Thermodynamic Properties of Rifampicin Redox Current Peaks in Human Blood Samples Using Nano-Sensor (Carbon Nanotubes / Glassy Carbon Electrode)

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Summary: The cyclic voltammetric electrochemical technique was utilized to investigate the effect of different temperatures on the redox current peaks of rifampicin (RF), a drug commonly used to treat many diseases including tuberculosis (TB), in vitro for human blood medium. A modified working electrode of glassy carbon electrode (GCE) with carbon nanotube (CNT) (CNT / GCE) was used as a sensitive nano-sensor to evaluate the impact of temperature on the blood medium in the presence of RF ions.

The results confirmed the presence of two oxidation and one reduction current peaks of RF in blood medium at 0.5, 1, and -0.5 V respectively. The redox current peaks of RF ions in blood medium were enhanced with increasing the temperature from 20 to 36oC. The activation energy (E*) values were determined by applying Arrhenius equation with oxidative and anti-oxidative peaks of Ea*(Ipa)= 9.252 and 11.026 kJ.mol-1.K-1,respectively. Other thermodynamic functions such as the change in each of activation Enthalpy (ΔH*), activation Gibbs energy (ΔG*) and activation Entropy (ΔS*) values were estimated using Eyring equation. The present results of the effects of different temperatures on the blood status in presence of RF lead to the explanation of the oxidative stress of the drug which used in an inflammatory of blood at different temperature.

Keywords: Rifampicin; Cyclic voltammetry technique; Blood medium; Nano-sensor; Different temperature.

Introduction

A number of recent studies have investigated the influence of medicines in blood medium to identify the potential oxidative stress of commonly used drugs on patients. Such proposed effects have been assessed by electrochemical analysis utilizing cyclic voltammetric technique with nano-sensors [1-6].

Rifampicin (RF) is one of the first line treatments of tuberculosis (TB) disease. Its chemical structure is 3-(4-methyl-1-piperazinyl) [7]. It is important to study this drug by techniques such as cyclic voltammetry (CV), differential voltammetry (DPV) and steady state amperometry under aerobic conditions. Nanobiosensor could be adapted to study the electrochemical properties of such drug. This is of importance since it would help to increase our understanding to the therapeutic mechanisms and bimolecular interaction of the drug of interest. It was found that 0.025 - 14 muM covers the peak of rifampicin serum level value of 0.045 muM [8]. Hepatic drug-metabolizing enzymes were found to be inducted by Rifampicin, and these enzymes increase the metabolism of many drugs making them ineffective. This highlights the significant of drug interactions which could help in tackling the threat of several diseases and improving the quality of life.. High-performance liquid chromatography (HPLC) is also utilized as a simplified measurement of rifampicin concentrations in blood [9]. Along with that, cyclic voltammetry is a commonly used approach to study the effect of thermal exposure on the electrochemical properties of environmental pollutants, such as Pb(II) ions, by in vitro assessing the redox current peaks in human blood medium [10]. A lead deposition reaction in different temperature ranges of 25 to 75 °C was studied on substrates of Pb, Cu, Ag, and C using linear and cyclic sweep perturbation in lead chloride and ammonium acetate. Adsorption isotherms, Tafel slopes, and diffusion coefficient were determined as a consequence of the increasing temperature [11]. Electrochemical analysis of the tuberculosis (TB) disease's drug by oxidation and flow injection analysis [12]. Another study of 6-benzylaminopurine on the nano sensor of MWCNT / GCE [13] and rifampicin study in high detection limit was studied [14].

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In this study a sensitive working electrode CNT/GCE was used in the determination of thermodynamic properties of Rifampicin drug in blood medium.

Experimental

Reagents and Chemicals

Rifampicin was purchased from Ajanta pharma limited (India), carbon nanotubes (purity 99%) were supplied by Fluka company (Germany), and normal saline from AdwicPharmaceticals Division (Egypt). Healthy human blood samples were obtained from the Iraqi Blood Bank in Baghdad Medical City, Baghdad-Iraq.

