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Full Paper

Electrochemical Behavior of Finasteride on Glassy Carbon Electrode Using Differential Pulse Voltammetric Technique

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Abstract- The direct and indirect electrochemical behavior of finasteride was studied using a differential pulse technique coupled with a three-electrode detection system consisting of 2 mm diameter glassy carbon as a working electrode, 2 mm diameter platinum wire as an auxiliary electrode, and silver/silver chloride saturated potassium chloride as reference electrode (Ag/AgCl sat KCl). The finasteride gives a weak reduction peak at -0.68 V. The calibration curve of finasteride was constructed using Briton- Robinson buffer solution (pH = 3), the plot of reduction peak current and concentration gives a linear relationship within the concentration range of 0.999×10^{-5}–19.607×10^{-5} M, with a correlation coefficient of 0.9903. To increase the sensitivity of the method, an indirect determination of finasteride through its interaction with cupric ion was investigated in acetate buffer solution (pH=2) and followed the decrease in reduction peak current of cupric ion as a result of adding sequence addition of finasteride solution. The calibration curve for finasteride was also constructed for its interaction with cupric ions by measuring the decrease of cupric reduction peak current with the sequence additions of finasteride. The calibration curve was linear within the concentration range of 4.997×10^{-6}-476.191×10^{-6} M, with a correlation coefficient of 0.9930. The binding constant (K) and the Thermodynamic parameters (ΔG, ΔH, and ΔS) for Cu^{2+}-finasteride interaction were calculated. The suggested method was successfully applied for the determination of finasteride in tablets.

Keywords- Finasteride drug; Glassy carbon; Indirect determination; Differential pulse voltammetry

1. INTRODUCTION

Finasteride (Fin.) is a chemical compound with the molecular formula $C_{23}H_{36}N_2O_2$ used primarily to treat prostate enlargement and can also be used for male pattern baldness. It is taken orally, where finasteride primarily belongs to a special drug group called 5-alpha-reductase inhibitors. This medication primarily works by preventing the hormone testosterone from converting into dihydrotestosterone (DHT), which is a hormone that may play a role in developing certain health problems such as benign prostatic hyperplasia (BPH). This medication is available in doses of 1 mg and 5 mg in tablet form for oral administration. Commercially, this medication is available under two different names, each serving a different purpose. The version designated for prostate issues is usually used to treat benign prostatic hyperplasia (BPH), a condition where the prostate enlarges significantly, obstructing or slowing down the normal flow of urine. This medication may help patients with this condition alleviate some accompanying symptoms such as difficulty urinating, frequent urination, and reducing the patient's chances of needing surgery. Secondly, the version of Fin. designated for baldness is typically used to treat androgenetic alopecia, which is the most common type of male pattern baldness. It is a condition where hair begins to thin and recede gradually from the scalp, usually starting from the frontal area of the scalp. Figure 1 represents the chemical structure Fin. [1-4].

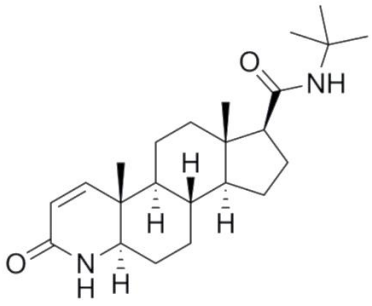

Figure 1. Chemical structure of Finasteride

Different methods were used for the determination of Fin. like spectrophotometric methods [5,6], chromatographic methods [7,8], voltammetric methods [9], and potentiometric methods [10].

2. EXPERIMENTAL SECTION

2.1. Apparatus

All experiments were conducted using a voltammetric analysis 797-AV Computrace-device consisting of a three-electrode system: the working electrode, which was a 2mm diameter glassy carbon electrode, the reference electrode (Ag/AgCl sat KCl), and the auxiliary electrode consisting of a 2 mm diameter platinum wire [11]. A pH meter from Philips was used

for pH measurements, and a thermostatic water bath of type Haake NK 22 was used to control the temperature.

2.2. Reagents

The finasteride pure material was supplied by Samarra Drug Industry (SDI), Iraq. 10^{-2} M of finasteride solution was prepared by dissolving 0.0186 g of pure finasteride in 5 mL of distilled water. A Briton–Robinson Buffer (BRB) solution was prepared from the following acids: boric acid 0.12 M, phosphoric acid 0.12 M, and acetic acid 0.12 M. The acetate buffer solution was prepared by mixing 0.2 M acetic acid (41 mL) and 0.2 M sodium acetate (9 mL), in a 100-mL volumetric flask and bringing the volume up to 100 ml with distilled water.

