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Research Article

Rifampicin: Electrochemical Effect on Blood Component by Cyclic Voltammetry Using Nano-Sensor

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Abstract

Rifampicin (RIF) compound was analyzed by electrochemical study using cyclic voltammetric method to characterize the electrochemical properties in blood medium. Glassy carbon electrode (GCE) was modified with carbon nanotubes (CNT) as a high sensitive sensor for using in the electro-analysis of RIF in blood medium. It was found that oxidation and reduction current peaks of RIF in blood medium were at the potential of 0.5 and -0.5 V, respectively. Different concentrations, pH, scan rates, reliability and stability of RIF in blood medium were studied. The diffusion coefficient of oxidation and reduction was determined using the Randles-Seveik equation. The result showed the average value of oxidation and reduction were 2.66×10^{-5} and 8.72×10^{-5} cm^2s^{-1}, respectively.

Keywords: Rifampicin; Blood medium; Cyclic voltammetry; CNT/GCE

Introduction

The important study for the most famous types of the treatment tuberculosis (Tb) disease in terms of its effects on blood components is namely rifampicin (RIF). Our study focused on the effect the oxidation and reduction of RIF of on blood medium by electrochemical analysis using highly accurse nano-sensors. In the recent fifteenth years, scientists have been focusing on the oxidative effect of the medicines in blood medium using oxidation-reduction method by cyclic voltammetric technique [1-7]. Rifampicin, also known as rifampin, is an antibiotic used to treat several types of bacterial infections, including tuberculosis. The structure of RIF compound is illustrated in Fig. 1 [8].

The electrochemical oxidation of RIF and isoniazid was studied by cyclic voltammetric technique in

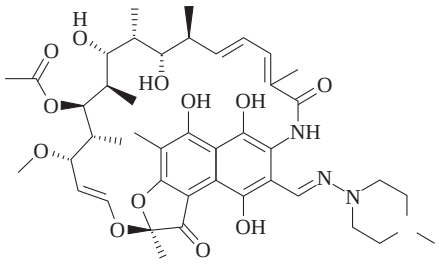

Fig. 1 Structure of rifampicin compound.

Britton Robinson buffer solutions. The oxidation current peak for rifampicin showed a quasi-reversible reaction and an irreversible reaction for the isoniazid [9]. Glassy carbon electrode (GCE) was modified with iron oxide nanoparticles (Fe_3O_4 NPs) and multiwalled carbon nanotubes (MWCNTs) composite to determine RIF by cyclic voltammetric technique. The new sensors were characterized by Fourier transform infrared spectroscopy (FTIR), transmission electron microscopy (TEM), thermogravimetric analysis (TGA) and X-ray diffraction (XRD) studies. The method was successfully applied for the determination of RIF in pharmaceutical tablets without any sample pre-treatment [10]. The technique of differential pulse voltammetry for the determination of RIF as a drug in the associated form was evaluated in the quality of medicine distribution. The potential cyclic voltammetric determination of RIF was achieved at the modified electrode, presenting two oxidation peaks for RIF at potentials approximately 0.09 V (peak 1) and 0.70 V (peak 2) in phosphate buffer solution with a linear range of 0.08-15.00 mM and a detection limit of 0.03 mM. The developed sensor was stable, reproducible and feasible for long-term use in biological samples with satisfactory results for RIF detection [11]. Adsorptive stripping voltammetry of antibiotics of RIF was investigated by cyclic voltammetry and differential pulse voltammetry. The results showed that the determination of highly sensitive oxidation peak current was the basis of a simple, pharmaceutical formulations and biological fluids by differential pulse adsorptive stripping voltammetry. The limits of detection for the determination of RIF in bulk forms were 6.0×10^{-8} mol/L and 1.3×10^{-8} mol/L, respectively [12].

In this work, GCE was modified with CNT for using in cyclic vltammetric technique. RIF compound was studied to find the oxidation-reduction current peaks in blood medium as application study.

