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Research Paper

ELECTROCHEMICAL BEHAVIOUR AND ANALYSIS OF FURAZOLIDONE IN PHARMACEUTICAL FORMULATIONS

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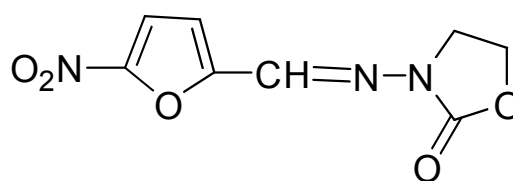
The electrochemical behavior of furazolidone is studied by employing Cyclic Voltammetry (CV) and Differential Pulse Polarography (DPP) in universal buffers of pH ranging from 2.0 to 12.0. The Kinetic parameters, such as transfer coefficients, diffusion coefficients, and heterogeneous forward rate constant values are evaluated by employing these techniques. Differential pulse polarography is employed for the estimation of furazolidone in selected pharmaceutical formulations.

Keywords: Furazolidone, Electrochemical behaviour, Analysis, Pharmaceutical formulations

INTRODUCTION

Furazolidone [3-(5-nitrofurfurylideneamino)-2-oxazolidone] (Figure 1) and other nitro furan derivatives have been used for more than 30 years in medicine for the treatment of gastrointestinal infections in animals and humans. The main pharmaceutical uses of nitro aromatic compounds (RNO₂) are as antibacterial and anticancer agents (D. Greenwood, 1995; Fotouhi L et al., 2006). They have been widely used in the treatment of caecal coccidiosis in chickens and necrotic enteritis in swine. They are generally added to animal feeds to prevent various poultry and swine diseases. In man these drugs are therapeutically effective as antibacterial and bactericidal agents (Morales A *et al.*, 1987).

Figure 1: Structure of Furazolidone



Furazolidone has been determined by spectrophotometry (Prasad CVN et al., 1999), conductimetry (Egerts V et al., 1963), gas-liquid chromatography (Ryan J J et al., 1975), High-performance Liquid Chromatography (Leitner A et al., 2001). A survey of the literature indicates that very little attention has been paid to the polarographic determination of these drugs

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(Fotouhi L et al., 2009; Fotouhi L et al., 2006). This work represents an attempt to understand in detail the voltammetric behavior of furazolidone by using advanced electrochemical techniques. It is also an effort to develop a simple, rapid differential pulse polarographic method for the estimation of furazolidone in selected pharmaceutical formulations.

MATERIALS AND METHODS

A PARC Model 364 polarographic analyzer equipped with BD 8 Kipp and Zonen X-t recorder was used for dc polarographic measurements. A three-electrode combination was employed, which consisted of a dropping mercury electrode (DME), a standard calomel electrode (SCE) and a platinum wire auxiliary electrode. Differential Pulse Polarographic (DPP) measurements were performed with a Metrohm E 506 Polarecord connected to an E 612 VA scanner. The electrode assembly consisted of a DME (with an area of 0.0223 cm^2) working electrode, a saturated Ag/AgCl(s), Cl⁻ reference electrode, and platinum wire auxiliary electrode. A digital Electronics 2000 X-Y/t recorder, which was connected to the Metrohm unit, was used for recording the cyclic voltammograms (the working electrode was a hanging mercury drop electrode having an area of 0.0433 cm^2). All the experiments were carried out at $25 \pm 1^\circ\text{C}$.

The Furazolidone sample was supplied by ESKAYEF Private Limited, Bangalore, and was used without further purification. All the chemicals used were of analytical reagent grade. An appropriate amount of furazolidone was dissolved in the required quantity of dimethylformamide (DMF) 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.

RESULTS AND DISCUSSION

Furazolidone was found to give rise to four waves i_A , i_B , i_C and i_D in acidic media (pH 2.0-4.0). At pH 6.0-8.0, waves i_B and i_C coalesced ($i_B + i_C$) and i_D disappeared. At pH 10.0 ($i_B + i_C$) was not observed, and only wave, i_A , was seen in the pH range 10.0-12.0. Wave i_A corresponded to the four-electron reduction of the nitro group to a hydroxylamine group; the subsequent reduction of the latter group to an amino group, in a two-electron step, was found to result in wave i_D . Wave i_B corresponded to a two-electron process result the reductive fission of the N-N bond in $>\text{C}=\text{N}-\text{N}$ linkage to an imine group ($>\text{C}=\text{NH}$), and wave i_C to the subsequent reduction of the imine group to an amino group, in a two-electron addition (Figure 2).

