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Polarographic behavior and determination of finasteride

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Abstract

The polarographic behavior of finasteride at the dropping mercury electrode (DME) was studied adopting direct current (DC_t), alternating current (AC_t) and differential-pulse polarography (DPP) modes. In Britton–Robinson buffer (BRb), finasteride exhibited cathodic waves over the pH range 6–12. At pH 10, a well-defined cathodic wave was obtained. The latter could be characterized as being irreversible, diffusion-controlled and partially affected by adsorption phenomenon. The number of electrons involved in the reduction process was accomplished and a proposal of the electrode reaction was presented. The current–concentration plots were rectilinear over the ranges 8–40 and 2–30 μg ml^{-1} using DC_t and DPP modes, respectively. The minimum delectability was 0.2 μg ml^{-1} (5.4×10^{-7} M), for the latter. The proposed method was successfully applied to the determination of finasteride in its commercial capsules and the results obtained were in good agreement with those given with a reference method.

Keywords: Finasteride; Pharmaceutical preparations; Polarography

1. Introductions

Finasteride, (5α, 17β)-*N*-(1,1-dimethylethyl)-3-oxo-4-azaandrost-1-ene-17-carboxamide), is a 5α-reductase enzyme inhibitor. This enzyme converts testosterone to the more potent androgen, α-dihydrotestosterone [1]. The drug provides a logical medical treatment for benign prostatic hyperplasia (BPH), as it induced a reduction in serum dihydrotestosterone and prostatic specific antigen levels with a concomittant increase in blood testosterone concentration [2]. Despite its widespread use, little has been published concerning its quantitation. A part from some reports on finasteride, no official methods for its assay has been reported. However, the reported methods for its determination in pharmaceutical preparations or in biological fluids include: HPLC [3–6], LC-MS-MS [7], and an isotop dilution mass-spectrometric methods [8], have been reported.

A review of the literature revealed that no reports have been published on the electrochemistry or polarographic activity of finasteride. The aim of the present work is to investigate the polarographic behavior of the drug and its application to pharmaceutical analysis using direct current (DC_t), differential pulse (DPP) and alternating current polarography (AC_t).

The presence in finasteride, of keto group conjugated with the double bond, which is susceptible to polarographic reduction [9], led to the present study.

2. Experimental

2.1. Materials and reagents

1) Finasteride and its prostride capsules were kindly provided by Egyptian Co. for Chemicals and Pharmaceuticals (ADWIA), Cairo, Egypt. Finasteride pure sample was used as received; (purity 99.68%).
2) Britton–Robinson buffer (BRb), 0.08 M [10], covering the pH range; 6.0–12.0.
3) Methanol, analytical grade (Aldrich).
4) A stock solution (0.25 mg ml^{-1}) was prepared in methanol and was further diluted with the same solvent to appropriate concentration.

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2.2. Apparatus

The polarographic study, DC_t and DPP were carried out using the polarecord E 506 Metrohm (Herisau, Switzerland). The electronically-controlled drop time obtained by a Metrohm 663 V A stand was 1 s. The polarogram were recorded using a potential scan rate of 10 mV s^{-1}. A three electrode system composed of dropping mercury electrode (DME), Ag/AgCl in saturated KCl as a reference electrode and a graphite rod as the auxiliary electrode.

Phase-selective AC_t polarography: AC_t polarograms were recorded with the same instrument, the superimposed alternating voltage being 15 mV at phase angle 90 °C.

The effect of mercury height was studied using 505 V A stand of the same company.

2.3. Procedures

2.3.1. Recommended analytical procedure

Transfer different aliquot volumes (0.2–4.0 ml) of finasteride stock solution into a 25 ml measuring flasks so that the final concentration is in the range of 2–40 μg ml^{-1}. Complete to 5 ml with 40% methanol, then add BRb of pH 10 to the mark. Mix well, then transfer the whole solution to the polarographic cell. Purge with pure nitrogen for 5 min, record the polarogram in both DC_t and DPP modes over the range from −1.2 to −1.6 V. Plot the produced current, uA versus the final concentration, mM to obtain the calibration graph and then derive the regression equation.

