Int. J. Electrochem. Sci., 10 **(2015)** 7147 - 7158

International Journal of
ELECTROCHEMICAL
SCIENCE
www.electrochemsci.org

Sensitive Electrochemical Determination of Pantoprazole Sodium in Pure Form Pharmaceutical Formulations and Biological Fluid at Glassy Carbon Electrode Using Differential Pulls and Square wave Techniques

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Received: 21 April 2015 / *Accepted:* 11 July 2015 / *Published:* 28 July 2015

The electrochemical behavior of pantoprazole sodium (PNT) was investigated by cyclic voltammetry, differential pulse and square wave techniques at a glassy carbon electrode in Britton-Robinson electrolyte (pH= 8).They gave one irreversible anodic oxidation diffusion controlled peak at 833 mV. The effect of experimental parameters has been examined. The oxidation peak current varied linearly with the concentration over the range of 0.5 - 7.5 µM (r = 0.999) and 0.675 – 4.375 µM (r = 0.992) for differential pulse voltammetry (DPV) and square wave voltammetry (SWV), respectively. The limits of detection and quantification were found to be 0.0318 and 0.106 µM (S/N = 3) for DPV and 0.0076 and 0.2535 µM (S/N = 10) for SWV, respectively. The proposed DPV and SWV methods have been applied with satisfactory results to the determination of pantoprazole sodium in pharmaceutical dosage forms and humane urine. Good analytical results being obtained upon comparison with the official method.

Keywords: Pantoprazole sodium (PNT); Cyclic voltammetry (CV); Differential pulse voltammetry (DPV); Square wave voltammetry (SWV) Glassy carbon electrode; Pharmaceuticals and urine samples.

1. INTRODUCTION

Pantoprazole sodium (PNT) is named as sodium 5-(difluoromethoxy)-2-[[(3,4-dimethoxy-2-pyridinyl) methyl] sulfinyl]-1*H*-benzimidazole sesquihydrate and its structure is shown in (Fig. 1) [1]. The treatment of gastric ulcers was widely carried out using pantoprazole sodium via inhibition of H^+,

K^+-ATPase in gastric parietal cells. It reduced the gastric acid secretion without taken into consideration the nature of stimulation [2].

An up-to-date literature survey revealed that several techniques have been developed for the quantitative determination of pantoprazol . Many of these methods rely on the use of high performance liquid chromatography [3-7], spectrophotometry [8-16] and capillary electrophoresis [17,18]. Electroanalytical techniques have some important advantages including speed, high sensitivity, relative simplicity and low costs compared to other techniques. This can be attained by a combination of square wave voltammetry (SWV) and a hanging mercury drop electrode (HMDE)[19]. New modern electrochemical methods, such as activation of glass carbon electrode at certain electric potentials have been purposed to solve the problem of sensitivity of pharmaceutical interest, and none of the methods can meet the practical needs [20-29].In the present work, a new rapid and sensitive method was developed using square wave voltammetry (SWV) at hanging mercury drop electrode (HMDE)[30-32] and differential pulse to investigate the voltametric oxidation behavior of pantoprazole at glassy carbon electrode in an addition to establish a simple electrochemical method for its determination of PNT in pure form, dosage forms and biological filed using the voltammetry technique.

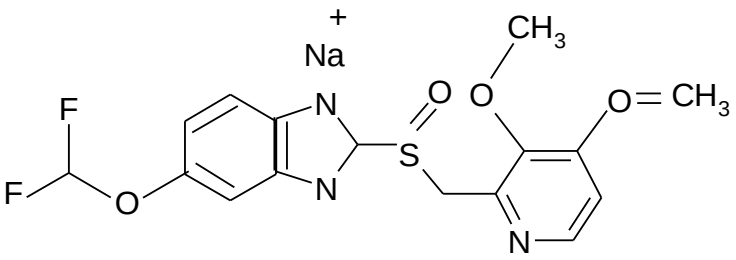


Figure 1. Chemical formula of pantoprazole sodium (PNT).