An anodic peak a_1 was noticed in the reverse scan of the cyclic voltammograms (Figure 3) taken at higher pH value (pH 10.0). In the second scan, another cathodic peak (c_2) at more positive potential than that of c_1 is noticed. The anodic peak a_1 may be attributed to the oxidation of hydroxylamine formed at c_1 to a nitroso derivative and the cathodic peak c_2 to the reduction of the nitroso derivative to the hydroxylamine group. This type of behavior also was observed by Morales et al., 1987 in the case of nitro-substituted furans.

In dc polarography, a maximum was noticed for the reduction of nitro group in all the supporting electrolytes employed. This maximum was suppressed in the presence of Triton X - 100 (0.02%).

The waves and peaks were found to be diffusion controlled and adsorption free (Egerts V et al., 1963) in the buffer systems taken, as

shown by the linear plots of i_d versus $h^{1/2}$ and i_m versus $t^{2/3}$ (where i_m is maximum current in DPP), which pass through the origin. Conventional log plot analysis and the variations of $E_{1/2}$, E_p and E_m (where E_m is the potential at maximum current in

DPP) values towards more negative potentials upon increasing the concentration of the depolarizer (Ryan *et al.*, 1975; Leitner A *et al.*, 2001) indicated the irreversible of the electrode process.

Figure 2: Typical Differential Pulse Polarogram of Furazolidone at pH 2.0 Concentration, 0.5 mM, Drop Time, 2 Seconds

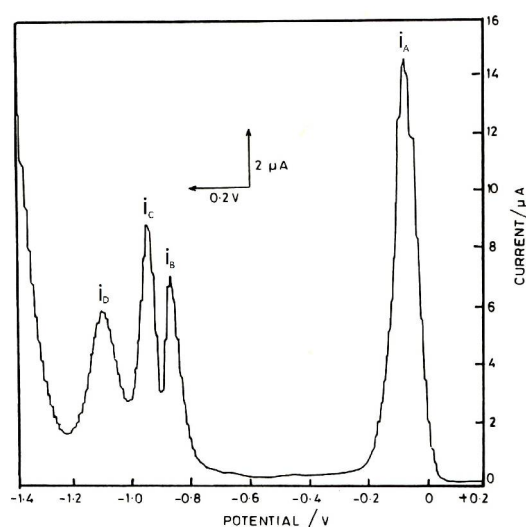
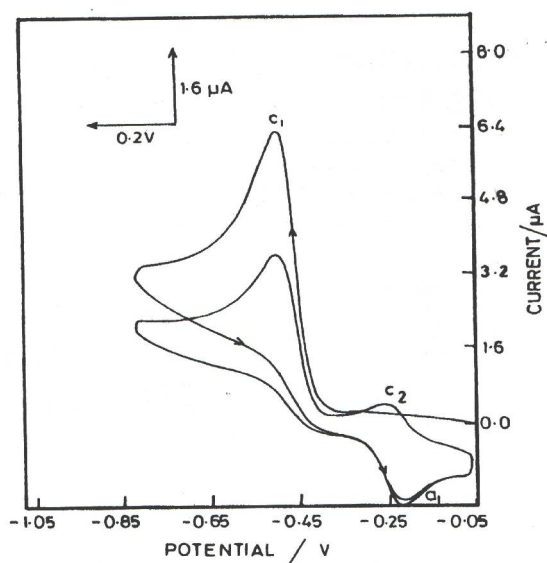


Figure 3: Typical Cyclic Voltammogram of Furazolidone at pH 12.0, Concentration, 0.5 mM, Scan Rate, 40 m V/s



The number of electrons involved in the reduction process was calculated from the results obtained with millicoulometry. At pH 2.0, n was found to be 4 for the first wave and 2 for the second, third, and fourth waves. At pH 12.0, only four-electrons addition was noticed; hence the reduction product of Furozolidone in basic media is likely to be hydroxylamine. Controlled potential electrolysis was carried out at pH 2.0 at -1.20 V vs SCE, and the product was identified as amine. The isolated amino product was confirmed by IR spectrometry

Kinetic data obtained with different techniques are summarized in Table 1. The diffusion coefficient values evaluated from all the

techniques are in good agreement. This is particularly evident because no adsorption complications were involved in the electrode process.

The rate constant values obtained for the reduction of the nitro group were found to be high when compared to those of the azomethine group because of the facile reduction of the former group, which is also evident from the less negative reduction potentials obtained. The rate constant values were observed to be high in acidic media, indicating that the rate of reaction is fast compared to that in basic media, since in acidic solutions proton involvement is high, which makes the reduction process easier.