2.3.2. Analysis of capsules

Weigh the contents of ten capsules and mix well. To a quantity of the powder capsules equivalent to 25 mg of the drug, add 20 ml methanol. Filter into a 100 ml measuring flask, wash the filter paper with another 20 ml methanol then dilute with the same solvent to the mark. Proceed as under procedure Section 2.3.1 and the finasteride content per capsule was determined either from the calibration graph or from the regression equation.

3. Results and discussion

Fig. 1 shows a typical polarogram of finasteride in pH 10 BRb containing 40% methanol, a well-defined cathodic wave with $E_{1/2}$ −1490 mV is produced. The reduction of finasteride at the DME was found to be pH-dependent. The $E_{1/2}$ values were shifted to less negative potentials upon increasing the pH (anodic shift) Fig. 2.

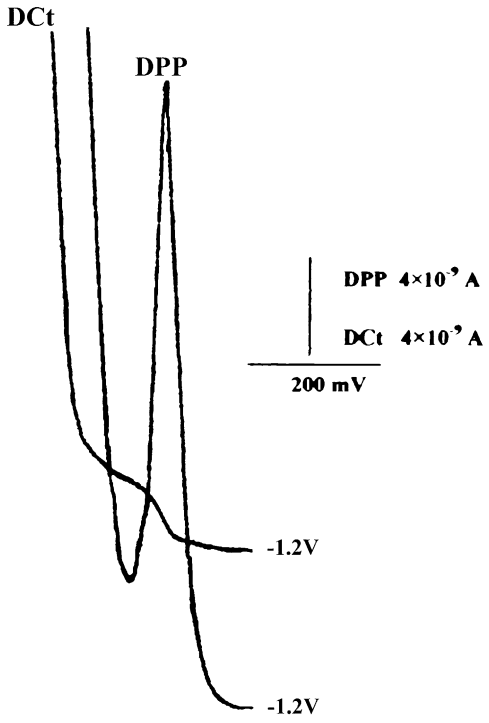


Fig. 1. Typical polarogram of finasteride (6.98×10^{-6} M) in 0.08 M BRb, pH 10.0 containing 40% methanol.

A plot of $E_{1/2}$ versus pH Fig. 3 shows a region of linearity with a break at about pH 8.5. As no evidence is offered on the dissociation constant of finasteride, the pK_a of the drug is assumed to be between 8 and 9 until more investigation is carried out.

Logarithmic analysis of the reduction waves obtained in BRb of different pH values (6–12) resulted in straight lines. The variable values of slopes proved that the reduction process is irreversible. The αn_a values were calculated according to the method of Meites and Israel [11]. At pH 10.0 the αn_a value was 0.81 indicating the high irreversibility of the reduction process (Table 1).

Increasing the mercury height (h) resulted in a corresponding increase in the wave height (w), plots of $\sqrt{h}$ versus w gave straight line and also, plots of log h versus log w gave straight line with a slop of 0.84 which indicate to a diffusion-controlled process, partially affected by adsorption phenomena.

Changing the buffer concentration over the range of 0.02–0.08 M resulted in a negligible decrease in the wave height. This observation adds another proof that the produced current is diffusion-controlled and adsorption phenomenon plays a limited role in the electrode process.

Fig. 4 shows the AC_t behavior of finasteride using a phase selective angle of 90° in BRb at pH 6, 7and 10.The summit potentials (E_s) were shifted 100, 85 and 100 mV more negative than the corresponding $E_{1/2}$ values,

