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SHORT COMMUNICATION

Voltammetric Behavior and Measurement of Nimorazole

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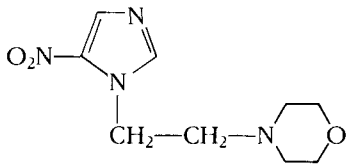
ABSTRACT

The electrochemical reduction behavior of nimorazole has been studied by employing dc polarography, differential pulse polarography, cyclic voltammetry, and chronoamperometry in the supporting electrolytes of pH ranging from 2.00 to 12.50. Parameters such as transfer coefficients, diffusion coefficients, and heterogeneous forward rate constant values are evaluated using these techniques. The analytical measurement of the drug is also discussed.

INTRODUCTION

Nimorazole (I) is an effective agent against a variety of protozoal diseases, including amoebiasis, trichominiasis, and balantidiasis [1–3]. Amoebic diseases are caused by *Entamoeba histolytica,* which is severe in subtropical and tropical regions, but *E. histolytica* has been effectively controlled by the drug nimorazole [4]. The pharmaceutical action of nimorazole is reflected by its selective toxicity to anaerobic microorganisms.



(I)

The nitro group of nimorozole behaves as an electron acceptor for the electron transport of proteins such as flavoproteins in mammalian cells and ferodoxins or their equivalent in bacteria [5].

Studies of the electrochemical reduction and determination of this compound have not been reported. We are not aware of other techniques that are used for this purpose. In the present investigation an attempt was made to explore the electrochemical properties and the quantitation of nimorazole employing dc polarography, cyclic voltammetry, chronoamperometry, and differential pulse polarography. Kinetic parameters are evaluated and reported.

EXPERIMENTAL

Polarographic assays were performed using an EG&G Polarographic Analyzer Model 364. A dropping mercury electrode (flow rate, 2.48055 mg s^{-1}) was used as the working electrode, and a saturated calomel electrode (SCE) was used as the reference electrode. Other techniques were carried out using a Metrohm unit with three electrodes: a Metrohm EA-1029/1 dropping mercury electrode (DME), a Metrohm E-427 Ag/AgCl(s), Cl^- reference electrode, and a Metrohm EA-425 platinum counterelectrode. All of the experiments were carried out at 30 ± 1°C.

The nimorazole sample was imported from the Federal Republic of Germany. The purity of the sample was tested with thin-layer chromatography. The chemicals used were of analar grade.

An appropriate amount of nimorazole was dissolved in required quantity of double-distilled water and accurately diluted with the supporting electrolyte to 10 mL. The solution was deoxygenated by purging with nitrogen gas for 5 minutes, and then the polarogram was recorded. The supporting electrolyte was used to prepare the various nimorazole solutions from the standard solution described previously.

RESULTS AND DISCUSSION

A single voltammetric peak [−0.75V vs. Ag/AgCl(s), Cl^- in Bates and Bower buffer (pH 12.50)] of nimorazole was observed in all of the supporting electrolytes studied (Figure 1). The peak is attributed to the reduction of the nitro group to the corresponding hydroxylamine. A small anodic peak (a_1) is observed in the reverse scan. In the second scan, another small cathodic peak (c_2) appeared at more positive potentials than c_1. The anodic peak may be the result of the oxidation of the reduced product at

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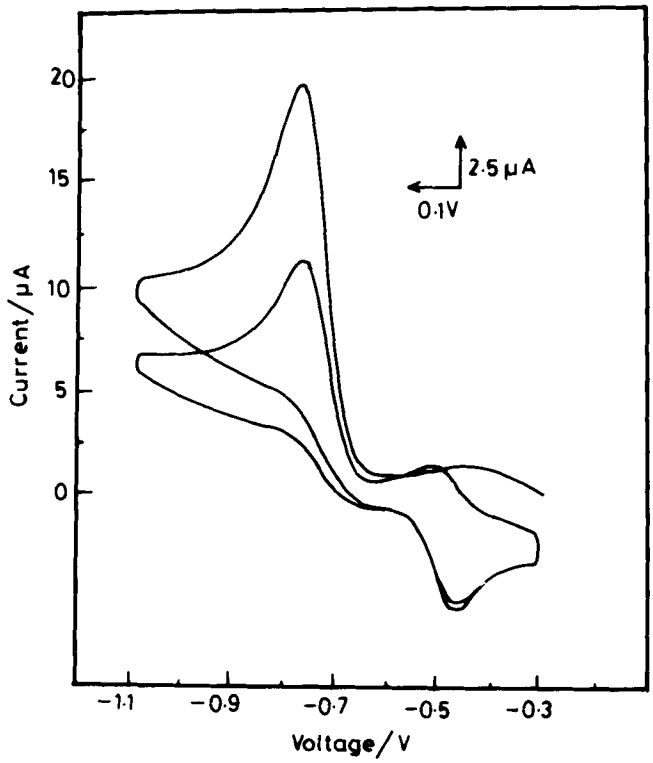


