RESEARCH PAPER

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Polarographic Determination of Nitro Group Containing Drugs in Tablets

Y.V. RAMI REDDY, P. RAJENDRA KUMAR REDDY, C. SURESH REDDY AND S. JAYARAMA REDDY*
Dept. of Chemistry, Sri Venkateswara University, Tirupati - 517 502.

A simple direct current polarographic method has been developed for the analysis of nitro drugs such as dimetridazole and nimesulide in tablets. The optimum pH range for obtaining well resolved waves for the quantitative determination of the drugs is found to be between 4.0 and 6.0. Both standard addition and calibration methods were used.

DIMETRIDAZOLE [1,2-dimethyl-5-nitroimidazole] is a veterinary antiprotozoal agent,[1] while nimesulide [N-(4-nitro-2- phenoxyphenyl) methane sulfonamide] is a antiinflammatory drug.[2] A review of the literature reveals that very little attention has been paid to the polarographic determination of these drugs.[3] The purpose of this work is to establish the experimental conditions that permit the study of the direct current polarographic (DCP) behaviour of dimetridazole and nimesulide and their determination in tablets. The proposed polarographic method involves cheaper instrumentation than those used in spectrophotometry and HPLC and is applicable for the routine analysis of nitro group containing drugs in small-scale Pharmaceutical industry.

EXPERIMENTAL

Apparatus and Conditions

Polarographic analyser model 364 supplied by PARC, USA coupled with BD 8 Kipp and Zonen x-t recorder was used to record all the d.c. polarograms. A dropping mercury electrode (DME) with a flow rate of 2.73 mg/s was used as working electrode and a saturated calomel electrode (SCE) as reference electrode. Platinum wire was used as counter electrode. Model LI-120 Elico digital pH was used for pH measurements. All the experiments were performed at 25 ± 1.0^{0}C.

Reagents and Solutions

Universal buffers of pH 2.0 to 12.0 were prepared by using 0.2 M boric acid, 0.05M citric acid and 0.1 M trisodium orthophosphate[4]. All the chemicals used were of analar grade.

A stock solution ($1x10^{-2}$ M) dimetridazole (ES-KAYEF Pvt. Ltd., Bangalore) or nimesulide (Sigma Chemical company, USA) was prepared in dimethyl formamide. An aqueous solution of Triton X- $100^{(0.2\%)}$ was used[5] to eliminate the polarographic maxima encountered throughout the polarogram.

Preparation of Calibration Graphs

Polarograms were recorded for different concentrations of the two drugs in the concentration range of 10^{-3}M - 10^{-5}M. A graph of measured diffusion current was plotted against the concentration. The lower detection limit (dl) was calculated[6] using the equation dl = 3sd/m, Where sd = standard deviation and m = slope of the calibration plot.

Analysis of Tablets (Marjan Assay Method)

Ten tablets were weighed and powdered, and the average mass per tablet was determined. A portion of the finely ground sample, corresponding to a stock concentration $1x10^{-3}$ M was accurately

weighed and transferred to a 100 ml calibrated flask containing 75 ml of DMF. The contents of the flask were shaken for 20 min, diluted to the mark with DMF and was filtered. One ml of the clear filtrate, 0.1 ml of Triton X-100 and 8.9 ml of the appropriate buffer of selected pH were placed in the Polarographic cell and the polarogram was recorded after deaeration for 10 min with nitrogen gas. After obtaining the polarogram, 1 ml of the standard solution was added to the cell, deaerated for 2 min and again polarogram was recorded under similar conditions. The mass of the drug per tablet was calculated using the following equation:[7]

$$\text{Mass of the drug per tablet (mg)} = \frac{abhx100}{[1.10H-h]W}$$

where a is the mass (mg) of the reference standard in 100 ml of standard solution; b is the average mass of a tablet (gm); W is the mass of sample (mg) taken for the polarographic determination; H is the wave height before standard additions; H is the wave height after standard additions; and 1.10 is the dilution factor.

RECOVERY EXPERIMENTS

In order to establish the reliability and suitability of the proposed method, known amount of the pure drug where added to various pre-analysed formulations of the drug and the mixtures were analysed by the above mentioned method.

