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Journal of Pharmaceutical and Biomedical Analysis
25 (2001) 387–391

JOURNAL OF
PHARMACEUTICAL
AND BIOMEDICAL
ANALYSIS

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Voltammetric determination of doxazosin in tablets using rotating platinum electrode

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Received 19 August 2000; received in revised form 27 September 2000; accepted 13 October 2000

Abstract

This study describes the voltammetric behaviour of doxazosin molecule based on the oxidation on the surface of platinum electrode in the stationary and rotating conditions and determine doxazosin in the tablets by differential pulse technique at only rotating condition. The experiments were carried out in the supporting electrolyte consisting of 0.2 M KCl and 0.2 M buffer solution in 10% (v/v) ethanol. The effect of initial potential was investigated and no adsorption effect was observed during use of + 500 mV. The influence of pH on the peak current and peak potential was examined and the most symmetrical peaks were obtained at 0.5 M H_2SO_4 for rotating conditions. In the rotation range of 50–1000 rpm and up to 1.0×10^{-5} M doxazosin, the factor affecting the voltammetric current was diffusional. The effect of rate of potential was tested between 2 and 20 mV for the stationary condition and the character of current was found to be diffusional up to 3×10^{-5} M concentration of doxazosin solutions. The voltammetric determination of doxazosin in tablets was realised in the optimum rotating system conditions and depending on the statistical evaluations, acceptable results were obtained. Therefore, the method proposed in this study is practical, sensitive and accurate for the analysis of doxazosin in the quality control laboratories.

Keywords: Voltammetry of doxazosin; Determination of doxazosin; Pharmaceutical application

1. Introduction

Doxazosin mesylate (DOX) 1(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(1,4-benzodioxan-2-yl-carbonyl) piperazine monomethansulphonate is a postsynaptic α-1 adrenoreceptor antagonist. It is structurally similar to prazosin. DOX as a potent anti-hypertensive agent is effective, when administered either orally or intravenously. It is slowly eliminated in man and its long half-life provides the basis for once-daily dosing [1,2].

It was encountered that several HPLC methods have been employed for the determination of DOX and these studies cover the determination of active material in the body fluids depending on the pharmacological evaluations [3–6]. In addition, it was reported in the several voltammetric methods such as polarography [7], cathodic stripping voltammetry [8], UV-spectrophotometry and

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PII: S0731-7085(00)00515-X

square-wave voltammetry [9] and adsorptive stripping voltammetry [10].

In the chromatographic methods, organic solvents and columns are used as mobile phase and requires same pretreatments of the test solutions, whereas this method does not face such problems and consequently reduces the cost of analysis. Additionally, the same solutions can be used many times by cleaning the surface of the electrodes.

The goal of this study is to examine the voltammetric behaviour of DOX molecule based on the oxidation of the surface of platinum electrode in the stationary and rotating conditions and to determine doxazosin in the tablets (Table 1) by differential pulse technique at only rotating condition and elucidate the optimum parameters and to determine it in tablets utilising the optimum parameters. UV-spectrophotometry was chosen as a comparison method to evaluate the validity of the techniques and all the results were evaluated statistically.

2. Experimental

2.1. Apparatus

Voltammetric system comprising of Polaropulse Model PRG-5; the electrodes dual-function EGMA type cell stand for polarography and voltammetry, with rotating platinum as working, platinum wire as auxiliary and saturated Ag/AgCl as reference electrodes (all Tacussel) were used. The polarograms were recorded by BBC Goertz Metrawatt Model SE 790 x-y recorder. A Model-P 114 pH-meter (Consort) was employed for measuring and adjusting the pH of the solution. Spectrophotometric studies were made using a Model-160 A spectrophotometer (Shimadzu). The system was termostated by MT Lauda M6 circulation thermostat.

2.2. Chemicals

Standard DOX (99.97%) was supplied from Pfizer Ilaç Sanayi AS (Istanbul) and it was used without further purification. All the other chemicals used in the experiments were the products of Merck Co. (Germany) and they were all of analytical grade. Double distilled water for the preparation of the solutions was employed. The commercial preparation of DOX (Cardura® tablet containing 4-mg active material) is produced and sold in the drugstore.