2.3. Procedure

A differential pulse voltammetry was used with an initial voltage -1.1 V and a final voltage -0.4 V, and the scan rate was 0.0322 V/s. The temperature of the voltammetric cell was controlled. The dissolved oxygen was removed by passing pure nitrogen gas for 5 minutes. Firstly, the voltammogram was recorded for 10 mL of a Britton-Robinson (pH=3) solution. Then, the voltammogram of Fin. was recoded for sequence additions of Fin. and the calibration curve was constructed.

For the indirect estimation of Fin. the same procedure was followed except the recording of a voltammogram of 2.93×10^{-6} M of cupric ion was done first and then record the voltammograms for sequence addition of Fin. to the same cell that contains a known concentration of cupric ion under the measured optimum conditions. The effect of temperature on the cupric - Fin. interaction was studied using a thermostatic water bath. A calibration curve was then constructed for the indirect determination of Fin.

3. RESULTS AND DISCUSSION

3.1. Direct Estimation of Fin.

The differential pulse voltammogram of 4.97×10^{-6} M a standard Fin. the solution was recorded in a Britton-Robinson buffer solution (pH=3), under the initial default conditions of the instrument, Table 1, Fin. exhibited a weak reduction peak at -0.68 V (Figure 2).

3.1.1. Optimum conditions

To examine the optimum conditions for measurement, 7.93×10^{-5} M Fin. solution was prepared, and many experimental and instrumental conditions that effect on the reduction process of Fin. were optimized including the effects of pulse amplitude, pulse time, voltage step, number of cycles, cleaning potential, cleaning time, deposition potential, deposition time, and equilibrium time Table 2 shows the tested optimum conditions.

Table 1. The default conditions of the instrument applied to the 4.97×10^{-6} M Fin. solution at pH 3

Parameters	Values
Start potential (V)	-1.1
End potential (V)	-0.4
Pulse amplitude (V)	0.3999
Pulse time (s)	0.01
Voltage step (V)	0.0299
Voltage step time (s)	0.9
Sweep rate (V/s)	0.0332
No. of cycles	3
Cleaning potential (V)	-0.0999
Cleaning time (s)	5
Deposition potential (V)	-0.0999
Deposition time (s)	60
Equilibrium time (s)	5

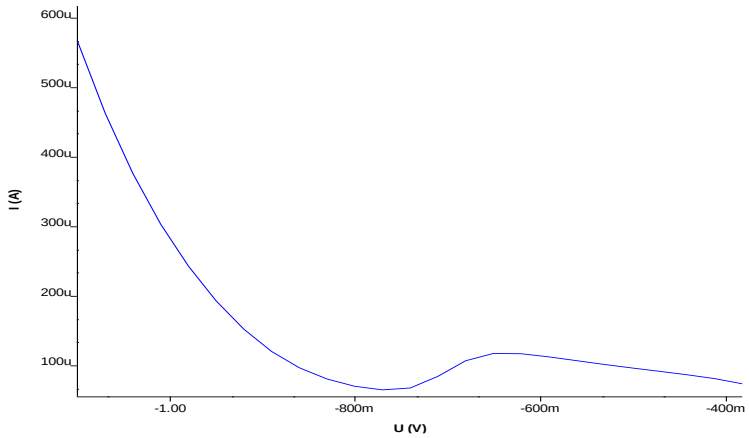

Figure 2. The reduction peak of Fin. under the default conditions of the instrument

Table 2. Shows the measured optimum conditions for direct determination of Fin.

Parameters	Values
Start potential (V)	-1.1
End potential (V)	-0.4
Pulse amplitude (V)	0.5
Pulse time (s)	0.01
Voltage step (V)	0.03
No. of cycles	5
Cleaning potential (V)	-0.2
Cleaning time (s)	5
Deposition potential (V)	-0.3
Deposition time (s)	50
Equilibrium time (s)	4
Scan rate (V/s)	0.0332

3.1.2 Effect of Time (Stability)

The effect of time on the reduction current of Fin. was studied by recording the differential pulse voltammogram for various durations time under the optimal measured conditions. The voltammogram was recorded for 7.93×10^{-5} M Fin. solution every five minutes for a total duration time of 35 minutes. It was observed that the current value remained almost constant within the studied time. The results are shown in Table 3.