RESULTS AND DISCUSSION

Under the experimental conditions, dimetridazole (I) and nimesulide (II) are found to show similar reduction behaviour. Compounds I and II are found to be reduced in a single wave at all the pH levels studied. This wave is attributed to the four electron reduction of the nitro group to a hydroxylamine group[8]. A typical polarogram is shown in **figure 1.**

The diffusion controlled and adsorption free nature of the wave of I and II is evidences from the

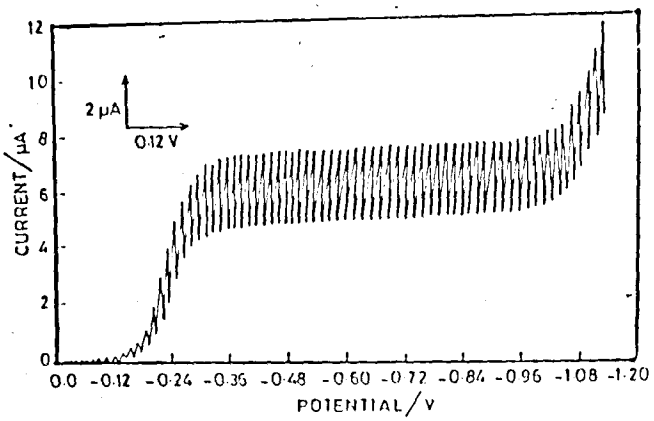

Fig.1: Typical d.c. polarogram of dimetridazole in pH 4.0
Concentration = 0.5 nM
Drop time = 3 Sec.

linear plots of i_d vs. $h^{1/2}$ passing through the origin. The irreversibility of the electron process is varified by logarithmic analysis of the wave.[9] The slope of E_{dc} versus log $i/(i_d-i)$- 0.546 log t graph exceeds appreciably 54.2/n mV. Further more, the reduction potentials ($E_{1/2}$) of compounds I and II are observed to be shifted towards more negative potentials with increasing concentrations indicating the irreversible nature of the electrode process.[10] The reduction potentials of dimetridazole and nimesulide are found to be dependent on pH and to shift toward more negative potentials with an increase in pH of the buffer solutions showing the proton involvement in the electrode process. The number of electrons involved in the over all reduction of the nitro group as determined by millicoulometry[11] is found to be 4.

Analysis is carried out using the currents obtained for nitro group reduction in compounds I and II. It is observed that at pH 2.0, the nitro group reduction appears at the start of the potential. In alkaline solutions (pH 8.0-12.0), the reduction of nitro group is not easily facilitated owing to less availability of protons. The optimum pH range for obtaining well resolved waves for the quantitative determination is found to be pH 4.0 and 6.0 **Tables 1 and 2** give the assay results of dimetridazole and nimesulide respectively. The recovery of 97.7-99.8% obtained

Table 1: Assay of dimetridazole tablets by direct current polarography

Concentration = 0.5 mM, Drop time = 3 sec.

Sample (Tablet)	pH of the buffer	Lebelled amount (mg)	Amount found (mg)	Recovery (%)	Standard deviation
Emtrylvet	4.0	25	24.6	98.5	0.015
Emtrylvet	6.0	25	24.8	99.3	0.012
Unizole	4.0	25	24.6	98.4	0.018
Unizole	6.0	25	24.7	98.9	0.013
Emtryl	4.0	25	24.8	99.3	0.016
Emtryl	6.0	25	24.4	97.7	0.015

Table 2: Polarographic assay of nimesulide dosage form by direct current polarography

Concentration : 0.5 mM, Drop time : 3 sec

Sample (Tablet)	Lebelled Amount(mg)	Amount found (mg)	Recovery (%)	Standard deviation
Nimesulide	10	9.95	99.6	0.021
Nimesulide	5	4.99	99.8	0.041
Riker	10	9.98	99.7	0.016
Riker	5	4.91	98.2	0.015

with the present polarographic method indicates its accuracy and reproducibility.

At pH 4.0, the calibration plots of dimetridazole and nimesulide is found to be linear in the concentration range $1.0x10^{-4}$ M to $2.1x10^{-5}$ M and $2.5x10^{-4}$ M to $2.5x10^{-5}$ M with a detection limit of 25 ug/ml and 32 ug/ml respectively.

None of the pharmaceutical excipients commonly employed in the tablet dosage form of dimetridazole and nimesulide are found to interfere with assay, making this method a simple, sensitive and rapid. Apparent variations of diffusion current-concentration relationship can be produced by potential impurities (if present) that react with electroactive substance actually responsible for the wave. There are only apparent because it is actually the concentration, that is affected in each instance, whereas the diffusion current is accurately proportional to the concentration of the electroactive substance that remains.[12] The polarographic method described here can safely be used as an alternative to the spectrophotometric method. Further, the proposed method or its simple modifications show promise for general application to a series of similar nitro group containing compounds.

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