Experimental

Materials and chemical reagents

RIF was received from Ajanta Pharma Limited, India. Normal saline was from ADWIC Pharmaceutical Division, Egypt. Carbon nanotubes (purity 99%) was supplied from Fluka Company, Germany. Other chemicals and solvents were of analytical grade and used as received from the manufacturer. Healthy human blood samples were received from Iraqi Blood Bank in Baghdad City of Medicine. Deionized water was used for the preparation of aqueous solutions.

Instrumentation

The EZstat series (potentiostat/glvanostat) provided from NuVant Systems Inc. Pioneering Electrochemical Technologies, USA was used in the present work. Electrochemical workstations of Bioanalytical system with potetiostate driven by electroanalytical measuring softwares were connected to a personal computer to perform cyclic voltammogram. Ag/AgCl (3 M NaCl) and platinum wire (1 mm diameter) was used as a reference and counter electrode, respectively.

Preparing the modification of glassy carbon electrode with carbon nanotube (CNT/GCE)

The mechanical attachment technical method to prepare the CNT/GCE working electrode was employed for preparation of the nano-sensor [13, 14]. The method of the modification of GCE included abrasive application of the multiwall carbon nanotubes (MWCNT) on the clean surface of GCE, forming an array of MWCNT as modified working electrode MWCNT/GCE and replaced in 10 mL of the diluted blood with normal saline ratio of 1 : 9 in the cyclic voltammetric cell; then all the electrodes (working electrode, reference electrode and counter electrode) were connected with the potentiostat.

Procedure

10 mL of the sample of blood with normal saline was replaced in cyclic voltammetry cell; then, each of modified working electrode (MWCNT/GCE), reference and counter electrodes was immersed in the blood sample and connected in the potentiostat and in turn with a personal computer to discuss the cyclic voltammogram of the compound in the cell. Afterwards, 1 uL of the 0.1 M RIF solution was added to every spike by micropipette in the blood medium to determine effect of the redox process of RIF on the blood component.

Results and Discussion

The current study was concerned with the electrochemical behavior of the RIF compound in blood medium which included different concentrations, pH, scan rate, and stability study of CNTs on the GCE as a high sensitive sensor.

Effect of different concentrations

Different concentrations of RIF compound in blood

medium were studied using nano-sensor (CNT/GCE) to determine the detection limit and the sensitivity of the method. Fig. 2 shows the cyclic voltammogram of RIF at different concentrations which enhanced the oxidation-reduction current peaks against the increasing concentrations of RIF in blood medium. Fig. 3 and 4 show the calibration curve of RIF compound in different concentrations of 0.5-4 mM in blood medium. Linearity of the plot of RIF concentration of up to 0.5 mM with a current sensitivity of close to 40.0 μA/mM was observed with curvature being detected at a concentration of greater than 0.5 mM. The calibration plots were performed at the CNT/GCE in RIF with blood medium; there also showed a good linearity of cathodic current versus different concentrations of RIF as described by y = 0.8842 x + 19.477, R^2 = 0.8925. The detection limit of the method based on CNT modified GCE for the determination RIF was found to be 0.5 mM.

Effect of different scan rates

Fig. 5 illustrates the cyclic voltammogram of RIF in blood medium at different scan rates from 0.01-0.1 V/sec. A good relationship between the oxidation and reduction current peaks and scan rates was found, as shown in Fig. 6 and 7, respectively.

A reasonably linear dependence of oxidation-reduction current peaks of RIF in blood medium on scan rate is described by y = 0.5701 x + 2.1399, R^2 = 0.9829, and y = 0.4745 x + 1.7706, R^2 = 0.9966, respectively. The slope of graph log plot (Fig. 6 and 7) is 0.47, which is quite comparable with the theoretical slope of 0.5 for diffusion controlled process [15].

