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ORIGINAL PAPER

Electrochemistry and voltammetric determination of furazolidone with a multi-walled nanotube composite film-glassy carbon electrode

Lida Fotouhi · Maryam Nemati · Majid M. Heravi

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Abstract This study describes the electrochemical properties of furazolidone (Fu) at a glassy carbon electrode (GCE) modified with a multi-walled carbon nanotube (MWCNT) composite film. Cyclic voltammetry and chronoamperometry techniques were used for diagnostic purposes. The electrode (MWCNT-film-modified GCE) exhibited excellent electrocatalytic behavior for the reduction of Fu as evidenced by the enhancement of the 4e-reduction peak current and the shift in the reduction potential to more positive potential (by 50 mV) in comparison with a bare GCE. The formal potential, $E^{0'}$, of Fu is pH dependent with a slope of 54.4 mV per unit of pH, close to the anticipated Nernestian value of −59 mV for a four-electron and four-proton processes. The transfer coefficient (α), standard rate constant of the surface reaction (k_s), diffusion coefficient (D), and surface concentration (Γ) for the MWCNT-film-modified GCE were calculated. On the other hand, Fu can be accumulated effectively on the MWCNT-film-modified GCE. Under the selected experimental conditions, i.e., solution pH 6, accumulation time 10 min, and accumulation potential −0.30 V, the peak current shows a dynamic linear range 3–800 μM with detection limit 2.30 μM. The method was successfully applied to analyze pharmaceutical formulations. The method used in this study was further applied for the determination of Fu.

Keywords Furazolidone · Multi-walled carbon · Cyclic voltammetry · Nanotube · Modified electrode

L. Fotouhi (✉) · M. Nemati · M. M. Heravi
Department of Chemistry, School of Science, Alzahra University, 1993891176 Tehran, Iran
e-mail: lfotouhi@alzahra.ac.ir

1 Introduction

Furazolidone (Fu) is a drug with a nitro group in its structure. It is a highly effective chemotherapeutic drug, widely used to control common infections in humans and animals. The main pharmaceutical uses of nitro-aromatic compounds (RNO_2) are found in their applications as antibacterial and anticancer agents [1, 2]. The reduction of these compounds is believed to be due to flavoproteins known as "nitro reductases" which have the ability to use nitro compounds as acceptors of one or two electrons [3].

Carbon nanotubes are an interesting class of non-metals offering high electrical conductivity, high surface area, significant mechanical strength, and good chemical stability. They have been known to promote electron transfer reactions when used as an electrode-modifying material. Utilization of these properties has led to the application of carbon nanotubes as scanning probes [4], electron field emission sources [5], sensors [6], nanoelectronic devices [7], and the electrocatalytic behavior toward many biomolecules such as proteins [8], hemoglobin [9], cytochrome *c* [10], DNA [11], acetaminophen [12, 13], and tyrosinase [14].

In a previous study, the authors have described the stabilization of RNO_2^- at a glassy carbon electrode (GCE) and obtained some of its kinetic parameters [15–17]. In continuation of the report on the redox chemistry of Fu, the authors have investigated the electrochemical response of Fu at the MWCNT-film-modified GCE based on the unusual properties of MWCNT. In this study, a MWCNT-film-modified GCE was constructed and used to study the electrochemistry of Fu. Some electrochemical parameters such as the standard rate constant of the surface reaction, transfer coefficient, diffusion coefficient, and surface concentration have been calculated by cyclic voltammetry and chronoamperometry.

2 Experimental

2.1 Apparatus

Electrochemical measurements were carried out with a Metrohm model 746VA trace analyzer connected to a 747 VA stand. The working electrode was a GCE (2-mm diameter). Before use, the working electrode was sequentially polished with graded 10 μM alumina powder, and rinsed with doubly distilled water. A platinum wire and a commercial Ag/AgCl-saturated KCl electrode from Metrohm were used as auxiliary and reference electrodes, respectively. The scan rate in cyclic voltammetry was 100 mV s^{-1}, with the exception of the experiments in which the influence of this variable was studied.

Chronoamperometric measurements were conducted using different concentrations of Fu in solution at the MWCNT-film-modified GCE. The initial potential (E_i) and step potential (E_s) were −0.30 and −0.50 V, respectively, with duration time 50 s.