FIGURE 1. Typical cyclic voltammogram of nimorazole in Bates and Bower buffer, pH 12.50. Concentration, 0.5 mM; solvent, 5% methanol; sweep rate, 40 mV s^{-1}.

c_1, and the cathodic peak c_2 may be due to the reduction of the oxidized product at a_1 as also observed by Morales *et al.* [6] in the case of nitro-substituted furans. The peak potential changed linearly with the pH. Adding methanol, ethanol, or DMF also caused a negative shift of the peak potential.

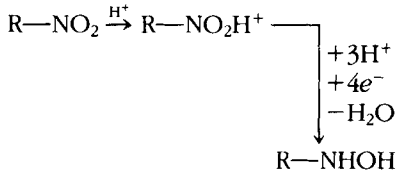
In dc polarography, a maximum was noticed in all of the supporting electrolytes employed. This maximum was suppressed in the presence of gelatin (0.05%).

The linear plots of i_d versus $h^{1/2}$ and i_p versus $V^{1/2}$, which pass through the origin, indicate that the electrode process is mainly diffusion controlled and free from adsorption complications. Conventional log-plot analysis, the variation of $E_{1/2}$ and E_p values toward more negative potentials on increasing the concentration of the depolarizer and the absence of an anodic peak for c_1 in the reverse scan in cyclic voltammetry as well as the disobedience of Tomes' criterion [7] indicate that the electrode process is irreversible.

Originally, colorless, the experimental solution became thick and yellow at higher pH values; this can be explained on the basis of nitro group tautomerism [8].

Millicoulometry was employed in Clarks and Lubs buffer (pH 2.00) and Bates and Bower buffer (pH 12.50) to determine the number of electrons involved in the electrode process. A value of four was obtained. The product of controlled potential electrolysis was identified as hydroxylamine. The number of protons involved in the rate-determining step was evaluated based on $E_{1/2}$ versus pH and E_p versus pH plots.

On the basis of the results of our own investigations as well as on data from the literature, the following schemes are given for the electrochemical reduction of nimorazole in different pH regions. In 2.00 < pH < 8.00,



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In 10.00 < pH < 12.50,

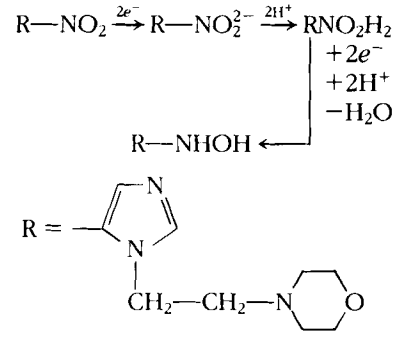

FIGURE 2. Typical differential pulse polarogram of nimorazole in Bates and Bower buffer, pH 12.50. Concentration, 1.0 × 10^{-5} M; solvent, 5% methanol; pulse amplitude, 50 mV.