Instruments

"NuVant Systems Inc., Pioneering electrochemical technologies, USA, was adapted in this study for the assessment of the Rifampicin electrochemical properties in vitro using EZstat series (potentiostat/glvanostat) device".

For the output of the Cyclic Voltammogram test, electrochemical workstations of the Bioanalytical Integral System are connected to personal computers with potetiostat operated by electroanalytical software. In addition to using Ag / AgCl (3 M KCl) to calculate the reference signal while using Platinum wire (1 mm diameter) as counter electrode

Preparation of modified GCE with CNT (CNT/GCE)

"The CNT / GCE working electrode was prepared using a modified mechanical attachment technique, which was then used to set up the nano-sensor [15,16]. The modification of GCE included abrasive application of carbon nanotubes (CNT) on the clean surface of GCE. This forms an array of CNT used as a modified CNT / GCE working electrode and put in the cyclic voltammetric cell of 10 ml of the diluted blood with a normal saline ratio of (1:9). The potentio-state was then connected to all electrodes (working electrode, reference electrode and counter electrode)".

Control of temperature

The temperature was controlled by using water bath, in which the cyclic voltammetric cell was placed, the gradual heating was done using a controlled heater, and the temperature was measured using a mercury thermometer.

Results and Discussion

Enhancement of redox currentpeaks using CNT/GCE

In this work a modified working electrode GCE with CNT (CNT/GCE) was used as a sensitive nano-sensor to determine the electrochemical properties of redox current peaks of Rifampicin(RF) in blood medium at different temperature (20–36ºC). Fig. 1 shows the cyclic voltammogram of RF exposed to different temperature. The cyclic voltammogram of RF showed two oxidation current peaks at 0.5 and 1V. Also, one of reduction current peaks at -0.5 V enhanced the redox current peaks by increasing temperature. This suggests a catalyst effect of the temperature changes [17].

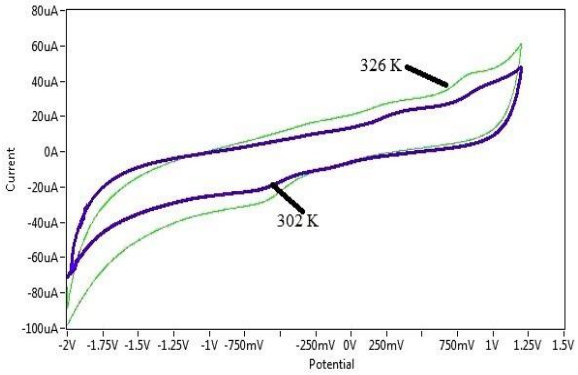

Fig. 1: Rifampicin cyclic voltammogram on modified working electrode (CNT / GCE) at different temperatures in the blood medium

Effect different temperatures on the blood medium redox current of RF

The potential effect of temperature change on blood composition was investigated in the present study. This was performed utilizing Cyclic voltammetric technique in the presence of RF compound by tracking the values of redox current peaks using electrochemical analysis. The results showed that blood medium incubated with RF be affected when it is exposed to increase the temperature degree, rising cell device prone to heat (20-36 C°). This effect was displayed as a change in the redox current peaks as demonstrated in Fig. 1.

Observing the apparent results, it was found that the peaks of the two oxidation current was at 0.5 and 1 V. with one of the reduction current peak at -0.5 V being enhanced upon decreasing the temperature.

The activation energy (E) value*

The influence of different temperature degrees on the redox reaction of RF in blood medium was investigated in this study by testing the reduction current peak patterns of the RF compound.

Activation energy was determined using Arrhenius equations (1) and (2) [18, 19]

$$\sigma = \sigma o Exp (- E^*/ RT) \quad (1)$$

$$D = DoExp (-E^*/ RT) \quad (2)$$

where σ / D refer to conductivity / diffusibility while σo /Do represent standard conductivity / the initial diffusibility

The chemical reaction rate at absolute temperature T (in kelvins) was estimated (quantified) using the equation of Arrhenius from the value of the rate constant k dependence.. For this equation, A represents the pre-exponential factor (or simply the pre-factor), whereas E***** refers to the activation energy and the symbol R to the universal gas constant:

$$"k = A EXP(-E^*/RT) \quad (3)$$

$$Log(Ip)=LogA – E^*/2.303RT \quad (4)$$

The slop linear line relation (-E*/2.303R) was calculated byplotting Log(Ip) against 1/T.