Table 1: Typical Electrode Kinetic Data for a Furozolidone Concentration of 0.5 mM

pH of the Supporting Electrolyte	Wave	dc Polarography: Drop time, 3 Seconds			Cyclic Voltammetry: Sweep Rate, 40 mV/s			Differential Pulse Polarography Drop Time, 2 Seconds		
		$-E^{1/2}$ (v)	$D \times 10^5$ (cm ² /s)	k^0f, h (cm ² /s)	$-E_p$ (v)	$D \times 10^5$ (cm ² /s)	k^0f, h (cm ² /s)	$-E_p$ (v)	$D \times 10^5$ (cm ² /s)	k^0f, h (cm ² /s)
2.0	1 st	0.09	2.94	1.02×10^{-3}	0.10	2.97	1.32×10^{-4}	0.08	2.97	2.01×10^{-3}
	2 nd	0.89	1.34	4.27×10^{-8}	0.89	1.40	3.72×10^{-8}	0.88	1.35	3.72×10^{-7}
	3 rd	0.98	1.05	5.38×10^{-10}	1.01	1.23	2.55×10^{-10}	0.96	1.20	1.22×10^{-9}
	4 th	1.16	1.45	3.72×10^{-11}	a			1.12	0.90	1.96×10^{-11}
4.0	1 st	0.18	2.82	2.04×10^{-4}	0.19	2.83	3.72×10^{-5}	0.12	2.79	4.92×10^{-4}
	2 nd	0.91	1.23	3.27×10^{-8}	0.95	1.34	8.69×10^{-9}	0.91	1.30	4.58×10^{-8}
	3 rd	1.02	1.01	6.31×10^{-11}	1.20	1.10	5.43×10^{-11}	0.98	1.05	2.80×10^{-10}
	4 th	1.21	1.07	7.88×10^{-13}	a			1.21	0.91	1.28×10^{-13}
6.0	1 st	0.23	2.74	3.83×10^{-6}	0.26	2.79	4.87×10^{-6}	0.21	2.69	2.17×10^{-5}
	2 nd	1.20	1.98	8.17×10^{-14}	1.24	2.07	6.54×10^{-13}	1.20	1.90	7.89×10^{-14}
8.0	1 st	0.31	2.70	5.18×10^{-7}	0.32	2.68	1.33×10^{-7}	0.29	2.58	5.70×10^{-7}
	2 nd	1.32	1.96	4.21×10^{-16}	1.33	2.69	4.15×10^{-15}	1.31	1.87	6.45×10^{-15}
10.0	1 st	0.40	2.42	5.72×10^{-8}	0.42	2.49	3.91×10^{-8}	0.38	2.37	1.03×10^{-8}
12.0	1 st	0.49	2.37	6.32×10^{-10}	0.52	2.40	9.33×10^{-10}	0.46	2.23	3.34×10^{-9}

Note: a – Merging with hydrogen evolution.

Based on the results obtained, the electrochemical reduction mechanism of Furozolidone may be proposed as follows (Figure 4).

ANALYSIS

Standard addition and calibration methods are used for the differential pulse polarographic analysis of Furazolidone. Peak i_A , responsible for the reduction of the nitro group, is used in the analytical estimation of the Furazolidone. The optimum pH range for obtaining well-resolved peaks for the determination of Furazolidone was found to be $4.0 \leq \text{pH} \leq 6.0$. The peak current was found to vary linearly with the concentration of the drug over the range 1.25×10^{-5} to 2.78×10^{-7} M. The lower detection limit was found to be 0.35×10^{-7} M. Furazolidone was analyzed by the

standard addition method in different pharmaceutical formulations.

The optimum conditions for the determination of the title compound in pH 4.0 were found to be a drop time of 2 seconds, pulse amplitude of 60 mV, and applied potentials of -0.18 V vs Ag/AgCl(s), Cl⁻. The relative standard deviation and correlation coefficient was 1.32% and 0.993, respectively, for 10 replications. Table 2 gives the assay results at pH 4.0 of different Furazolidone containing tablets.