2.MATERIALS AND METHODS

2.1 Instrumentation

The voltammeric measurements were carried out using computerized polarographic trace analyzer 797 VA Computrace Software 1.0 (Metrohm, Switzerland). With a Three-electrode configuration: ELCD 641/656 glassy carbon electrode as working electrode, a silver/silver chloride/saturated KCl as the reference electrode and a platinum wire as an auxiliary electrode. A JEANWAY 3510 digital pH/mV- meter with a glass electrode was used for the preparation of the buffer solution. Matter balance (Sartorius) was used for weighing the solid materials, double-distilled water used through the present study was supplied from a Hamiton-Aqua-Maticbidistilled water solution and a micropipette (Eppendorf-multipette plus) was used throughout the present experimental work.

2.2 Materials

Pantoprazole sodium (PNT) was supplied from Medical Union Pharmaceuticals Company (MUP) (Badercity, Egypt) and were used without further purification. A stock solution of 1.0 x 10^{-3} M

pantoprazole sodium (PNT) was prepared by dissolving an accurate mass of the drug in appropriate volume of double-distilled water, which was then protected from light at 4 ^{0}C. Britton-Robinson [33] buffers (pH 2-12) were used as supporting electrolyte. All solutions were prepared by using analytical grade reagents in double-distilled water.

2.3 Tablet Assay Procedure

Ten tablets of pantoprazole sodium (PNT) accurately and finely powdered. A suitable amount of this powder was accurately weighed. The sample was shaken with 25 ml double-distilled water and then sonicated for 5 min. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant liquid and diluting them with double-distilled water in order to obtain a final solution of $1.0X10^{-3}$ M pantoprazole sodium (PNT). Voltammograms were recorded following the voltammetric procedure. The content of the drug in tablet was determined referring to the regression equation of the adsorptive stripping voltammetry.

2.4 Urine Analysis Procedure

Aliquot quantity of urine is collected from a healthy volunteer and added into the voltammetric cell containing Britton-Robinson buffer of (pH= 8, 0.04M, 9:1 v/v urine: buffer). The voltammograms are recorded for the blank urine sample and then a certain concentration of PEN is added into the voltammetric cell and DPV and SWV are recorded at optimum condition for each voltammetry. Quantification performed by means of calibration curve method [34].

2.5 Pretreatment of Working Electrode

The glassy-carbon surface was polished with alumina (BAS CF-1050) on an alumina polish pad (BAS MF-1040) for 60s to each chemical measurement and then rinsed with double-distilled water and gently dried with a tissue paper. The supporting electrolyte was placed in the cell and several potential sweeps were applied to obtain a low background.

2.6 General Procedure for the Determination of PNT in the Pure Form

A 25 ml aliquot of background electrolyte was introduced into the voltammetric cell. Then, the accumulation potential (0.0 mV) was applied to the working electrode for 50s while the solution was stirred continuously at 1200 r.p.m. Then stirring was stopped and after 5 s rest period was allowed for the solution to become quiescent. An aliquot of the standard PNT solution was introduced into the cell with a micropipette and the adsorptive voltammugram was repeated using a new mercury drop as before.

3. RESULTS and DISCUSSION

3.1 Cyclic Voltammetry

The electrochemical behavior of PNT in Britton-Robinson buffer (pH= 8) as supporting electrolyte at GCE was described. The cyclic voltammetric behavior of PNT has been performed over the pH range of 2 -12 in Britton-Robinson buffer solutions and at a scan rate of 100 mV/s. It exhibits one well defined oxidation peak developed in the potential range from 0.0 V to +1.0V with no peak on the reverse scan, indicating the irreversible nature of the electrode reaction in the cathodic scan. Fig. 2 shows the cyclic voltammogram of 2.5µM PNT in Britton-Robinson buffer (pH 8.0. 0.04M).