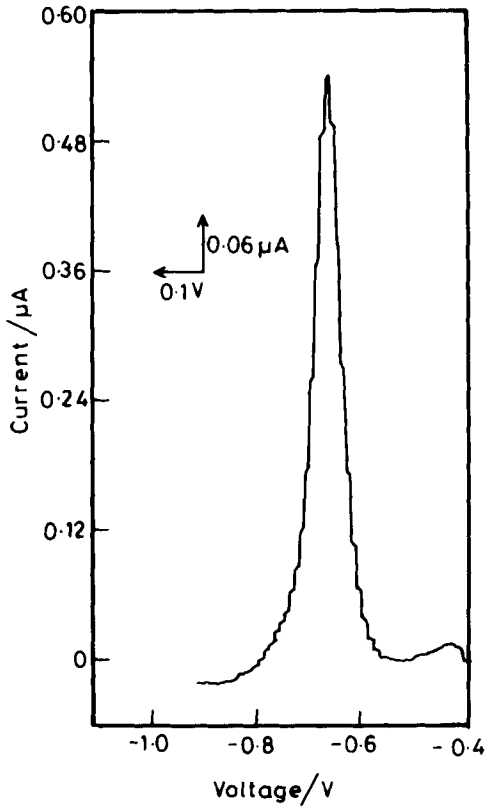

TABLE 1 Typical Electrode Kinetic Data for Nimorazole[a]

	dc Polarography (Drop Time, 3 seconds)			*Cyclic Voltammetry (Sweep Rate, 40mV s^{-1})*			*Chronoamperometry*			*Differential Pulse Polarography (Drop Time, 3 seconds)*		
Supporting Electrolyte	$-E_{1/2}$ (V)	$D \times 10^6$ ($cm^2\ s^{-1}$)	$k^o_{f,h}$ ($cm\ s^{-1}$)	$-E_p$ (V)	$D \times 10^6$ ($cm^2\ s^{-1}$)	$k^o_{f,h}$ ($cm\ s^{-1}$)	$D \times 10^6$ ($cm^2\ s^{-1}$)	$k_{f,h}$ ($cm\ s^{-1}$)	*Step Potential*	$-E_p$ (V)	$D \times 10^6$ ($cm^2\ s^{-1}$)	$k^o_{f,h}$ ($cm\ s^{-1}$)
Clarks and Lubs buffer (pH 2.00)	0.31	9.35	6.01×10^{-4}	0.16	8.40	1.43×10^{-6}	8.16	8.20×10^{-9}	0.14	0.28	2.53	1.59×10^{-11}
Acetate buffer (pH 4.00)	0.43	6.11	1.95×10^{-8}	0.43	11.37	1.99×10^{-8}	2.60	5.19×10^{-10}	0.40	0.44	1.17	3.51×10^{-13}
Citrate buffer (pH 6.00)	0.51	5.33	4.50×10^{-12}	0.55	11.83	7.06×10^{-11}	4.31	2.34×10^{-11}	0.52	0.50	1.10	2.42×10^{-12}
Phosphate buffer (pH 8.00)	0.58	5.03	1.09×10^{-12}	0.63	10.17	1.29×10^{-12}	0.98	3.81×10^{-17}	0.60	0.58	0.96	4.92×10^{-20}
Carbonate buffer (pH 10.00)	0.69	4.66	4.76×10^{-15}	0.74	8.40	1.75×10^{-15}	0.90	8.12×10^{-18}	0.71	0.57	1.74	4.08×10^{-16}
Bates and Bower buffer (pH 12.50)	0.63	4.74	4.54×10^{-15}	0.75	12.26	1.45×10^{-15}	0.68	2.11×10^{-18}	0.73	0.66	0.66	1.00×10^{-21}

[a] Concentration, 0.5 mM.

Kinetic data obtained with the different techniques are summarized in Table 1. As expected, the heterogeneous forward rate constant values decrease with increasing pH. The rate constant values are high in acidic media, which indicates a fast reaction because the protonated form is reduced in acidic medium. The heterogeneous forward rate constant values obtained in dc polarography are in good agreement with the cyclic voltammetric values. The diffusion coefficients calculated using different techniques are observed to be in good agreement (Table 1).

Analytical Utility

The analytical method described here is based on the results obtained with dc polarography and differential pulse polarography at a dropping mercury electrode. The peak responsible for the reduction of the nitro group is used in the analytical estimation of nimorazole. The optimum conditions for the analytical determination are found to be a differential waveform with a drop time of 2 seconds and a pulse amplitude of 50 mV. A typical response is shown in Figure 2. Coupled with the standard addition method, this allowed the determination of nimorazole in different pharmaceutical formulations. The lower detection limit is found to be 2.5×10^{-7} M, and the relative standard deviation was 2.1%. The electroactivity of the drug may be used for amperometric detection following liquid chromatography of complex samples.

ACKNOWLEDGMENTS

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