Determination of diffusion coefficient from scan rate

Diffusion coefficient value was determined from the Randles-Sevcik equation which describes it as

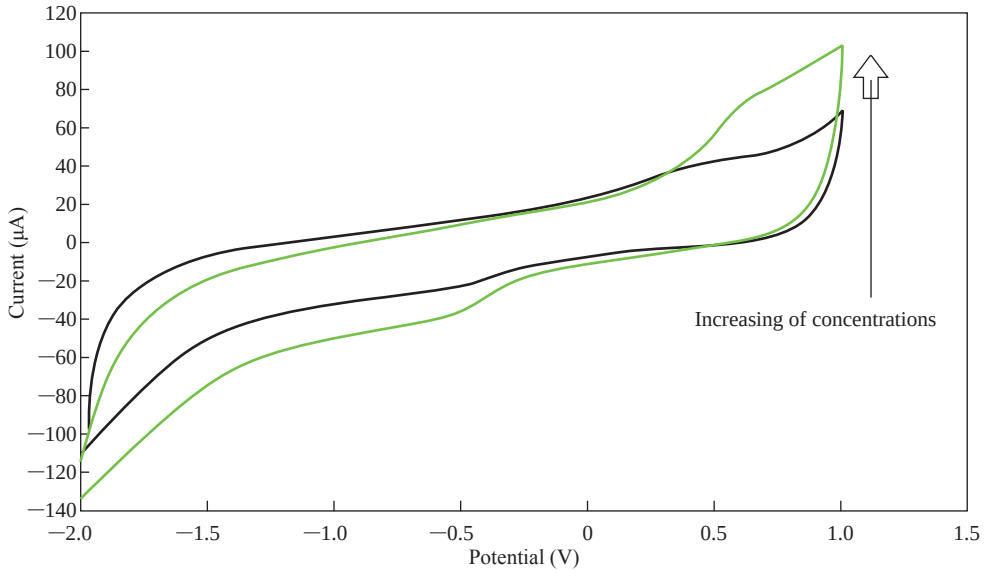

Fig. 2 Cyclic voltammogram of rifampicin at different concentrations in blood medium on CNT/GCE as working electrode versus Ag/AgCl as reference electrode at the scan rate of 100 mV/sec.

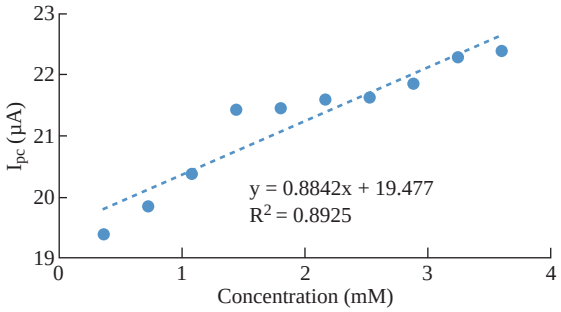

Fig. 3 Calibration curve of reduction current peak of rifampicin in blood medium against different concentrations.

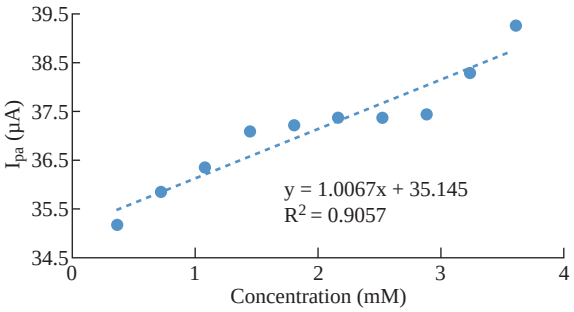

Fig. 4 Calibration curve of oxidation current peak of rifampicin in blood medium against different concentrations.