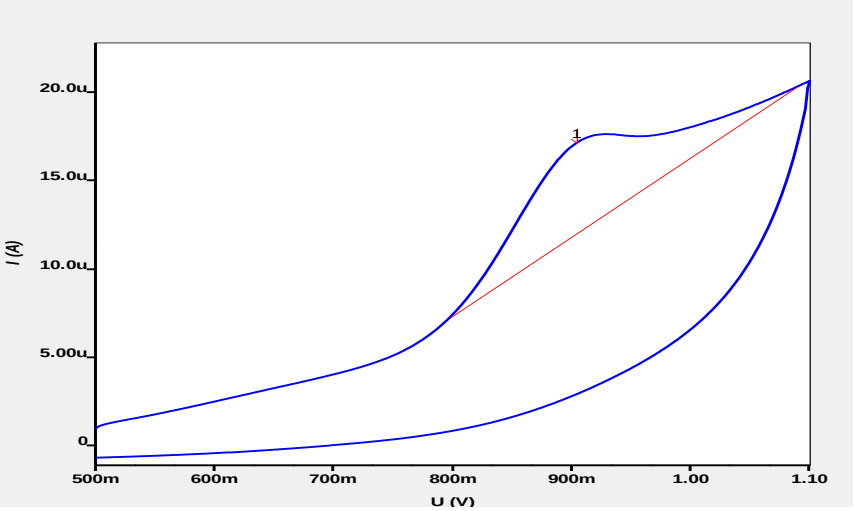


Figure 2. Cyclic voltammograms of 3µM PNT solution in BR buffer of pH 8.2 GCE at a scan rate100 mV/s.

3.2 Scan Rate

The effect of scan rate on the redox reaction of PNT on GCE was carried out by cyclic voltammetry. Cyclic voltammograms for 3 µM PNT (0.04 M) in Britton-Robinson buffer solution (pH= 8) at the GCE with scan rates (20 - 300 mV s^{-1}) are shown in Fig. 3. The increase of potential scan rate promoted the increase of peak current in redox reaction of PNT. Linear relationship was obtained between the logarithmic peak currents and the logarithmic scan rate. The regression equation was log Ip(A) = 4.9349+ 0.3569 log υ (Vs^{-1}) with r^2 = 0.9989 and a slope value 0.3569 which is close to the theoretical theoretically expected value of 0.5, indicating that the oxidation current is of diffusional nature [35]. Moreover, the peak potential was shifted toward more positive values 0.861 to 0.936 V with absence of the cathodic wave in cyclic voltammetry that confirmed the irreversibility of the oxidation process of PNT at glassy carbon [36], (Fig. 4).

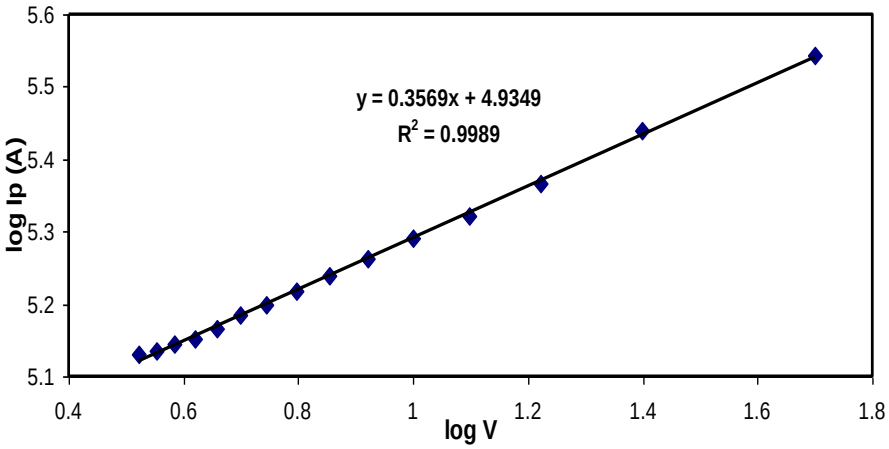


Figure 3. Dependence of CV anodic peak current logarithm, log Ip, of 3µM PAN on GCE in B-R buffer at pH 8.0.