2.2 Chemical and reagents

Furazolidone (Fu) was obtained from Sigma. All other reagents used were of analytical grade and used without further purification. A Fu solution (1 mM) was used in a Britton–Robinson (B–R) buffer (pH 6.0)-30% DMF solution. A stock B–R buffer solution 0.04 M with respect to boric acid, orthophosphoric acid and acetic acid was prepared from proanalysis reagents. From this stock buffer solutions with various values of pH were prepared by the addition of 0.2 M sodium hydroxide solution. Multi-walled carbon nanotubes with purity 95% (10–30 nm diameter and 5 μm length) were obtained from io-li-tec, Ionic Liquid Technologies. Solutions were deaerated by bubbling high purity argon gas for 10 min through them prior to the experiments. All electrochemical experiments were carried out at room temperature.

2.3 Preparation of the MWCNT film-modified GCE

The GCE was sanded using ultrafine sand paper, polished with 10 μm alumina slurry in sequence and sonicated successively in water and ethanol, respectively, for 5 min.

MWCNT (4 mg) was added to 0.5 mL DMF. A homogeneous and stable suspension of 8 mg mL^{-1} was achieved with the aid of ultrasonic agitation for about 5 min. The GCE was coated by casting with a 1 μL suspension of MWCNT-DMF and dried in air.

2.4 Procedure for analysis of real samples

A tablet after weighing and finely powdering was dissolved in 20 mL DMF. Then the solution was filtered after shaking well for 10 min. 0.10 mL of the filtrate was transferred to a 10 mL calibrated flask and diluted to the required volume with B–R buffer (pH 6.0)-30% DMF solution for determination.

An identical procedure was applied to the determination of Fu in the Fu suspension by taking an appropriate volume 0.50 mL.

3 Results and discussion

3.1 Electrochemical behavior of Fu at the MWCNT-film-modified GCE

It was shown previously [15–17] that Fu at protic media shows two cathodic peaks due to the 4e-reduction of the nitro group to the corresponding hydroxylamine (RNHOH) and 2e-reduction of the corresponding hydroxylamine to the amine (RNH_2), respectively, as is reported for nitroaromatic compounds [18, 19]. In this study our current interest is devoted to the study of this 4e- irreversible reductive peak in the B–R buffer (pH 6.0)-30% DMF solution on the MWCNT-film-modified GCE as working electrode.

The electrochemical behavior of 0.5 mM Fu has been investigated in a protic medium at MWCNT-film-modified GCE (Fig. 1). In the absence of Fu, no redox peaks were observed at either the bare or modified GCE electrodes during the cyclic voltammetry measurements within the potential window of −0.30 to −0.80 V (Fig. 1, curves a, c). Compared with the bare GCE (Fig. 1, curve a) a large background current was observed at the MWCNT-film-modified GCE

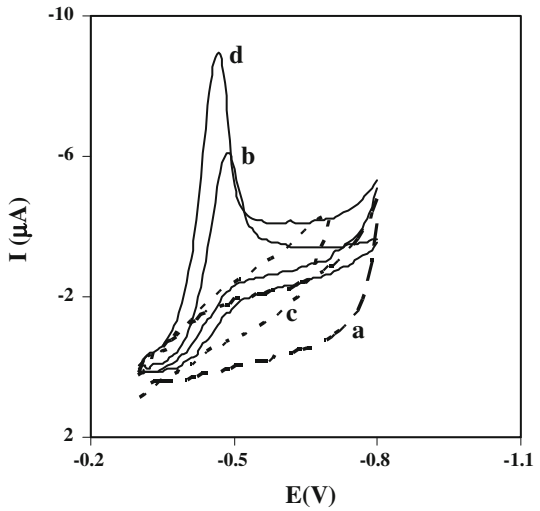

Fig. 1 Cyclic voltammograms of (*a*) Bare GCE in blank solution, (*b*) MWCNT-film-modified GCE, in blank, (*c*) Bare GCE in the presence of 0.5 mM Fu, (*d*) MWCNT-film-modified GCE in the presence of 0.5 mM Fu. B–R buffer (pH 6.0)-30% DMF solution, scan rate: 100 mV s^{-1}

(Fig. 1, curve c) during the cyclic voltammetric scan, which is probably due to a high double layer capacity [20]. The cyclic voltammogram of Fu at bare GCE demonstrates an irreversible peak at −0.50 V due to the 4e- reduction of the nitro group to hydroxylamine (Fig. 1, curve b). In comparison, at a MWCNT-film-modified GCE, the cathodic peak was observed at the more positive potential of −0.45 V and clearly showed an increased peak current (about two times) compared with the bare GCE (Fig. 1, curve d). The increased current as well as the positive shift of the cathodic peak demonstrated an efficient catalytic reduction of Fu on the MWCNT-film-modified GCE.