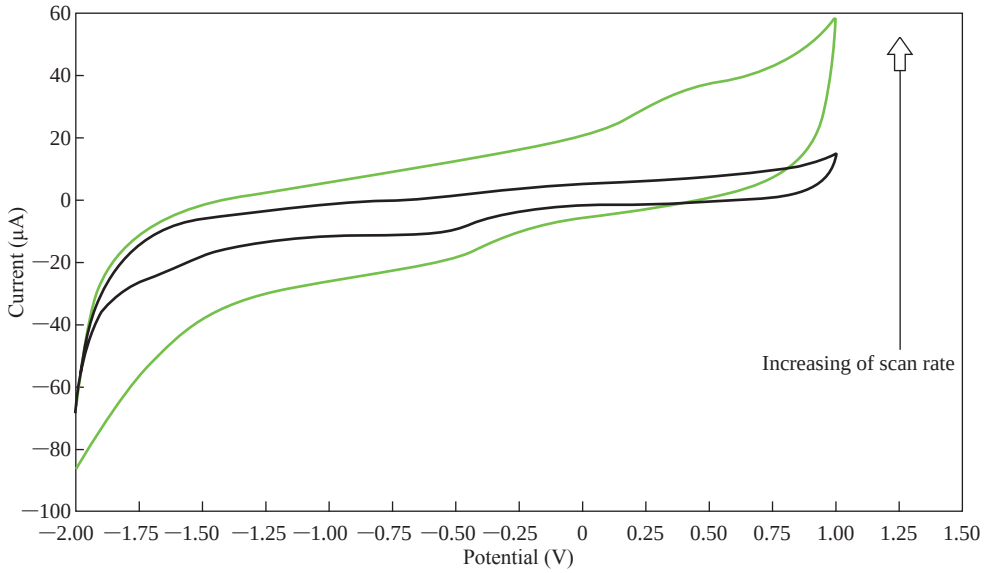

Fig. 5 Cyclic voltammogram of rifampicin at different scan rates from 0.01-0.1 V/sec in blood medium on CNT/GCE as working electrode versus Ag/AgCl as reference electrode.

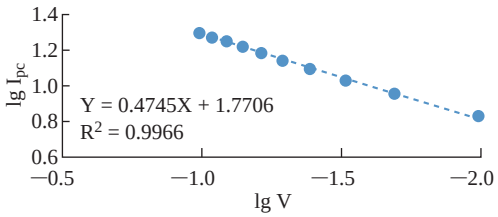

Fig. 6 Plot log I_{pc} against log V of rifampicin compound in blood medium using CNT/GCE as working electrode versus Ag/AgCl as reference electrode at different scan rates from 0.001-0.1 V/sec.

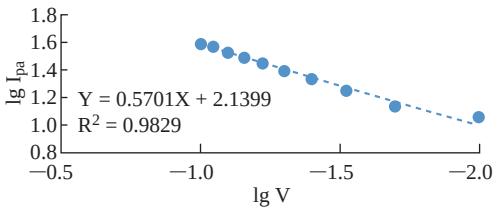

Fig. 7 Plot log I_{pa} against to log V of rifampicin compound in blood medium using CNT/GCE as working electrode versus Ag/AgCl as reference electrode at different scan rates from 0.001-0.1 V/sec.

reversible redox couple peaks [16, 17]:

$$I_p = 2.69 \times 10^5\ n^{3/2}\ AC\ D_f^{1/2}\ V^{1/2}, \quad (1)$$

where I_p is the current peak (μA), n is the number of moles of electrons transferred in the reaction, A is the area of the electrode (cm^2), D_f is the diffusion coefficient (cm^2/sec), and V is the scan rate of the applied potential (V/sec).

The diffusion coefficient values of oxidation-reduction reaction (D_{fa}, D_{fc}) for RIF in blood medium was determined from equation (1), as shown in Table 1. The average values of oxidation and reduction were 2.66×10^{-5} and 8.72×10^{-5} cm^2/sec, respectively.

Table 1 Diffusion coefficient values at different scan rates of oxidation-reduction current peaks of rifampicin compound in blood medium

Scan rate	E_{pa} (mV)	I_{pa} (μA)	E_{pc} (mV)	I_{pc} (μA)	D_{fa} (cm^2/s,10^{-3})	D_{fc} (cm^2/s, 10^{-3})
0.01	1199	11.12	899.2	6.87	0.026416	0.010083
0.02	493.8	13.68	897.7	9.125	0.019989	0.008894
0.03	517.9	17.54	896.1	10.84	0.021908	0.008368
0.04	538.1	21.1	898.9	12.52	0.023777	0.008372
0.05	553.8	24.44	897.9	13.99	0.025521	0.008362
0.06	561.8	28.01	897.9	15.47	0.027934	0.008521
0.07	566.2	30.79	898.6	16.79	0.028932	0.008603
0.08	582.2	33.01	898.6	18.03	0.029098	0.008681
0.09	589.9	36.29	898	19	0.031260	0.008569
0.1	599.2	38.36	899.3	20.17	0.031435	0.008691

Diffusion coefficient of oxidation-reduction for RIF in blood medium was determined through cyclic voltammetric technique and compared with the values in literature. The contribution of the fractal surface of the modified electrode (CNT/GCE), and the possibility of involving of subsequent chemical reaction to the redox current peak affecting the diffusion coefficient were analyzed [18].