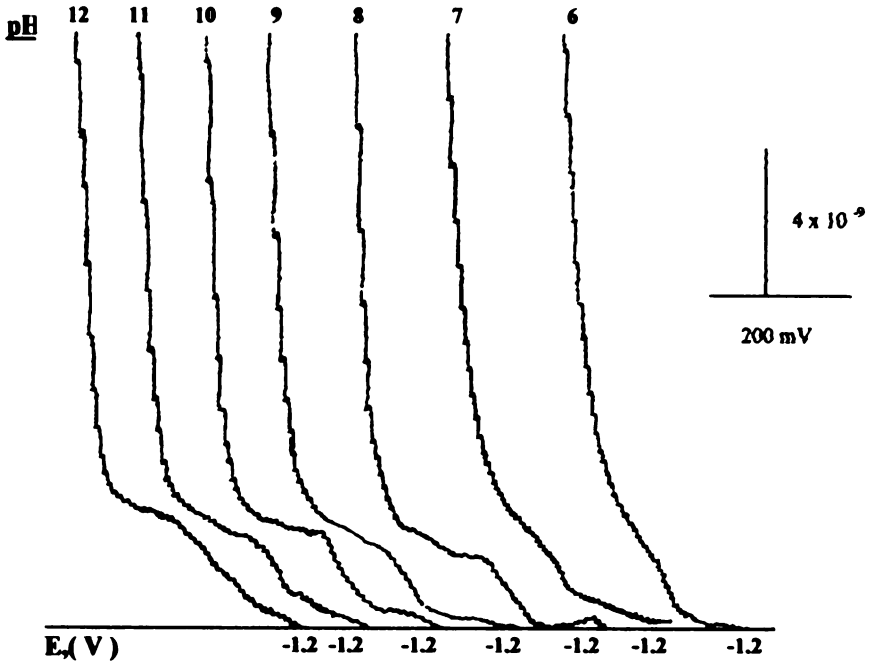


Fig. 2. Effect of pH on the development of the polarographic waves of finasteride (6.98×10^{-6} M) in 0.08 M BRb.

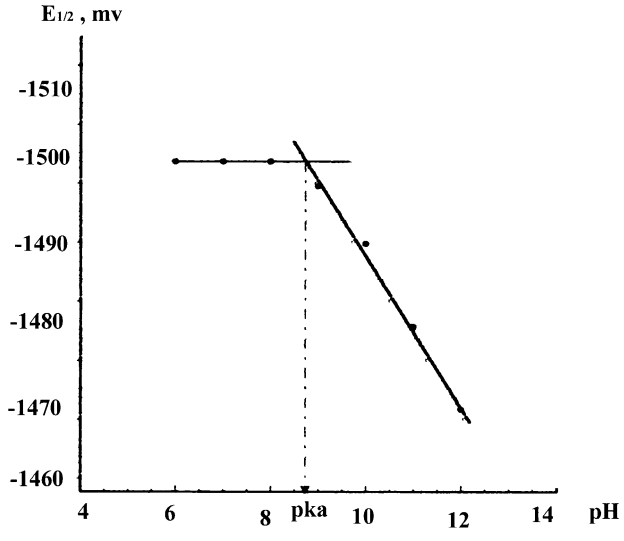


Fig. 3. Effect of pH on the half wave potential ($E_{1/2}$) of finasteride.

Table 1
Effect of pH on the development of the polarographic waves of finasteride

pH	$E_{1/2}$ (mV)	αn_a	$W_{1/2}$ (mm)
6	−1500		8.5
7	−1500	0.78	8
8	−1500	0.78	7.5
9	−1497	0.77	9
10	−1490	0.81	6.5
11	−1480	0.77	8
12	−1470	0.72	10

Where, $E_{1/2}$ is the half-wave potential in DC_t. $W_{1/2}$ is the half-peak width in DPP. α is the transfer coefficient, and the value of αn_a is obtained through logarithmic analysis of the waves.

respectively. At all the pH studied, only the depolarizer but not its reduction product was adsorbed to the mercury surface.

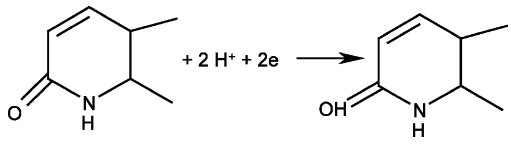
The relation between limiting current (i_d) in μA and the concentration (C) in mM obtained by both DC_t and DPP modes was found to be linear over the ranges cited in (Table 2).

The diffusion current constant Id and the diffusion coefficient (D) were calculated according to Ilkovic equation for various concentrations of finasteride. The results obtained show that the values are reproducible.

Linear regression analysis of the data gave the corresponding regression equation shown in the same table. Statistical evaluation [12] of regression form gave small values of the standard deviation of the residuals ($S_{y/x}$), slope (S_b) and intercept (S_a), as shown in Table 2.

