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Polarographic Determination of Metronidazole

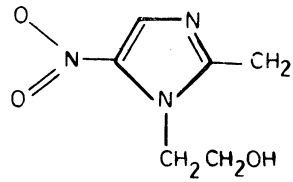
P. SIVA SANKAR and S. JAYARAMA REDDY*

Department of Chemistry, Sri Venkateswara University
Tirupati–517 502, India

The advanced electrochemical technique, differential pulse polarography is used to develop analytical procedure for the determination of metronidazole in buffered aqueous media. The procedure described has been used for the determination of metronidazole in different tablet formulations without any prior separation.

INTRODUCTION

Metronidazole(I) (1-2-hydroxyethyl-2-methyl-5-nitroimidazole) is an effective agent for a variety of protozoal diseases including trichominiasis,



giardiasis, amoebiasis and balantidiasis[1]. The first studies on the mode of action of metronidazole indicated that it inhibited the output of hydrogen gas from T. vaginalis before that of carbon dioxide, which causes the cell death[2]. The reduction of nitro group makes the metronidazole to be active. HPLC[3], spectrophotometry[4], gas chromatography[5] and gravimetry[6] have been reported to be useful in the determination of metronidazole. Edwards[7] has studied the polarographic behaviour of metronidazole in presence of DNA. In this communication, a detailed polarographic determination procedure has been described for metronidazole based on the well defined cathodic peak/wave obtained for this electroactive species.

EXPERIMENTAL

Metronidazole was supplied by unique Pharmaceutical Labs Pvt. Ltd., Bombay. The polarograms were recorded with polarographic analyser Model-364 coupled with BD 8 Kipp and Zonen recorder. Differential pulse polarograms were obtained by 'Metrohm unit' Model E 506 polarecord. The dropping mercury electrode of flow rate 2.48055 mgs^{-1} was used as working electrode and SCE/Ag/AgCl.(s),Cl^- as the reference electrodes in DCP/DPP measurements while platinum electrode served as the auxiliary electrode. All the experiments were carried out at $25 \pm 1°C$.

An appropriate amount of metronidazole was disolved in required quantity of water and accurately diluted with the supporting electrolyte to 10 ml. The solution was deoxygenated by passage of nitrogen gas for 5 minutes and then the polarogram was recorded. As far as tablets are concerned, about 100 mg or complete tablet of powdered sample was dissolved in 250 ml of water with repeated extractions. Supporting electrolyte was used to prepare various desired concentrations of metronidazole solutions from the standard solution prepared.

RESULTS AND DISCUSSION

Only one polarographic wave or peak is exhibited by metronidazole in Clarks and Lubs buffer of pH 2.00. Addition of methanol or ethanol or dimethyl formamide is noticed to shift the half-wave potentials and summit potentials to more negative values because of the decreased solubility of metronidazole. The solution pH is seen to have a marked influence on the half-wave potentials and on the summit potentials. These are found to increase with the increase in pH of the supporting electrolyte upto pH 9.25 and then remain almost constant. The limiting current and peak current are dependent on pH and decreases linearly with pH of the supporting electrolyte. A maximum is observed in all the supporting electrolytes except in Clarks and Lubs buffer of pH 2.00 in d.c. polarography which can be suppressed by using (0.1 to 0.3 ml) gelatin of 0.05%. In view of the well defined peaks/waves obtained in Clarks and Lubs buffer of pH 2.00 and because of the absence of the polarographic maximum in this medium, estimation procedure is worked out using this supporting electrolyte. The wave/peak obtained for metronidazole (1.5×10^{-4} M/2.5×10^{-7} M) in Clarks and Lubs buffer of pH 2.00 is not found to be disturbed by successive additions of other nitro group imidazoles like tinidazole, ornidazole of concentrations (1.0×10^{-3}M/2.5×10^{-6}M) (Fig. 1).