Table 3. Shows the measured effect of time

Time (min.)	E_p (V)	Ip (µA)
0	-0.801	3.09
5	-0.801	3.15
10	-0.801	3.23
15	-0.801	3.24
20	-0.801	3.32
25	-0.801	3.33
30	-0.801	3.50
35	-0.801	3.42

3.1.3. Calibration curve

The calibration curve was constructed by adding sequence additions of a 10^{-2} M Fin. standard solution under the previous fixed optimum conditions, using Britton-Robinson buffer solution (pH=3). The voltammogram was recorded for each addition. The plot of reduction peak current versus concentration gives a straight line (Figure 3) with a calibration equation y= 4.4336x+79.446 and a correlation coefficient equal to 0.9807.

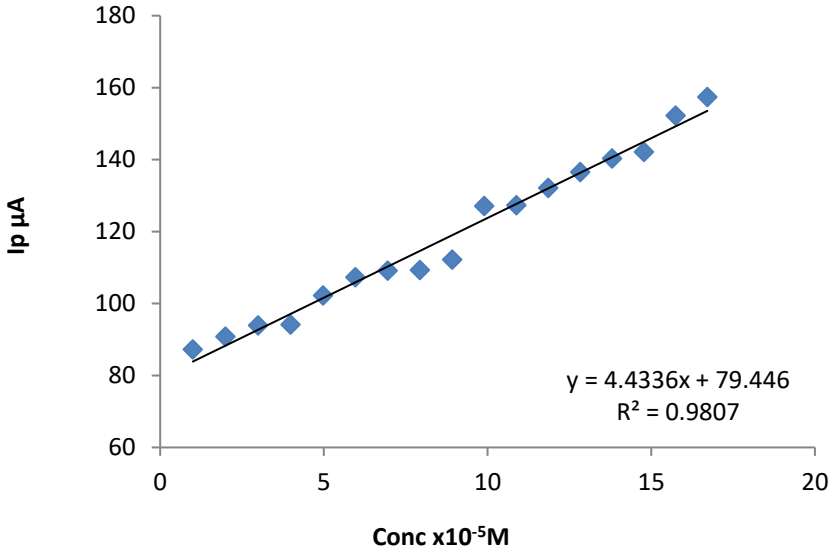

Figure 3. Calibration curve for the Fin.

3.2. Indirect Estimation of Finasteride Through its Interaction with Cupric Ion

Indirect estimation of Fin. was carried out through its interaction with cupric ion on a glassy carbon electrode using acetate buffer solution (pH=4) and followed the decrease in the reduction peak current of cupric ion as a result of Fin. addition. Fin. gives a weak reduction peak, so its indirect determination through its interaction with cupric ions may lead to enhancing the sensitivity of the measurement. For this purpose, a differential pulse voltammogram of 2.93×10^{-6} M cupric ion solution was recorded under the initial default conditions (Table 4), using acetate buffer solution (pH=4). Cupric ion shows a well-defined reduction peak (Figure 4) at -0.28 V versus Ag/AgCl saturated KCl reference electrode.

Table 4. The initial default conditions for cupric ion reduction

Parameters	Values
Start potential (V)	-1.0
End potential (V)	0.5
Pulse amplitude (V)	0.6
Pulse time (s)	0.08
Voltage step (V)	0.01999
Voltage step time (s)	0.6
Sweep rate (V/s)	0.0222
No. of cycles	1
Cleaning potential (V)	0.0998
Cleaning time (s)	2
Deposition potential (V)	-0.8
Deposition time (s)	50
Equilibrium time (s)	5