3.1. Mechanism of the reduction

Depending on the presence of a conjugated carbonyl group [13], and through comparison with spironlactone [9], two electrons were involved in the electrode reaction of finasteride and the postulated mechanism is as follows:



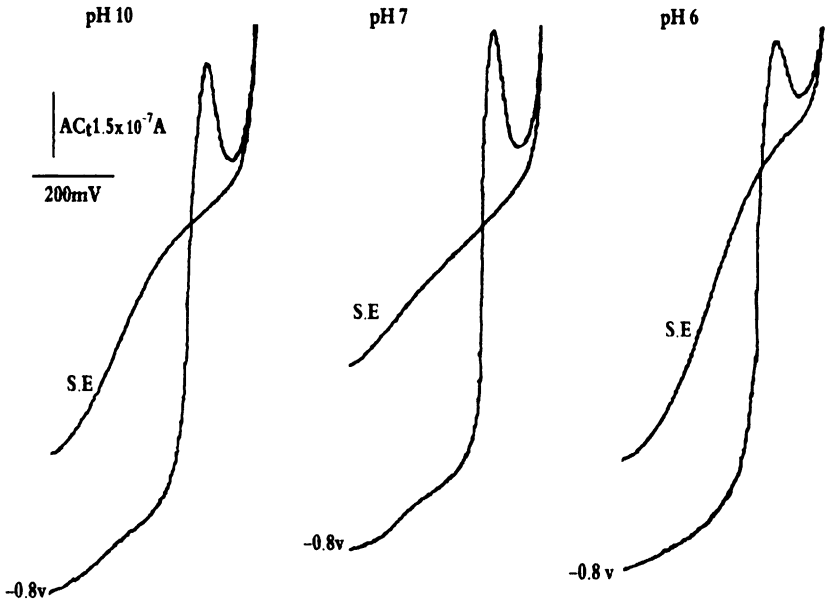


Fig. 4. AC_t behavior of finasteride (0.0805 mM) in BRb (0.08 M) containing 40% methanol at phase selective angle 90°.

Table 2
Performance data for the proposed method

Parameters	DC_t	DPP
pH	10	10
$E_{1/2}$ (V)	−1.490	−1.940
Concentration range (mM)	0.02–0.1	0.005–0.08
Regression equation $Y(i_d) = Bx_{(conc.)} + A$	$Y = 0.8246x + 0.0012$	$y = 1.337x + 0.0018$
Correlation coefficient	0.9990	0.9997
$S_{y/x}$	1.34×10^{-6}	1.168×10^{-7}
S_a	3.419×10^{-6}	7.78×10^{-7}
S_b	1.84×10^{-5}	1.909×10^{-5}
Diffusion current constant (Id)	0.704 ± 0.32	1.179 ± 0.046
Diffusion coefficient (D) $cm^2\ s^{-1}$	$3.52 \times 10^{-7} \pm 0.52$	$9.44 \times 10^{-7} \pm 7.4 \times 10^{-8}$

$S_{y/x}$, standard deviation of the residual; S_a, standard deviation of the intercept; S_b, standard deviation of the slope.

3.2. Analytical application

The best developed DC_t polarographic wave was observed in BRb, pH 10.0 containing 40% methanol (Fig. 1). At this pH, the DPP peak was the steepest, the half-peak width ($W_{1/2}$) was the smallest (Table 1) and the current was a linear function of concentration, for 0.02–0.1 mM and 0.005–0.08 mM in the DC_t and DPP modes, respectively with a detection limit of 5.4×10^{-7} M, for the latter.

DC_t and DPP modes were successfully applied to the assay of finasteride in commercial capsules. The percentage recoveries of different concentration were based on the average of three separate determinations. The results obtained were favorably compared with those obtained with a reference method [14]. Statistical analysis [12] of the results obtained by both methods using Student's t-test and the variance ratio F-test, showed no significant difference between the performance of both methods, regarding accuracy and precision, (Table 3).

Table 3
Application of the proposed method and the reference method to the determination of finasteride in capsules

Preparation	Percentage recovery		Reference method [a]
	DC_t mode	DPP mode	
Prostride capsules (5 mg finasteride per capsule)	97.8	99.3	
	99.2	99.8	
	98.7	99.4	
	99.6	98.8	
X	98.57	99.33	98.89
SD	0.71	0.41	0.33

[a] HPLC method [14].

No interference was observed from the additives coformulated with finasteride in its capsule.

4. Conclusion

The proposed method is simple, sensitive, selective and less time consuming than the reference HPLC methods.

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