Effect of different pH

RIF compound had especial electrochemical behavior for oxidation-reduction current peaks at different pH from 4-10, which is illustrated in Fig. 8 and 9, respectively. The oxidation peak was enhanced in acidic medium and disappeared in alkaline medium, while the reduction peak remained in both media (acid and base). The relationship of oxidation-reduction current peaks of RIF in blood medium at acidic and alkaline pH is shown in Fig. 8 and 9, respectively [19]. It is very important to look for the effect of pH on the blood component with RIF drug in treatment of patients. It was found that oxidation current peak of RIF enhanced at neutral pH of the blood medium as shown in Fig. 8, while the reduction current peak of RIF enhanced at neutral pH as shown in Fig. 9; hence, RIF functioned as a good treatment in pH 7 of blood medium.

Reliability and stability Study

RIF compound in blood medium was studied by nano-sensor (CNT/GCE) in cyclic voltammetry. To ensure that the results were reliable in this study, ten times of scanning was used for the voltammogram (Fig. 10), and the relative standard deviation (RSD) was determined for both oxidation-reduction current peaks of RIF as of ± 0.329% and ± 0.411%, respectively [20-24]. A good nano-sensor was used in this study, i.e. CNT/GCE as working electrode with high sensitivity

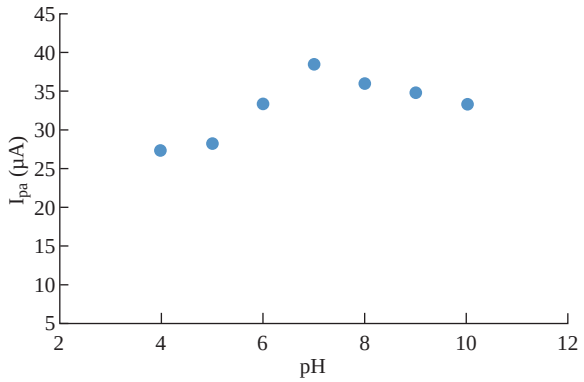

Fig. 8 Relationship between oxidation current peak and different pH of 4-10 in blood medium.

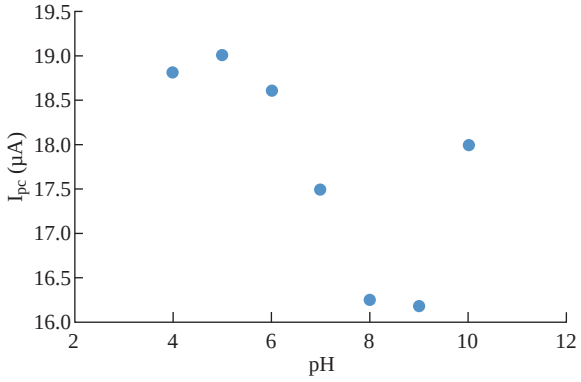

Fig. 9 Relationship between reduction current peak and different pH of 4-10 in blood medium.