2.3. Supporting electrolyte

An aqueous solution containing 10% ethanol (v/v), 0.2 M KCl and acetate or phosphate buffer was the most suitable supporting electrolyte. The pH of the buffers was adjusted by 2 M HCl or NaOH solutions.

2.4. Procedure

2.4.1. Pre-treatment of platinum electrode

Working electrode, platinum rotating disk, was polished by sweeping with alumina. Then, it was cleaned by methanol, rinsed with double distilled

Table 1
The statistical evaluations of assay results of 4-mg DOX in Cardura® tablet using rotating platinum electrode by DC, DP-voltammetry and UV-spectrophotometry[a]

Modes	Rotating DP-voltammetry	Rotating DC-voltammetry	UV-spectrophotometry
Recovery mean ($n = 8$)	4.03	4.03	4.05
S.D.	0.04	0.07	0.06
R.S.D. (%)	0.12	0.17	0.16
CL	± 0.03	± 0.05	± 0.04
t-tests of significance	0.45	0.78	$t_{0.05} = 2.26$
F-tests of significance	1.86	1.19	$F_{0.05} = 3.18$

[a] Abbreviations: S.D., standard deviations; R.S.D., relative standard deviations; CL, confidence limits.

water and it was dried using non-abrasive tissue paper. This procedure was repeated prior to each experiment.

2.4.2. Voltammetric studies

Ten ml supporting electrolyte containing 1.1×10^{-4} M DOX was put into the voltammetric cell to investigate the optimum voltammetric parameters. The investigations were carried out by scanning anodically against saturated Ag/AgCl reference electrode potential. The other parameters used during the experiments are given in the related sections. All the experiments were conducted in ambient temperature.

2.4.3. Spectrophotometric studies

The aqueous solution of 1.0×10^{-3} M DOX solution was prepared and a series of standard solution in the concentration range of 1.0×10^{-5} and 5.0×10^{-5} M diluted from the stock solution. The spectrophotometric measurements were made at 330 nm using quartz cuvets and double distilled water was used as a blank solution.

2.4.4. Analysis of pharmaceutical dosage form

For the pharmaceutical analysis, 20 tablets (each containing 4 mg active material) were weighed, the average weight of a tablet was calculated and they were powdered in a mortar. The powder of Cardura® tablet containing DOX equivalent to 4 mg were weighed accurately, transferred into a 100-ml flask and added some supporting electrolyte to dissolve the active material. The solution was stirred magnetically for 10 min and made up to volume of 100 ml with supporting electrolyte. Sufficient amount of the solution was pipetted into a tube and centrifuged for 5 min. The clear solution was diluted either with supporting electrolyte for the voltammetric or with distilled water for the spectrophotometric determination of the active material.

3. Result and discussion

DOX is a water soluble compound. Acidity increases its solubility. Therefore, aqueous supporting electrolyte having 10% ethanol, 0.2 M KCl and 0.5 M H_2SO_4 was preferred for the voltammetric investigation of DOX. Voltammograms of 4.2×10^{-5} M DOX solution having 0.5 M H_2SO_4 was prepared and were recorded each day. Although, the prepared solutions give the same polarograms during a week time. It is not always possible to obtain the true stability of the molecule. For this aim, HPLC or TLC methods are recommended.

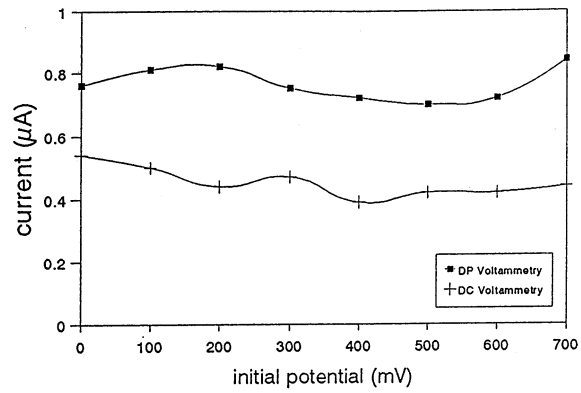

Fig. 1. The variation of peak current of 6.7×10^{-5} M DOX versus initial potential on DC and DP voltammetry.