The analytical method described here is based on the results obtained with d.c. polarography and differential pulse polarography at the dropping mercury electrode. The polarograms are recorded over the range of applied potential from +0.1 V to −0.9 V. A series of polarograms for 5×10^{-4}M metronidazole in all buffers (pH ranging from 2.0 to 12.00) are recorded. The linear plots of the limiting current, i_d vs. $h^{1/2}$ and i_m vs. $t^{2/3}$, passing through the origin indicate that the electrode process is diffusion controlled. Different concentrations of metronidazole (1×10^{-5}M to 1×10^{-3}M for d.c. polarograms and 1.0×10^{-8}M to 1×10^{-5}M for DPP) are examined in Clarks and Lubs buffer of pH 2.00. The plots i_d vs. C and i_m vs. C are also found to be linear passing through origin. The calibration plot is seen to be linear upto 1.5×10^{-4}M to 1×10^{-3}M in d.c. polarography and 2.5×10^{-7}M to 1×10^{-5}M in differential pulse polarography.

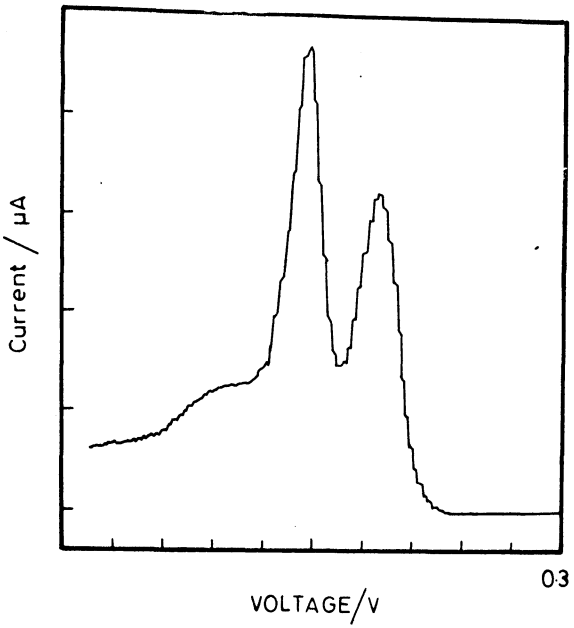


Fig. 1 Typical differential pulse polarogram of metronidazole in presence of tinidazole in phosphate buffer of pH 8.00: Concentration of metronidazole: 0.4×10^{-5}M; Concentration of tinidazole: 0.4×10^{-6}M; Drop time: 2 sec; Amplitude: 50 mV.

Differential pulse polarographic technique is found to be more suitable at still lower concentrations due to its high sensitivity and resolution. The relative standard deviations are evaluated to be 3.5% and 2.3% and the correlation coefficients 0.9731 and 0.9982 in d.c. polarography and in differential pulse polarography respectively (from 20 replicants).

Analysis of Metronidazole

Metronidazole can be determined successfully in different pharmaceutical formulations without any prior separation by using differential pulse polarography. Tests on the effect of pulse amplitude (E) on the peak height of the polarogram indicated that a value of 50 mV gives the best response. Standard addition method[8] with differential pulse polarography is used for the analysis of metronidazole. The results are shown in Table 1.

The relative standard deviation and correlation coefficient are found to be 2.4% and 0.9913 respectively.

The procedure described can be employed for the successful estimation of metronidazole (1) without prior separation of diloxanamide furoate or furazolidone commonly available in certain pharmaceutical formulations (2) without interference from other nitroimidazoles such as trinidazole, ornidazole and nimorazole.

TABLE 1

S.No.	Tablet	Composition	$i_m/\mu A$	Amount of compound	
				Observed mg	Prescribed mg
1.	Dyrade-M	Metronidazole & Diloxanamide furoate	2.98	398.7	400
2.	Metron	Metronidazole	3.71	198.6	200
3.	Furoxone	Metronidazole & Furazolidone	3.73	197.1	200
4.	Flagyl	Metronidazole	3.77	199.1	200
5.	Metrogyl	Metronidazole	7.42	396.4	400

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