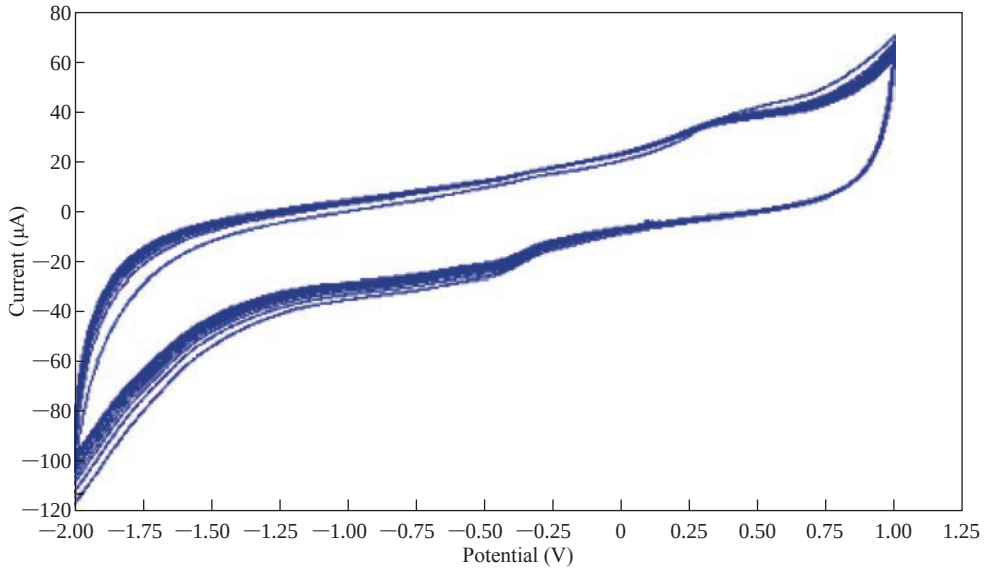

Fig. 10 Cyclic voltammogram of rifampicin in blood medium at tenth times recording.

Table 2 Relative standard deviation of using modified working electrode (CNT/GCE) for oxidation current peak of rifampicin in blood medium

Number	E_{pa} (mV)	I_{pa} (μA)	Mean I_{pa}	I_{pa} - mean	$(I_{pa}$ - mean$)^2$	RSD
1	595.2	33.7	33.017	0.683	0.466489	
2	604.7	33.4	33.017	0.383	0.146689	
3	611	33.19	33.017	0.173	0.029929	
4	612.3	33.07	33.017	0.053	0.002809	
5	608.1	32.93	33.017	-0.087	0.007569	0.328521
6	610	32.87	33.017	-0.147	0.021609	
7	611.4	32.85	33.017	-0.167	0.027889	
8	613.2	32.79	33.017	-0.227	0.051529	
9	608.7	32.71	33.017	-0.307	0.094249	
10	610.9	32.66	33.017	-0.357	0.127449	

Table 3 Relative standard deviation of using modified working electrode (CNT/GCE) for reduction current peak of rifampicin in blood medium

Number	E_{pc} (mV)	I_{pc} (μA)	Mean	I_{pa}-Mean	$(I_{pa}$-Mean$)^2$	RSD
1	898.8	20.14	20.188	-0.048	0.002304	
2	898.8	20.31	20.188	0.122	0.014884	
3	899	20.33	20.188	0.142	0.020164	
4	897.9	20.27	20.188	0.082	0.006724	
5	898.1	20.14	20.188	-0.048	0.002304	0.410999
6	899.4	20.1	20.188	-0.088	0.007744	
7	899.4	20.12	20.188	-0.068	0.004624	
8	898.6	20.15	20.188	-0.038	0.001444	
9	898.7	20.15	20.188	-0.038	0.001444	
10	898.7	20.17	20.188	-0.018	0.000324	

with good stability of nanomaterials on the surface of GCE of low RSD at ten times recording in cyclic voltammetry as shown in Fig. 10.

Conclusions

The effects of rifampicin compound on blood components were studied by electrochemical analysis method using nano-sensor CNT/GCE in cyclic voltammetric technique. The oxidation current peak of rifampicin compound in blood medium appeared in the cyclic voltammogram at potential of +0.5 V which caused an oxidative stress of blood compound by producing free radicals in this medium, and so the pharmacokinetics study of effect of the rifampicin was induced in blood medium through using it as a drug in different metabolic actions of these chemical compounds in human body. However, in some patients the hypoglycemic effect of using rifampicin may be affected during concomitant treatment with rifampicin.

Conflict of Interests

The authors declare that no competing interest

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