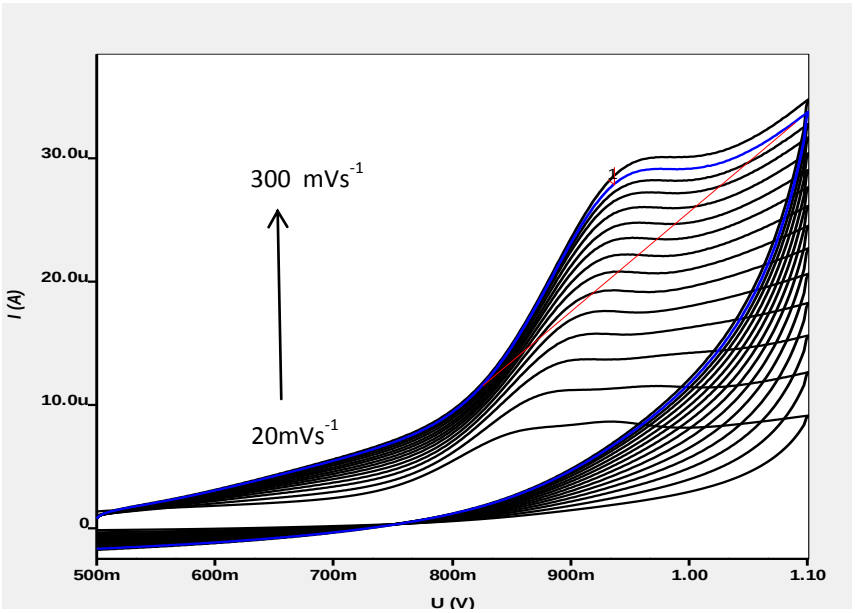


Figure 4. Cyclic voltammetry of 3µM PNT solution in BR buffer of pH 8.0 at different Scan rate (20-300 mv/sec) at GCE.

3.3 Effect of pH

The pH effect on the electrochemical behavior of PNT was studied by cyclic voltammetry using Britton-Robinson buffer at the pH range from 2 to 12. It was found that electrochemical behavior of PNT is dependent on the pH value of the aqueous solution and the pH of the solution has a significant influence on the peak current and potential of the oxidation of PAT. Fig. 5 shows the plot of peak current (Ip) vs. pH indicating that the peak current reaches its maximum value at pH 8 which is the optimal value selected. It was found that the peak potential gradually decreases linearly with increasing pH from 5.0 - 10.0 and the shift in potential (E) depends on the optimal pH value for the

redox reaction which was accompanied by transferring of protons. It gave a linear regression equation of E(V) = 1.3843–0.0596pH, with the correlation coefficient of 0.9931 (Fig. 6).

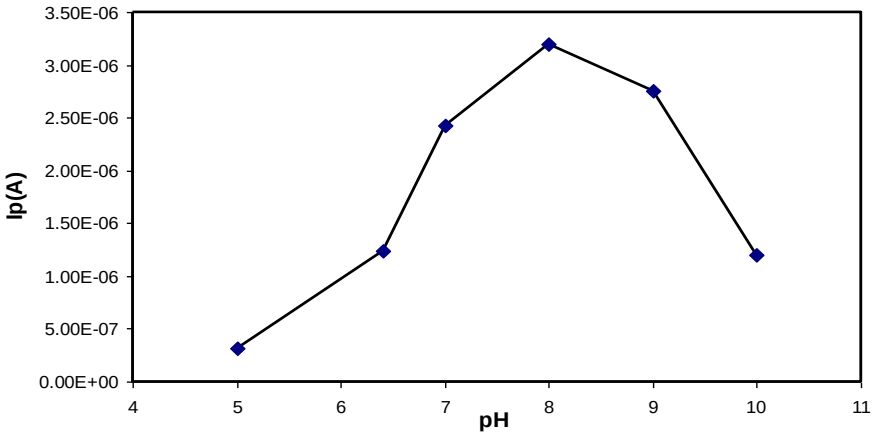


Figure 5. The relationship of anodic peak current response vs. solution pH value of 3μM PNT solution in B-R buffer on GCE at a scan rate 100 mV/s.