3.1. Voltammetric behaviour of DOX

Initial potential dramatically effects the species of voltammetric current and morphology of the current. Therefore, the variation of the limiting current of 6.7×10^{-5} M DOX in 0.5 M H_2SO_4 versus initial potential in the range of 0 and + 700 mV was examined by rotating platinum electrode employing DC and DP techniques, respectively. Well-defined and morphologically good oxidation curves were obtained in the range of 0 and + 700 mV initial potential and the plots of the limiting current by DC and peak current by DP voltammetric techniques versus initial potential are given in Fig. 1. This dependence for each technique shows that the systems do not exhibit any adsorption phenomena because of almost equivalent currents and it was decided to employ + 500 mV as initial potential for both techniques.

The variation of the limiting current (DC) or peak current (DP) of 1.1×10^{-4} M DOX in the supporting electrolyte consisting of 10% ethanol,

0.2 M KCl and 0.2 M acetate buffer at various pH versus pH were examined by using rotating platinum electrode with 500 rpm recording from + 500 mV initial potential applying 30 s. The plot of current and peak potential including 0.5 M H_2SO_4 against pH are demonstrated in Fig. 2a. The variation of the limiting currents exhibit an increase due to the decrease of pH. The most reproducible and symmetrical voltammograms appeared in H_2SO_4.

The dependence of half-wave (DC) and peak potential against pH are in Fig. 2b. It is observed that there are two intersection points for both DC and DP techniques. One point around pH 5 probably corresponding the pK_a of molecule, which was reported as 4.8, earlier [11].

To elucidate the factor which influence the voltammetric current, the rotation effect in the range of 50–1000 rpm was investigated by DC technique. The plot of square-root of rotation rate, $\omega^{1/2}$, versus current of 4.2×10^{-5} M DOX. Straight line which almost passes through origin with a little intercept was obtained in the whole rotational range. The equation of the curve was computed to be [i (μA) = 0.089 $\omega^{1/2}$ + 0.065, r = 0.9853]. This result shows that the system obeys the Levich law [12], which indicates that the character of current is diffusional. It was observed that there is a relation between rotation rate and concentration of the bulk material. Adsorption phenomena diminishes with the use of low rotation rate. Thus, 500 rpm was preferred for the rest of the study.

The effect of pulse height of 1.1×10^{-4} M of DOX solution on the peak currents was investigated in the range of 2–100 mV and linear dependence were obtained with little slopes for rotating DC and DP techniques. Thus, it was decided that 50 mV is the most convenient pulse height value for each technique and it was used for the quantification studies. Almost symmetrical peaks of 6.7×10^{-5} M DOX were appeared using rotating platinum electrode by DC and DP techniques utilising the optimum analytical and voltammetric conditions; initial potential of + 500 mV, rotation rate of 500 rpm and pulse height of 50 mV, in the employment of 0.5 M H_2SO_4 as demonstrated in Fig. 3.

Then the calibration studies were achieved and straight line, which almost passes through origin was obtained for the examination of DOX dilutions in the range of 1.0×10^{-5}–6.1×10^{-5} M. The equations of the calibration curves were computed to be [i (μA) = 7.7×10^{-3} + 9245C(M); r = 0.9996] for DC and [i (μA) = 3.7×10^{-2} + 8655 C(M); r = 0.9996] for DP. The linearity of the calibration curves with its good correlation coefficient and little intercept value indicate them to obey the Fick's law and it corresponds that they allow us to determine DOX confidentially in the pharmaceutical preparations by these techniques.