3.2 Determination of electrochemical active surface area

In order to measure the electrochemically active surface areas of the bare and modified electrodes, the chronoamperogram of 0.1 mM potassium ferrocyanide as the redox probe was recorded. In chronoamperometric studies, the current i, for the electrochemical reaction of ferrocyanide (at a mass-transfer-limited rate) that diffuses to an electrode surface is described by the Cottrell equation [21]:

$$i = \frac{nFAD^{\frac{1}{2}}C^*}{\pi^{1/2}t^{1/2}} \quad (1)$$

where A is the electrochemically active area, D is the diffusion coefficient, C^* is the bulk concentration of ferrocyanide, while the remaining parameters have their usual meanings. Under diffusion control, a plot of i vs. $t^{-1/2}$ will be linear and, from the slope, the value of A can be obtained, since the precise value of the diffusion coefficient of ferrocyanide is well known (6.20×10^{-6} cm^2 s^{-1}). The electrochemically active areas of the MWCNT-film-modified GCE were 0.50 cm^2.

3.3 The effect of the scan rate

Figure 2A shows the cyclic voltammograms of Fu at the MWCNT-film-modified GCE when the scan rate (υ) varies from 20 to 6000 mV s^{-1}. As shown in Fig. 2B, the cathodic peak current of Fu is proportional to the scan rate, which indicates that the electrode process is surface controlled. However, at higher scan rates (more than 2000 mV s^{-1}), the plot of i vs. $\upsilon^{1/2}$ was linear, most likely due to the diffusion-controlled Fu reduction (Fig. 2C). From the observations, it can be concluded that the electrochemical process consists of a mixture of diffusion- and adsorption-controlled processes, depending on the scan rate [22–25]. Furthermore, from the slope of the linear plot of i vs. υ (0.0475), the surface concentration of the electroactive species (Γ) can be estimated to be about 7.05×10^{-11} mol cm^{-2} according to the following equation [26]:

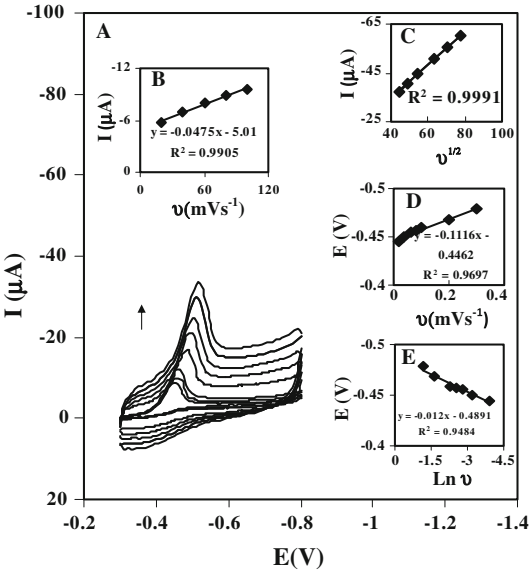

Fig. 2 (*A*) Cyclic voltammetric responses of 1.0 mM Fu at MWCNT-film-modified GCE (B–R buffer (pH 6.0)-30% DMF solution) at scan rates, (inner to outer) 60–600 mV s^{-1}. (*B*, *C*) The plots of peak currents vs scan rate and square root of scan rate, respectively. (*D*, *E*) The variations of peak potential vs. υ and Ln υ, respectively

$$i_p = \frac{n^2 F^2 \upsilon A \Gamma}{4RT} \quad (2)$$

As shown, with increasing scan rate, the peak potential is shifted to a more negative potential. Because of the irreversible electrode process of the reduction reaction of Fu, the Laviron's equation [27] was used to estimate αn and k_s values, as follows:

$$E_p = E^0 + \frac{RT}{\alpha nF}\left[\ln\left(\frac{RTk_s}{\alpha nF}\right) - \ln \upsilon\right] \quad (3)$$

where α is the electron transfer coefficient, k_s is the standard rate constant of the surface reaction, υ is the scan rate, n is the electron transfer number, and E^0 is the formal potential. k_s and αn values can be calculated from the intercept and slope of the linear plot of E_p with respect to Ln υ, if the value of E^0 is known.