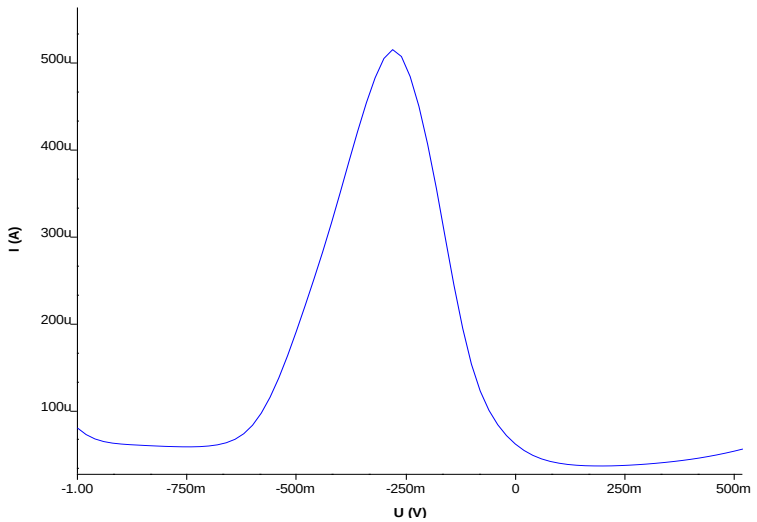

Figure 4. The reduction peak of cupric ion in acetate buffer solution

3.2.1. Optimum conditions

To test the optimum conditions for Fin. cupric ion reduction, 2.93×10^{-6} M of cupric ion was used. The effects of pulse amplitude, pulse time, voltage step, voltage scan rate, number of conditioning cycles, cleaning potential, cleaning time, deposition potential, deposition time, and equilibrium time were investigated. The results obtained are summarized in Table 5.

Table 5. Measured optimum conditions for cupric ion reduction using acetate buffer (pH=4) as supporting electrolyte

Parameters	Values
Start potential	-1.0
End potential(v)	0.5
Pulse amplitude(v)	0.6
Pulse time (s)	0.01
Voltage step (v)	0.02
Scan rate(V/S)	0.0333
No. of cycles	4
Cleaning potential(v)	0.03
Cleaning time(s)	5
Deposition potential (v)	-0.4
Deposition time (s)	90
Equilibrium time(s)	3

3.2.2. The effect of time (stability)

The effect of time on the reduction current of cupric ion was studied by recording the differential pulse voltammogram of 2.93×10^{-6} M cupric ion for 35 min. The voltammogram was recorded every five minutes for a duration of 35 minutes Table 6. It was observed that the current remained stable during the studied period.

Table 6. Shows the measured effect of time

Time (min)	E_p (V)	I_p (mA)
0	-0.0404	2.08
5	-0.0404	2.03
10	-0.0404	2.03
15	-0.0404	2.04
20	-0.0604	2.06
25	-0.0604	2.10
30	-0.0604	2.09
35	-0.0604	2.07

3.2.3. The Effect of pH

Different pHs (2-6) were used to examine their effect on the Fin.– cupric interaction using 2.93×10^{-6} M cupric ion. The results obtained are summarized in Table 7.

Table 7. Shows the measured effect of pH

pH	E_p (V)	I_p before (Cu) mA	I_p after (Cu) (mA)	ΔI_p (Fin.) (mA)
2	-0.36	2.58	2.29	0.29
3	-0.1	1.69	1.56	0.13
4	-0.0404	0.939	0.892	0.047
5	-0.1	0.871	0.789	0.082
6	-0.24	0.181	0.158	0.023

The results indicate a maximum change (decrease) in the diffusion current and the best voltammogram shape was at pH 2. Therefore, it was chosen as the ideal media for studying the electrochemical behavior of Fin. in the presence of cupric ions.

3.2.4. Calibration curve of Fin.-cupric interaction

The calibration curve of Fin.-cupric interaction was constructed by adding a series of additions of 10^{-2} M Fin. standard solution in the presence of 2.93×10^{-6} M cupric ion in acetate buffer solution (pH=2). The differential pulse voltammogram was recorded for each addition under the optimum measured conditions (Table 5), by scanning the potential between -1.0 – 0.5 V and following the decrease in peak current at -0.34 V (Figure 5).