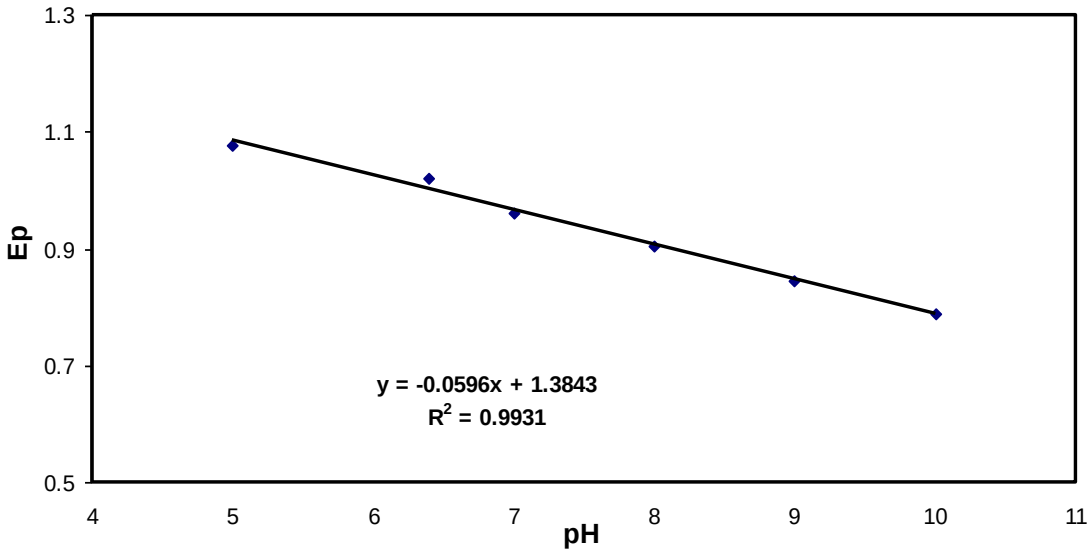
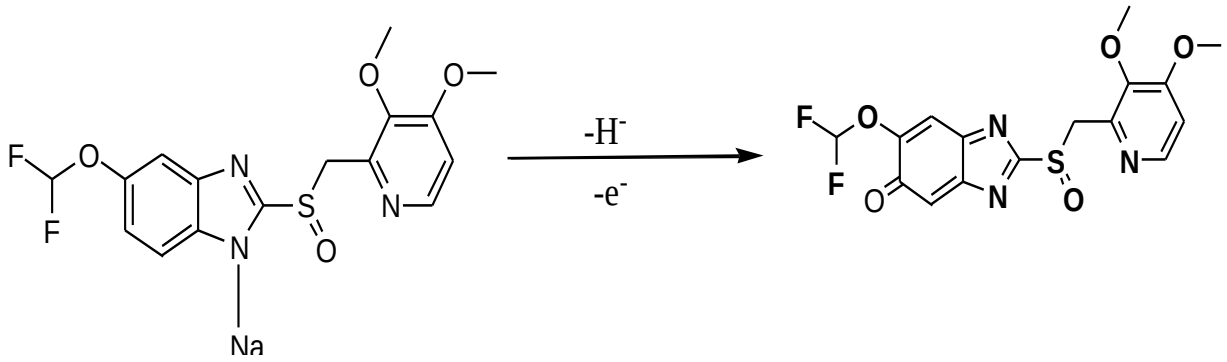


Figure 6. The relationship of Epvs. solution pH of PNT 3μM at GCE electrode at a scan rate 100 mV/s.

The slope value of 59.6 mV/pH was very close to the anticipated Nernstian value of 59 mV for electrochemical processes involving the same number of protons and electrons [37], which suggested that processes involving the same number of one proton transfer coupled to one electron transfer. The mechanism of anodic oxidation of PNT can be proposed according to the equation:



4. ANALYTICAL PARAMETERS AND VALIDATION OF THE DEVELOPED METHODS

4.1. Differential Pulse Voltammetry

Differential pulse experiments were performed on the GCE in Britton-Robinson buffer solution of pH 8 with experimental conditions were, scan rate 5 mV/s; pulse amplitude 50 mV; sample width of 40 ms; pulse width of 50 ms and pulse period 40 ms. The potential was scanned anodically from an initial to a final potential of 500 - 1000 mV. The resulting voltammograms shown in Fig. (7) reveal that the peak potential remained almost constant at 0.833V. The DVP results for the determination of the PNT is shown in Fig.(8). It is obvious that linear relation between the peak current (Ip) and PNT concentration (C) was found in the concentration range of 0.5 - 7.5 µM according to the equation:

Ip = 0.0698C (µM) +0.0539 r^2 = 0.9904

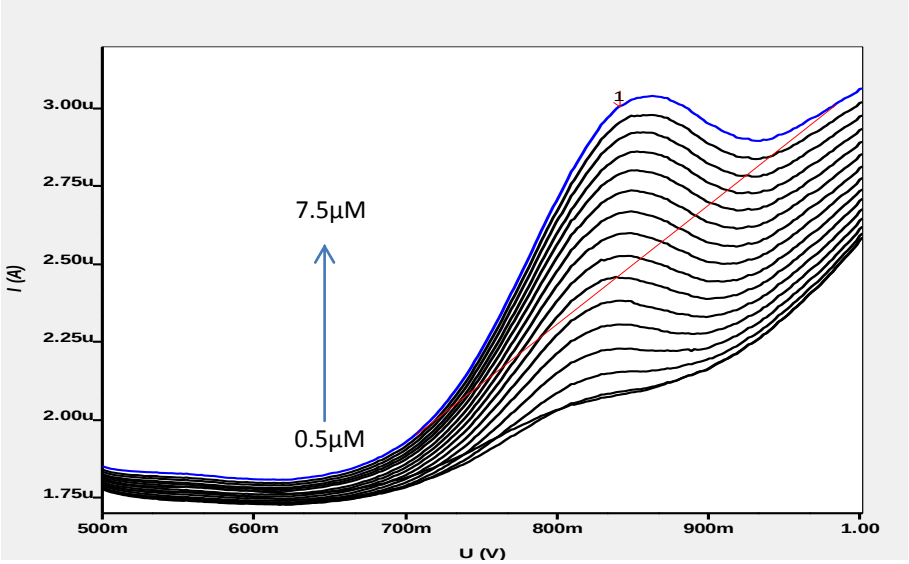


Figure 7. Differential pulls voltammetric responses for successive additions of PNT from 0.5µM to7.5 µMin BR buffer solution (pH 8.0) at GCE.

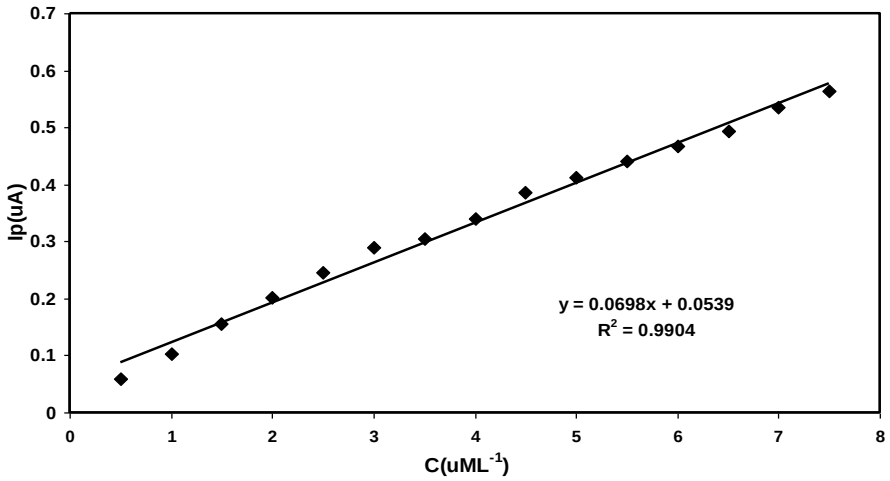


Figure 8. Background corrected DPV response for different concentrations of PNT0.5µM to 7.5 µM in BR buffer solution (pH 8.0) at GCE.

4.2 Square-Wave voltammetry

Square-wave voltammetry was performed at GCE in 25 ml of Britton-Robinson buffer solution of pH 8.0 with the experimental conditions optimized at 20 mV square-wave amplitude, 2 mV potential step, potential range of 500 to 1000 mV and frequency 50 Hz.