The E^0 value at both the bare and MWCNT-film-modified GCE can be deduced from the intercept of E_p vs. υ plot on the ordinate by extrapolating the line to $\upsilon = 0$ (Fig. 2D). Knowing E^0 and from the graphical representations of E_p vs. Ln υ for Fu in the presence of MWCNT (Fig. 2E), the values of $\alpha n = 2.12$, and $k_s = 2.33$ s^{-1} were obtained from the slope and intercept, respectively.

3.4 The effect of pH

Figure 3 shows the cyclic voltammogram of Fu at different values of pH on the MWCNT-film-modified GCE. By increasing the pH from 3 to 7, the cathodic peak potential

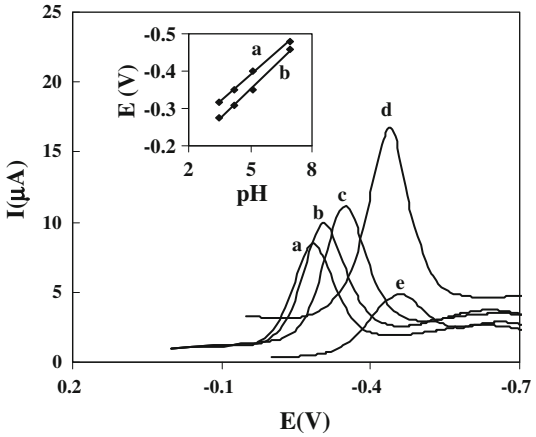

Fig. 3 Cyclic voltammograms of Fu 1.0 mM at MWCNT-GCE for pH values of (*a*) 3, (*b*) 4, (*c*) 5, (*d*) 7, and (*e*) 8 in B–R buffer-30% DMF solutions, scan rate 60 mV s^{-1}. *Inset* plot $E^{0'}$ vs. pH for (*a*) bare GCE, (*b*) MWCNT-film-modified GCE

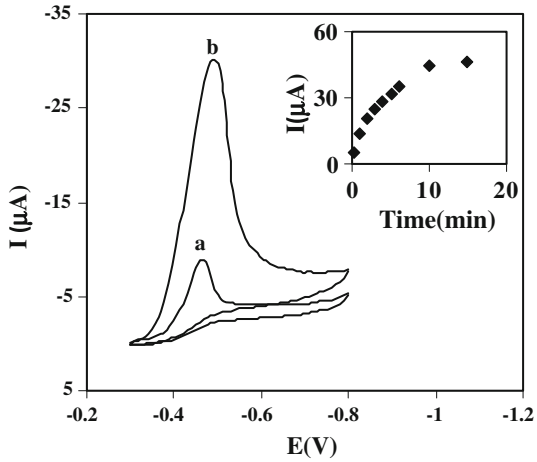

Fig. 4 Cyclic voltammograms of Fu at MWCNT-film-modified GCE (*a*) without accumulation, (*b*) with accumulation at −0.30 v for 2 min. *Inset* the plot of current vs. time

of Fu shifts to more negative potentials up to pH 7 and then becomes constant. The curve showing formal values of $E^{0'}$ is linear with pH in the range 3–7, and with a slope 54.4 mV/pH. This value is close to the theoretical value of 59 mV/pH [21] indicating the participation of the same proton and electron numbers in the electrochemical process.

The position of the break in the $E^{0'}$/pH plot implies that the protonation site is associated with the electrode reaction, which has an apparent pK_a value of about seven (data not shown).

3.5 Chronoamperometric studies

Chronoamperometry can be used for the determination of the diffusion coefficient (D) of Fu. We have obtained chronoamprogram at a fixed potential of −0.50 V over 50 s in B–R buffer (pH 6.0)-30% DMF solution. From the slope of a plot of i vs $t^{-1/2}$, $D = 8.30 \times 10^{-6}$ cm s^{-1} was estimated according to the Cottrell equation [21].

3.6 The influence of accumulation time and accumulation potential

The peak current increases (about six times) when the MWCNT-film-modified GCE is accumulated at potentials where no electrolysis occurs (Fig. 4). The influence of accumulation potential was tested from −0.20 to −0.43 V. The peak current of Fu increases with increasing accumulation potential up to −0.30 V and then becomes constant. Thus, the optimum accumulation potential was selected to be about −0.30 V.

The peak current increases with increasing accumulation time. However, when it exceeds 10 min (the optimum accumulation time) for 0.5 mM Fu solution (Fig. 4, inset), the peak current remains almost unchanged, meaning that an accumulation/or extraction equilibrium is achieved at the electrode/solution interface.