"In the above equation: k is the rate constant that replaced with Ip, which refers to the current peak of the oxidation or reduction produced by the electrochemical reaction".

The relationship between ln(Ipa), ln(Ipc) and 1/T are shown in Figs 2 and 3. It was found from the slope of the strait line that the activation energy of oxidation-reduction of RF have values of 9.031 and 11.024 KJ/mol K, respectively

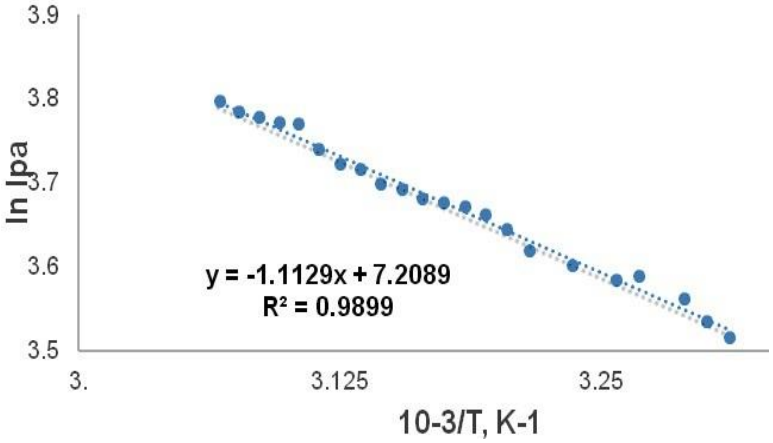

Fig. 2: Relationship between ln(Ipa) against to inverse temperature of the oxidation current peak of RF in blood medium at different temperature using CNT/GCE and Ag/AgCl at SR=100mVs^{-1}.

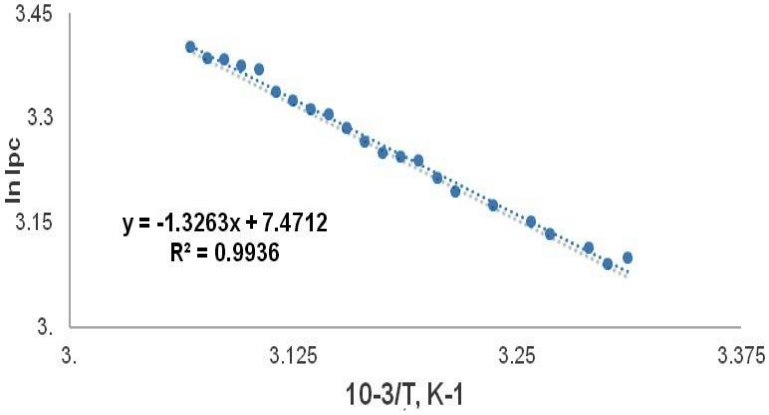

Fig. 3: Relationship between ln(Ipc) against to inverse temperature of the reduction current peak of RF in blood medium at different temperature using CNT/GCE and Ag/AgCl at SR=100mVs^{-1}.

Table-1: Thermodynamic functions (ΔH*,ΔG*, and ΔS*) of redox peaks of Rifampicin in blood medium.