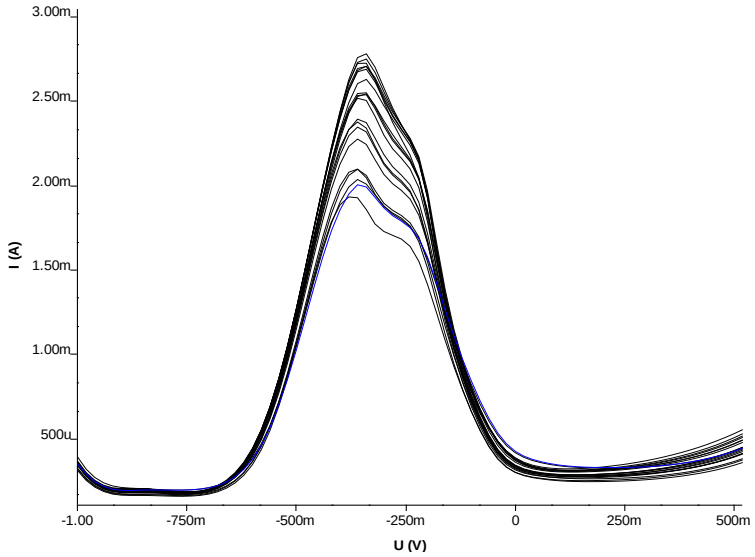

Figure 5. The differential pulse voltammogram of cupric ion in the presence of Fin. under optimum measured conditions

The relationship between concentration and reduction peak current (Figure 6) was linear in the concentration range 4.997×10^{-6}–476.191×10^{-6} M, with a correlation coefficient equal to 0.9862 and a calibration curve equation of y = 0.0034x + 0.0954.

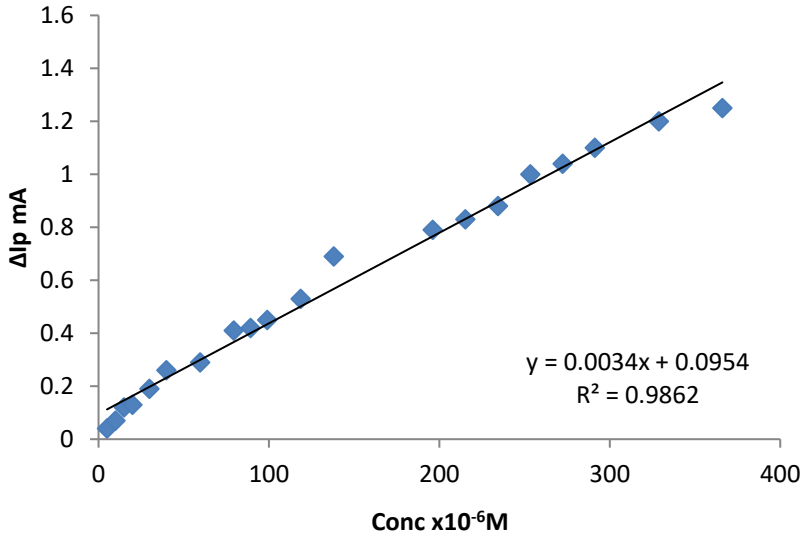

Figure 6. Calibration curve for the finasteride in the presence of cupric ion

3.2.5. Applications

The suggested method was successfully applied for the determination of Fin. in two pharmaceutical preparations, Accord 5 mg tablet supplied by Accord company, England, and Prosteride5 mg tablet supplied by S.D.I company, Iraq. The recovery percentage was calculated for three different concentrations, the results are shown in Table 8, a good recovery was obtained for all the concentrations used for Accord tablets whereas for Prosteride tablets bad recovery was obtained may have been due to the manufacturing fault.

Table 8. Recovery values for finasteride in pharmaceutical preparations used

Drug	Taken conc.×10^{-6} (M)	ΔI_p (mA) tab.	ΔI_p (mA) pure	Recovery (%)	Found conc.×10^{-6} (M)
Accord 5 mg/tab	39.840	3.59	3.80	94.47	39.840
	234.375	1.70	1.70	100.00	234.375
	403.071	1.35	1.33	101.50	403.071
S.D.I company 5 mg/tab.	29.910	1.29	2.39	53.97	29.910
	234.375	1.06	2.32	45.68	234.375
	366.088	0.576	1.70	33.88	366.088

3.2.6. Thermodynamic Calculations

The binding constant of Fin.-cupric was calculated according to equation 1.

$$\ln (I_p/(I_p^o - I_p)) = \ln (1/[\text{Conc.(M)}]) - \ln K \quad (1)$$

Where I_p^o is the reduction current of cupric ion alone, I_p is the reduction current of Fin. – cupric complex, Conc. is the molar concentration of cupric ion (1.37×10^{-3} M), and K_b is the binding constant of Fin.–cupric complex. The binding constant was calculated at different temperatures (298, 303, 308, 313, and 318) K, and the results obtained are shown in Table 9.