3.7 The effect of the amount of MWCNT composite

The effect of the amount of MWCNT on the cathodic peak was examined by varying the amount from 2 to 6 mg in 0.5 mL of DMF. The results showed that the peak current reached a maximum at 4 mg and decreased after that. The effect of the injected volume of MWCNT composite film was also investigated and a maximum current is obtained at 4 μL. However, the background current is also increased by increasing the injected volume. Thus, the optimum of the amount of MWNCT was selected to be about 1 μL.

3.8 Analytical application, analytical figures of merit

The relationship between the variation of the optimum current and Fu concentration was found to be linear over the entire range of Fu concentration. Under optimum conditions, the calibration curve shows a dynamic linear range of 3–800 μM (Fig. 5). The limit of detection (LOD), was obtained from $Y_{LOD} = X_B + 3S_B$, where Y_{LOD} is the signal at the limit of detection, and X_B and $3S_B$ are the mean and the standard deviation of the blank signal, respectively [28]. Under optimum experimental conditions, the limit of detection (LOD) was 2.3 μM.

The reproducibility of the method was checked by successive determinations (n = 8) of Fu. The relative standard deviations (R.S.Ds.) were less than 1.9%.

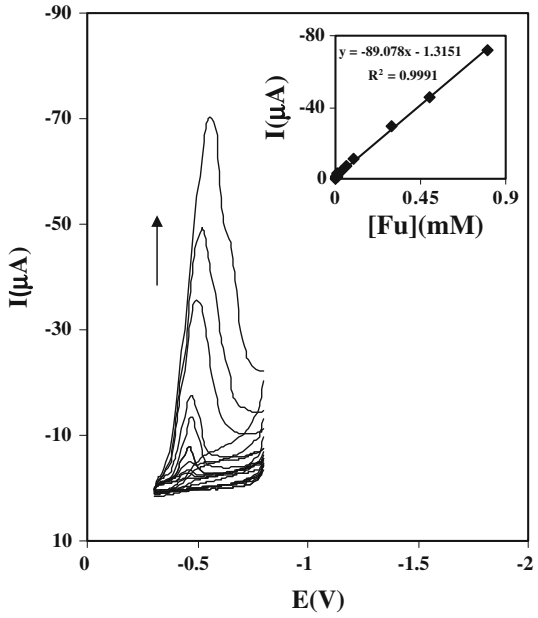

Fig. 5 Cyclic voltammograms of Fu in B–R buffer (pH 6.0)-30% DMF solution at scan rate 100 mV s^{-1} with various concentrations of Fu (3–800 μM). *Inset* the plot of the current vs. Fu concentration

Table 1 Results of analysis of real samples

Sample	Added (mg)	Found (mg)	Actual concentration in real sample (mg)	Recovery (%)	R.S.D. (%) ($n = 3$)
Tablet	–	0.517	0.500	–	–
	0.45	0.957	0.500	103.5	2.4
Suspension	–	0.118	0.125	–	–
	0.08	0.194	0.114	91.4	1.1

3.9 Interferences

The possible interferences of several metal ions such as K^+, Li^+, Ni^{2+}, Ca^{2+}, Ba^{2+}, Pb^{2+}, Cd^{2+}, Al^{3+}, Cu^{2+}, Mg^{2+}, Zn^{2+}, Cl^-, ClO_4^-, NO_3^-, and SO_4^{2-} were investigated. Amino acids such as glycine, L-asparagine, L-phenylalanine, L-cysteine, AND L-leucine were investigated but did not show any interference effect.

3.10 Application to real matrices

To evaluate the applicability of this method on real matrices, assays were performed in pharmaceutical formulation. The results showed that satisfactory recovery for Fu could be obtained. Table 1 summarizes the data obtained for Fu assays performed on the matrices studied using the optimized experimental methodology.

4 Conclusions

In this article, a MWCNT-film-modified GCE, which was easily produced, was used to investigate the detailed electrochemical behavior of Fu. The reported modified electrode significantly improved the electrochemical response of Fu and clearly demonstrated the excellent electrocatalytic activity of the MWCNT-film-modified GCE toward the redox reaction of Fu. Some electrochemical parameters such as the standard rate constant of the surface reaction, transfer coefficient, diffusion coefficient, and surface concentration of the electroactive species have been calculated. Under optimized experimental conditions, good analytical performance was obtained, including suitable precision, excellent linear dynamic range, and detection limits at the trace level. The method is sensitive enough for the analysis of lower concentrations of Fu. Furthermore, the proposed method has advantages like requiring neither expensive instruments nor critical analytical reagents.

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