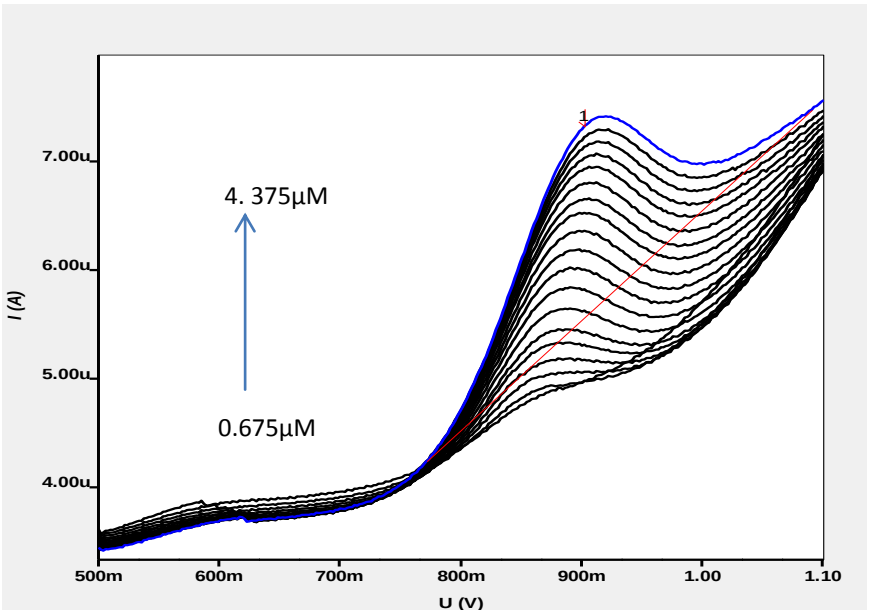


Figure 9. Background corrected SWV response for different concentrations of PNT0.675µM – 4.375µM in BR buffer solution (pH 8.0) at GCE.

The resulting voltammograms are shown in Fig.(9). It reveals that the peak potential remained almost constant at 0.89V. SWV for the determination of the PNT drug under investigation as shown in

Fig. (10) gives a linear relation between the peak current (Ip) and PNT concentration (C) in the concentration range of 0.675–4.375 µM. The data obtained from calibration plots were described by the following equation:

$Ip = 3.5279\ C(\mu M) + 3.1353 \qquad r^2 = 0.9925$

The process of validation (within-day variations) was studied by analyzing four replicate samples of 2µM PNT for both techniques. The regression equation plots showed that there was linear dependence of the peak current intensity on the PNT drug concentration by both SWV and DPV over the previously reported concentration range and the results of the statistical analysis of the experimental data such as slope, intercept, correlation coefficients, standard deviation (SD) of intercept (Sa) and limit of detection (LOD) are given in Table. 1. Between-day variation of the same concentration of PNT was studied for analyses made during four consecutive days by performing five measurements.

