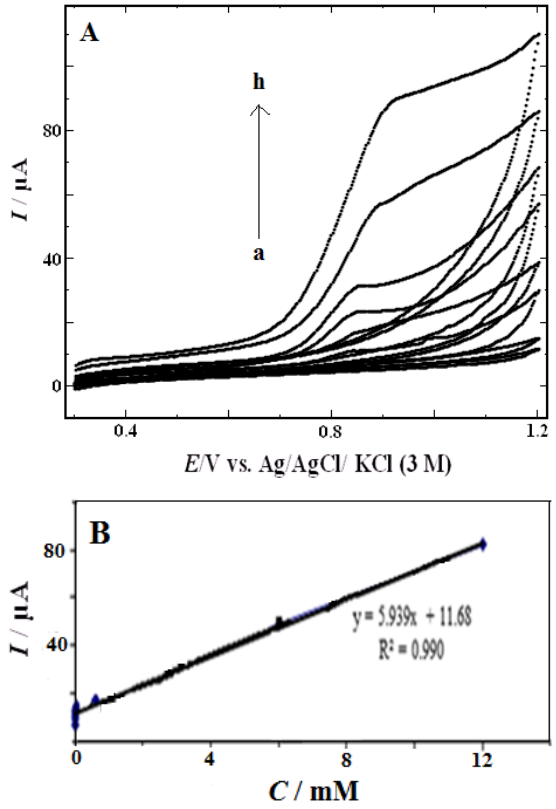

Fig. 4. (A) Cyclic voltammograms of MWCNT-CPE in 0.1 M phosphate buffer solution (pH=5) containing 0.003, 0.008, 0.01, 0.02, 0.04, 0.6, 6 and 12 mM of cefixime from a to h at 20 mV s^{-1} (B) Plot of catalytic current *vs* cefixime concentration.

Real sample analysis

In order to examine the applicability of the proposed method, we tested the determination of cefixime in commercial tablet sample using the standard addition method for preventation of any matrix effect under the optimized conditions. All samples were diluted with phosphate buffer solution (pH=5) and then appropriate amounts of cefixime standard samples were transferred to the electrochemical cell for the determination of it. There is a linear relationship between the I_{pa} versus cefixime concentration. It was found that the drug concentrations determined using this method is in good agreement with the reported values. The value of experimentally determined drug and the declared value in tablet are tabulated in Table 1.

Effect of scan rate

The dependence of the anodic peak current response on the potential scan rate during the electrocatalytic oxidation of cefixime was examined employing CV by varying the scan rate from 10 to 1000 mV s^{-1} (not shown). Results indicated that there is a linear relationship between the anodic peak current (I_{pa}) and the square root of the scan rate ($v^{1/2}$) in the scan rates of 10–1000 mV s^{-1} for cefixime (I_{pa}=1.033 $v^{1/2}$–0.019). This indicates that the oxidation of cefixime at MWCNT-CPE is a diffusion-controlled process.

Chronoamperometric studies

We employed chronoamperometric method for the investigation of electrochemical processes at MWCNT-CPE. Fig. 5 represents the current–time profiles obtained by setting the working electrode potential at 850 mV for various concentrations of cefixime. Plotting of the net current as a function of the inverse square root of time, gives a linear relationship (Fig. 5B), resulting in a diffusion controlled process. The diffusion coefficient of cefixime can be obtained by using the slope of this straight line, according to Cottrell equation [22]:

$$I = nFAD^{1/2}C^{*}\pi^{-1/2}t^{-1/2} \qquad (1)$$

Table 1. Determination of cefixime in pharmaceutical preparation using MWCNT-CPE

Sample	Amount Labeled / g	Amount Founded / g	Recovery %	RSD %, n=5
Cefixime tablet	0.4	0.422	105.5	2.5

Table 2. Comparison of performances of some electrodes in determination of cefixime

Electrode	Modifier	pH	LDR /µM	LOD/ µM	Reference
CPE	Gold nanopartcle	3	1.2-200	1	[23]
GC	MWCNT/$NiFe_2O_4$	8	1.8-600	1.74	[24]
SPGE[a]	Gold nanopartcle	2.6	10-1000	———	[25]
HMDE[b]	———	2.6	9.85-50.4	9.62	[26]
CPE	MWCNT	5	3-12000	2.5	This work

[a]Screen printed gold electrode
[b]Hanging mercury dropping electrode

Where D is diffusion coefficient and C^* is the bulk concentration of cefixime. The value of diffusion coefficient of cefixime was found to be 2.48×10^{-5} $cm^2\ s^{-1}$.