T/K	100/T	lnIpc	ΔHipa	ΔHipc	ΔG Ipa	ΔGipc	ΔS* Ipa	ΔS*Ipc
302	3.311	3.099	-2.501	-2.499	65.171	-66.214	-0.224	0.210
303	3.300	3.091	-2.519	-2.519	65.346	-66.462	-0.223	0.211
304	3.289	3.113	-2.527	-2.527	65.503	-66.633	-0.223	0.210
306	3.267	3.132	-2.544	-2.544	65.879	-67.040	-0.223	0.210
307	3.257	3.150	-2.552	-2.552	66.116	-67.221	-0.223	0.210
309	3.236	3.174	-2.569	-2.569	66.517	-67.613	-0.223	0.210
311	3.215	3.194	-2.585	-2.585	66.921	-68.017	-0.223	0.210
312	3.205	3.214	-2.593	-2.593	67.079	-68.193	-0.223	0.210
313	3.194	3.238	-2.602	-2.602	67.256	-68.356	-0.223	0.210
314	3.184	3.244	-2.610	-2.610	67.452	-68.568	-0.223	0.210
315	3.174	3.250	-2.618	-2.618	67.664	-68.779	-0.223	0.210
316	3.164	3.264	-2.627	-2.627	67.876	-68.967	-0.223	0.209
317	3.154	3.285	-2.635	-2.635	68.070	-69.14	-0.223	0.209
318	3.144	3.305	-2.643	-2.643	68.274	-69.314	-0.223	0.209
319	3.134	3.312	-2.652	-2.652	68.451	-69.520	-0.222	0.209
320	3.125	3.325	-2.660	-2.660	68.659	-69.71	-0.222	0.209
321	3.115	3.336	-2.668	-2.668	68.833	-69.909	-0.222	0.209
322	3.105	3.369	-2.677	-2.677	68.977	-70.047	-0.222	0.209
323	3.095	3.374	-2.685	-2.685	69.193	-70.259	-0.222	0.209
324	3.086	3.383	-2.693	-2.693	69.402	-70.462	-0.222	0.209
325	3.076	3.385	-2.702	-2.702	69.605	-70.682	-0.222	0.209
326	3.067	3.402	-2.710	-2.710	69.792	-70.862	-0.222	0.209

Thermodynamic functions (ΔH, ΔG*, ΔS*) of Rifampicin in blood medium*

The activation free energy (G^*), enthalpy (H^*) and entropy (S^*) of Rifampicin in blood medium values on the modified electrode CNT/GCE were determined using Erying equation and thermodynamic equations [19]:

$$\Delta G^* = -RT \, Ln \, (k \, h / T \, k_B) \quad (3)$$

Eyring equation

$$\Delta H^* = \Delta G^* + T \, \Delta S^* \quad (4)$$

$$\Delta H^* = \Delta G^* + T \, \Delta S^* \quad (5)$$

"where gas constant R =8.314 $J.mol^{-1}k^{-1}$, Boltzmann constant k_B =1.381x10^{-23} $m^2kg.sec^{-2}k^{-1}$, and Plank constant h =6.66 x 10^{-34}J.sec. with multiplier of temperature T (K)".

The thermodynamic functions of Rifampicin in blood medium were determined from the above mentioned equations 3, 4, and 5. The results showed that the spontaneous reaction of redox Rifampicin process in blood medium at different temperature was done according to the law Gibbs Helmholtz free energy, not only depend on change in enthalpy (ΔH*) (Table-1). This redox process is becoming spontaneous when the value of free energy (ΔG*) is negative and enthalpy change (ΔH*) is negative too which can be seen in the reversible reaction of cathodic current peak, but entropy (ΔS*) is showed to have a positive value [20] as it is illustrated in table 1. Moreover, the nanoparticles (CNT) act as a catalyst for redox reaction of rifampicin in blood medium especially the anodic process [21].

Conclusion

In this work the effect different temperature on the redox process of Rifampicin compound in blood medium using nano-sensor (CNT/GCE) was analyzed by cyclic voltammetric method to identify the thermodynamic functions such as activation energy (E_a^*), activation free energy (G^*), enthalpy (H^*) and entropy (S^*) using Arrhenius equations and Eyring equation. It was found from the results that Rifampicin compound has the process of redox current peaks in blood medium as a spontaneous reduction action which is indicated by the negative values of both free energy (ΔG*) and enthalpy change (ΔH*), but nonspontaneous of oxidation reaction. The study's results also suggested a key role for the nano-sensor (CNT/GCE) in the diffused ions in the cyclic voltammetry in blood medium.

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