CONCLUSION

The work describes the voltammetric behaviour of Furazolidone based on the reduction of azomethine group at dropping mercury electrode and hanging mercury drop electrode. The

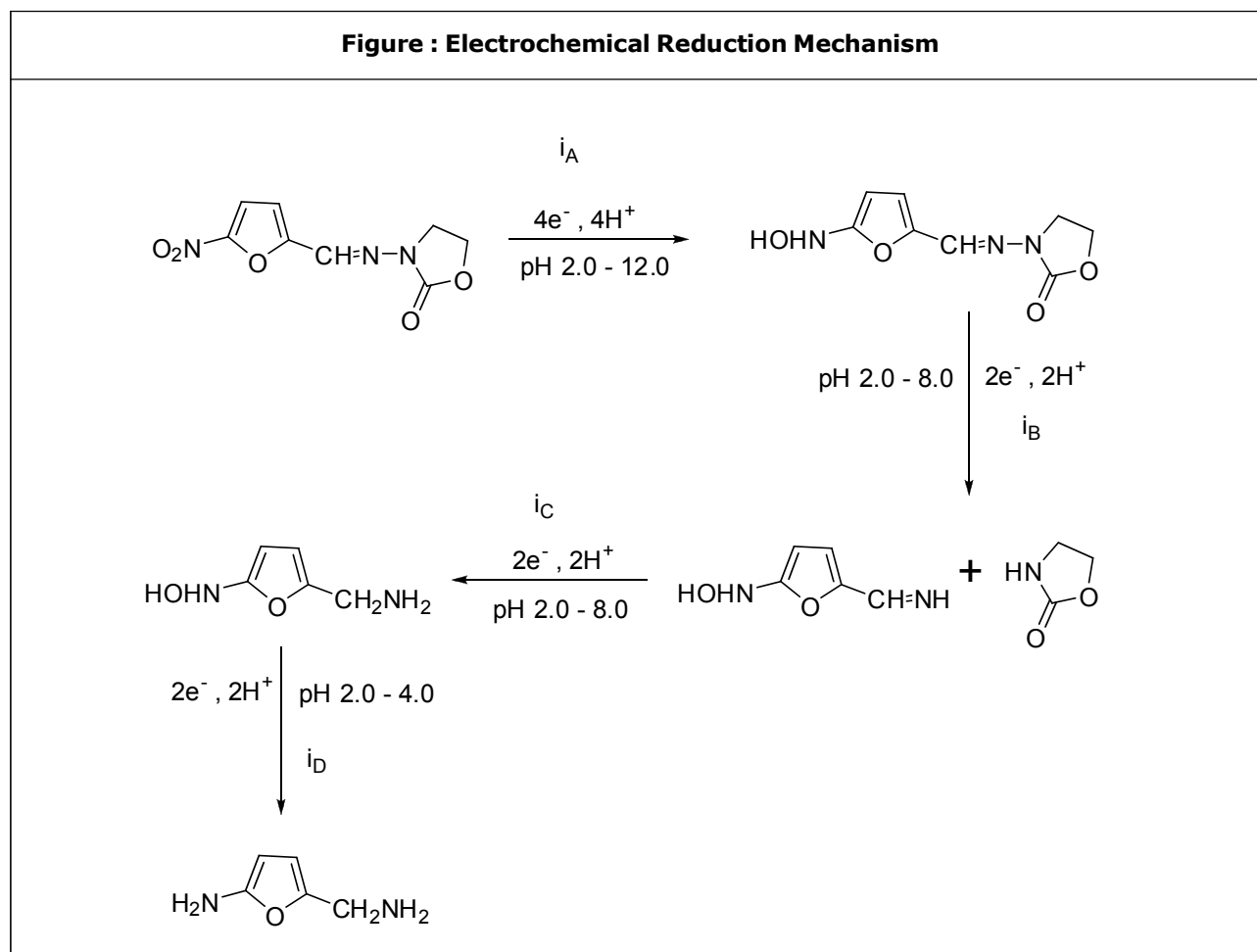


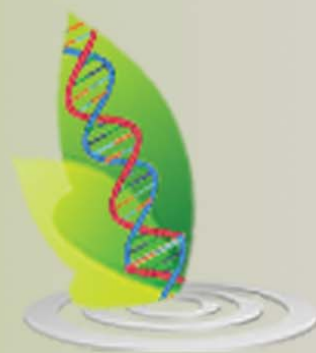
Table 2: Assay of Furazolidone Dosage Form by Differential Pulse Polarography at pH 4.0: Pulse Amplitude, 60 mV, Drop Time 2 Seconds

Sample (Tablets)	Labeled Amount (mg)	Amount Found (mg)	Recovery (%)	Standard Deviation
Furazolid	20	19.63	99.04	0.014
Nominol	20	19.85	99.20	0.018
Nitrofin	20	99.54	98.93	0.015
Furazolid	100	99.65	99.65	0.019
Nominol	100	98.79	98.79	0.019
Nitrofin	100	98.79	98.79	0.022

recovery result shows that differential pulse polarography is a simple, reliable and inexpensive method for the determination of Furazolidone in formulations. The main advantage of the proposed method over the other one is that the excipients do not interfere and a separation procedure is not necessary.

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