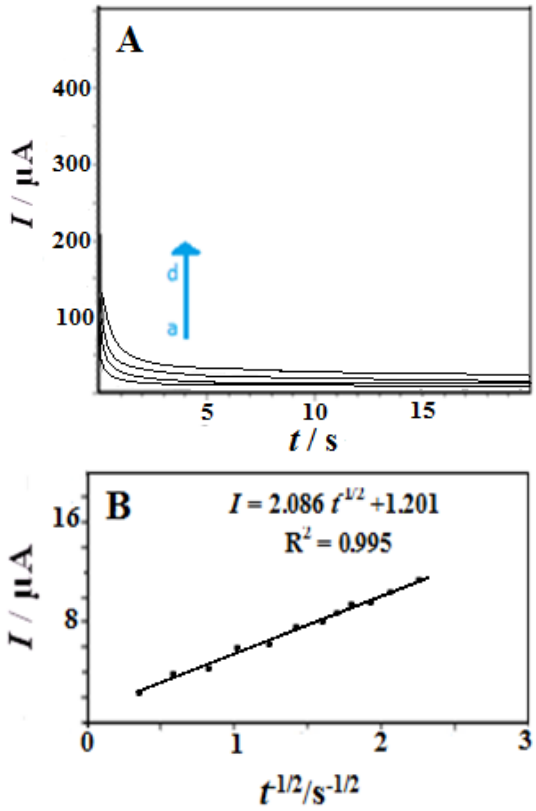

Fig. 5.(A) Chronoamperograms of MWCNT-CPE in 0.1 M phosphate buffer solution (pH=5) with different concentrations of cefixime: (a) 0, (b) 0.1, (c) 0.6 and 6 mM (B) Plot of I *vs.* $t^{-1/2}$

Stability of the modified electrode

The long-term stability of MWCNT-CPE was also studied by storing the electrode for 2 weeks at room temperature. The current response was only decreased by 0.5% after two weeks. It confirms the stability of modified electrode.

CONCLUSION

The study has described successfully the modification of CPE with MWCNT. This modified electrode acts as an active suitable catalyst for the oxidation of cefixime. At the surface of this electrode, the operating potential can be reduced more than 380 mV compared to CPE. The oxidation currents are directly proportional to cefixime concentration in a wide range, which illustrates the potential applications of this type of electrode for the anodic determination of cefixime. Table 2 compared the proposed electrode for cefixime determination with electrodes reported in literatures. As shown, the proposed electrode is comparable with other electrodes. Also, the proposed method provides a fast, sensitive and simple approach to the determination of cefixime in real samples.

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ПРИЛОЖЕНИЕ НА ЕЛЕКТРОД С ВЪГЛЕРОДНА ПАСТА, МОДИФИЦИРАН С МНОГОСТЕННИ ВЪГЛЕРОДНИ НАНОТРЪБИ КАТО ПРОСТ И ЕФЕКТИВЕН КАТАЛИЗАТОР ЗА ОПРЕДЕЛЯНЕТО НА ЦЕФИКСИМ В РЕАЛНИ ПРОБИ

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(Резюме)

В това изследване е приготвен модифициран електрод чрез смесването на графит с многостенни въглеродни нанотръби (MWCNT-CPE). Този модифициран електрод има много добра активност спрямо окислението на цефиксим в разтвор на фосфатен буфер (pH = 5). При оптимални експериментални условия максималният ток нараства линейно с концентрацията на цефиксим в интервала 3-12×10^3 μM. Границата на чувствителност (3δ) на метода е 2.5 μM. Затова използването на този електрод позволява просто, бързо и ефективно определяне на цефиксим във фармацевтични препарати.