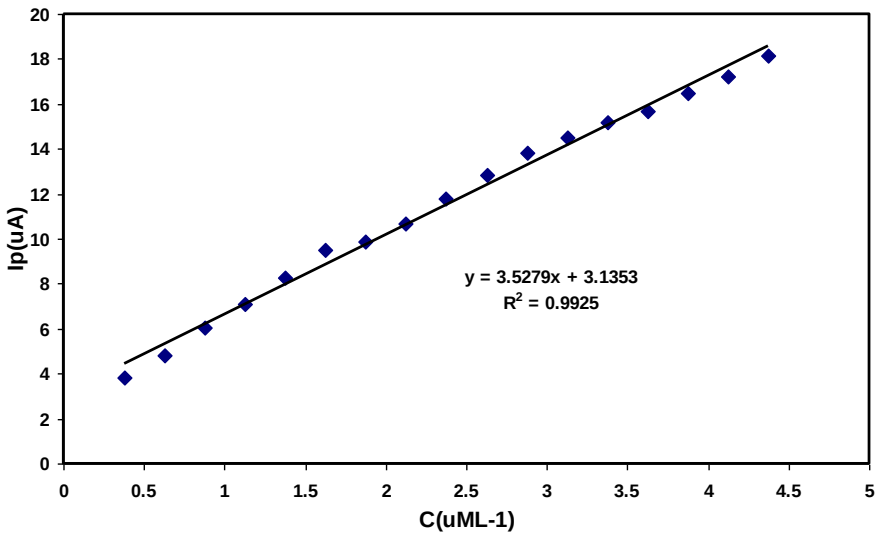


Figure 10. Square wave voltammetric responses for successive additions of PNT from 0.675µM – 4.375µM in BR buffer solution of pH 8.0at GCE.

Table 1. Characteristics of PNT calibration plots using proposed voltammetric methods.

Parameters	DPV	SWV
Slope (mV decade^{-1})	0.0698	3.5279
Intercept (mV)	0.0539	3.1353
Correlation coefficient	0.994	0.9925
Limit of detection (µmol L^{-1})	0.3731	0.1801
Limit of quantification (µmol L^{-1})	1.243	0.6005
Working pH	8	8
Concentration range, µmol L^{-1}	0.5 - 7.5	0.675 – 4.375
Average recovery (%)	98.95-99.79	98.64-99.55
RSD%[a]	0.4009	3.05

[a] Average of five determinations.

5. ANALYTICAL APPLICATION

5.1Tablet analysis

DPV and SWV methods have been applied to determine PNT in pharmaceutical preparation (Pantoloc tablet). The results of the proposed methods have been evaluated statistically as compared to results of official method [38]. There was no significant difference between the proposed and reported methods in terms of accuracy and precision Table 2.This is supported also by the value of F- and t-tests.

Table 2. Evaluation of the accuracy and precision of the proposed and official methods for the determination of PNT in its pharmaceutical forms at GCE.

Pantoloc	[Drug] mg	Proposed method ±%RSD, n = 5	Official method ±%RSD, n= 5	F-test	T-test
DVP	20 40	100.1 ± 0.32 99.98 ± 1.02	100.0± 2.2 99.92 ± 0.87	1.2 1.33	2.13 2.12
SWV	20 40	100.0 ± 0.1 99.96 ± 1.11	100.0± 1.1 99.92 ± 0.76	1.42 1.23	2.01 2.23

5.2 Assay of pantoprazole sodium in spiked human urine

The suggested method was successfully applied to the determination of PNT in spiked human urine samples using DPV and SWV techniques. The results are summarized in Table.3. The described voltammetric methods were carried out without extraction of the drug before the analysis. DPV and SWV voltammograms of PNT in spiked human urine recorded under the optimum operational conditions of the described voltammetric methods and the quantitative analysis carried out by adding the standard solution of PNT into the detect system of urine samples. The peak linearly increased in height. The calibration graph was used for the determination of spiked PNT in urine samples.

Table 3. Determination of PNT in spiked urine samples.

Urine	Spiked	Detected[(a)] (μ M)		Recovery (%)		RSD%	
		DPV	SWV	DPV	SWV	DPV	SWV
Sample 1	0.2	0.198	0.203	99.8	100.01	1.11	0.95
Sample 2	0.5	0.502	0.492	100.1	99.9	0.88	0.89
Sample 3	0.7	0.697	0.701	99.75	100.2	0.93	0.98

([a])Mean average of five determinations

6. CONCLUSION

The proposed DPV and SWV methods are direct and rapid for the determination of PNT and do not include any extraction process. They are precise, accurate, less expensive and easy be to use. The developed methods are also selective and sensitive enough to determine PNT in commercial preparations and urine samples without any interference from the additives. The reliability and stability of the glassy carbon electrode offers a good possibility for extending the technique in routine analysis of PNT in the pharmaceutical preparations and in urine. Thus, the glassy carbon electrode as PNT sensor had a better application prospect.

ACKNOWLEDGEMENT
The author gratefully acknowledges the financial support of the Faculty of Pharmacy, October 6 University for helping to execute this work.

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