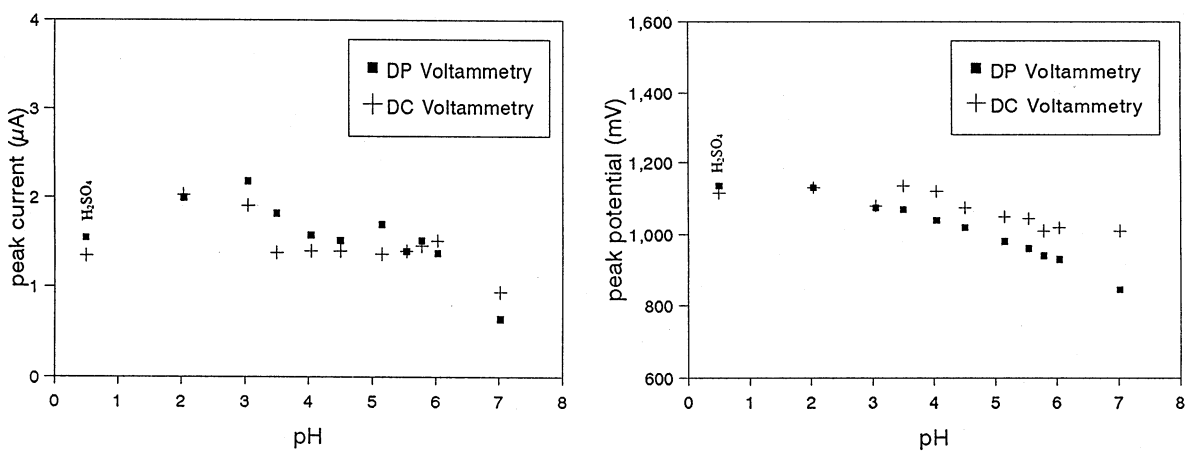

Fig. 2. The dependence of peak current values (a) and peak potential values (b) 1.1×10^{-4} M DOX against pH in the DC and DP voltammetry.

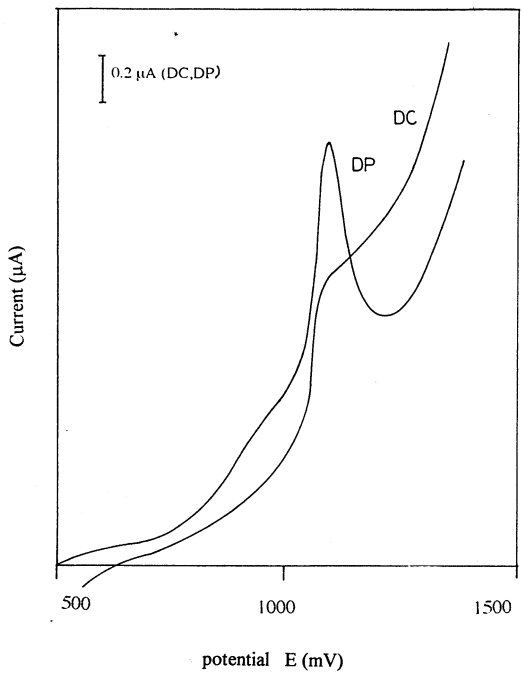

Fig. 3. The DC and DP voltammograms of 6.7×10^{-5} M DOX solution.

Reproducibilities were found to be (inter-day for 6 days) 1.37%, for DC and 1.16%, for DP. Detection limits were calculated to be 2×10^{-6} M and 1.5×10^{-5} M DOX accepting signal-to-noise is equal to 3, for DC and DP, respectively.

3.2. Application of voltammetric techniques to DOX tablets

The validity of the method proposed with this study was applied to tablets, Cardura® tablets, which contain 4 mg DOX. Tablets were processed as described under the experimental studies and optimum voltammetric conditions were employed for the quantification. Since additives in the tablet are electrochemically inactive, they have no interference effect. Therefore, the proposed method can be used for the analysis of pharmaceutical preparations.

UV-spectrophotometry was used as a comparison method. Calibration studies were done preparing standard DOX solutions in the range of 1×10^{-5}–5×10^{-5} M concentration. Calibration graph was drawn and no deviation appeared. The equation was computed to be utilising the absorbance values against concentrations of DOX as [$A = 3.0 \times 10^{-3}$–9084 C(M); $r = 0.9999$] at 330 nm.

The results of the methods were compared with each other by common statistical tests at the 95% probability level. The results of the statistical evaluations are in Table 1. According to the results of *t*- and *F*- tests, insignificant difference was observed between the methods. The quantification results also show a parallelity with the study, which was achieved voltammetrically. Besides, the content of a tablet was providing the official requirements, as well [13].

In conclusions, the advantage of the proposed method over the procedure described in [7], is that this method does not need to use the toxic and potentially pollutant mercury electrode. The method proposed in this study is practical, sensitive and accurate for the analysis of DOX preparations in the quality control laboratories.

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