Table 9. The binding constant of Fin.–cupric complex at different temperatures

Temp (K)	1/T	Ln K
298	0.0034129	7.8574
303	0.0033003	7.4669
308	0.0032467	5.7504
313	0.0031948	3.9931
318	0.0031446	0.5974

Thermodynamic parameters were calculated, in Figure 5, according to equation 2 (Van't Hoff equation)

$$\text{Ln K} = -\frac{\Delta H}{RT} + \frac{\Delta S}{R} \quad (2)$$

Enthalpy (ΔH) was calculated from the slope (equation 3)

$$\Delta H = \text{- Slope} \times R \quad (R= 8.314 \text{ J. mole}^{-1} \text{ . K}^{-1}) \quad (3)$$

The free energy (ΔG) was calculated from the equation4

$$\Delta G = -R \times T \times \ln K \quad (4)$$

Entropy (ΔS) was calculated from the intercept (equation 5)

$$\Delta S = \text{Intercept} \times R \quad (5)$$

The plot of ln K versus 1/T gives a straight line with R^2 equal to 0.9114, Figure 7. Thermodynamic values for Fin.–cupric interaction was calculated (Table 10).

Table 10. Thermodynamic values for Fin.-cupric interaction

Temp. (K)	Binding constant $K_b \times M$	ΔH ($KJ.mol^{-1}$)	ΔG ($KJ.mol^{-1}$)	ΔS ($J.mol^{-1} \cdot K^{-1}$)
298	2.05914	-281.919	-19.467	-873.136
303	2.00822		-18.810	
308	1.74730		-14.725	
313	1.38301		-10.391	
318	0.51458		-1.5790	

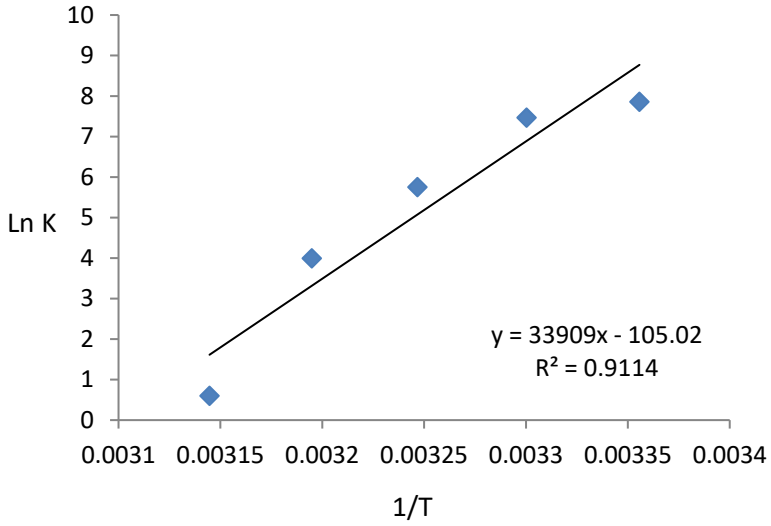

Figure 7. The relation between ln K and 1/T

The negative value of ΔH indicates that the interaction between Fin. And cupric ion was exothermic and the binding constant decreased with increasing temperature. Also, ΔG becomes more positive with increasing temperature means the spontaneous of binding decreased, whereas the negative value of ΔS indicates that the system became more ordered. The negative ΔH and ΔS values for the interaction of Fin. and cupric ion indicate that the binding is mainly enthalpy and entropy-driven, and the interaction may involve a coordination bond between copper and Fin. [12-19].

4. CONCLUSION

The electrochemical behavior of Fin. shows a weak reduction peak current at -0.68 V versus Ag/AgCl sat. KCl in Britton-Robinson buffer solution using direct estimation method which suffers from lack of sensitivity and narrow linear range of calibration curve, so to increase the sensitivity of its estimation and calibration linearity range, the indirect method was used by following the decrease in cupric reduction peak current which is appeared at -0.28 V in acetate buffer solution (pH=2) with the increasing amount of Fin. added. The binding constant was calculated and thermodynamic values were studied, the result of the thermodynamic study indicates that the binding is mainly enthalpy and entropy-driven, and the interaction may involve a coordination bond between copper and Fin. The suggested method was successfully applied for the determination of Fin. in two manufacturing companies for pharmaceutical preparations.

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Declarations of interest

The authors declare no conflict of interest in this reported work.

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