

DETERMINATION OF NITROFURAZONE IN PHARMACEUTICAL DOSAGE FORMS BY REDUCTION AT ROTATING PLATINUM ELECTRODE

Zühre ŞENTÜRK*

SUMMARY

The electroreduction of nitrofurazone has been studied by voltammetry at platinum rotating wire electrode in different buffer systems. The experimental results show that in Britton-Robinson buffer pH 12, the drug produces two well-defined reduction waves. According to the second wave with half-wave potential of -0,71 V, the limiting current is proportional to the concentration, in the range of 19, 81 to 198, 14 $\mu\text{g ml}^{-1}$. The proposed method permits this drug to be determined in pharmaceutical formulations.

Key Words: Nitrofurazone determination, voltammetry, rotating platinum electrode, pharmaceutical formulations.

DÖNER PLATİN ELEKTROT KULLANARAK REDÜKSİYON YOLUYLA NİTROFURAZON'UN FARMASÖTİK PREPARATLARDA MİKTAR TAYİNİ

ÖZET

Döner platin tel elektrot kullanılarak farklı tampon çözeltilerinde voltametrik yöntemle nitrofurazonun elektroedüksiyonu incelenmiştir. Deneysel sonuçlar, ilacın pH 12 Britton-Robinson tamponu içerisinde iki redüksiyon dalgası verdiğini göstermiştir. Yarı dalga potansiyeli -0,71 V olan ikinci redüksiyon basamağı esas alındığında sınır akımının 19, 81 ile 198,14 $\mu\text{g ml}^{-1}$ aralığında derişimle orantılı olduğu görülmüş ve bu yöntemle ilacın farmasötik ilaç şekillerinde miktar tayininin yapılabileceği saptanmıştır.

* Department of Analytical Chemistry, Faculty of Pharmacy, Ankara University, 06100, Tandoğan, Ankara

INTRODUCTION

Nitrofurazone (5-nitro-2-furaldehyde semicarbazone) is a synthetic nitro-furan derivative with a nitro group at the 5-position on furan ring. It has been used as an antibacterial agent.

This compound has been determined by spectrophotometry (1), colorimetry (2,3), and thin-layer (4), gas (5) and high-pressure liquid chromatography (6-8). Further, nitrofurazone and its formulations are listed in the US Pharmacopoeia (9) and the British Pharmacopoeia (10) where the recommended assay is by spectrophotometry at 375 nm.

The electrochemical behaviour of nitrofurazone is based on the ease of reduction of the nitro group at a dropping mercury or solid electrode. A review of the literature indicates that very little attempt has been made to study the voltammetric behaviour of nitrofurazone using solid electrodes (11,12). Studies of the electrochemistry of this drug have almost been limited to its polarographic determinations at a dropping mercury electrode (13-16).

In our previous paper (17) the results of voltammetric investigations of nitrofurazone in dimethylformamide using stationary platinum and ruthenium electrodes were described.

The rotating platinum electrode may be used as the working electrode in a simple direct current procedure (18-21). The aim of this work was to investigate the reduction of nitrofurazone at the rotating platinum electrode and develop a simple and rapid method for the determination of this drug in pharmaceutical formulations.

MATERIALS and METHODS

Apparatus

A PRG-3 polarographic analyser system (Tacussel) together with an EPL-2 recorder (Tacussel) were used for all voltammetric measurements performed at a scan rate of 5 mVs^{-1} .

The three electrode cell with the rotating platinum electrode with a surface area of $0,07 \text{ sq.cm.}$ was used. The electrode was rotated with a synchronous motor at a rate of 1800 r.p.m. The auxiliary electrode was platinum wire. Potentials were referred to the saturated calomel electrode (SCE).

Pre-treatment of Electrode

The surface of a solid electrode changes with time due to contamination with species from solution and oxide formulation. To reactivate the electrode, prior to each experiment, a pretreatment operation is applied to the electrode surface for a satisfactory reproducibility of the curves.

In the present work, electrode pretreatment was performed by holding electrode potential at -0.10 V vs SCE during the deaeration with nitrogen for 5 min in solutions being studied.

Chemicals

Stock solutions of nitrofurazone were prepared by dissolving the appropriate amount in dimethylformamide and stored in the dark.

All of the chemicals used were of either AnalaR grade from BDH or general-reagent grade from Merck.

Four different buffer systems, namely acetate (pH 4), Mc Ilvaine H5,94), borate (pH 8.5) and Britton-Robinson (pH 12) were prepared in distilled water. The other solutions containing various concentrations of nitrofurazone were obtained by dilution of the stock solution with the selected buffer.

The stream of nitrogen was allowed to flow gently over the surface on the solution during the electrode reaction.

Assay Procedure for Pharmaceutical Formulations

Two nitrofurazone formulations, soluble ointment (0.2 %) and nasal drop (0.2 %) were used for analysis.

The required amount of ointment corresponding to a stock solution of concentration ca. 10^{-3} M was accurately weighed and transferred into a 100-ml volumetric flask containing 80 ml of dimethylformamide. The contents of the flask were stirred magnetically for 15 min to effect complete dissolution and then diluted to volume with dimethylformamide and filtered through a Whatman No. 42 filter paper. Appropriate solutions were prepared by taking suitable aliquots of the clear filtrate and diluting them with the selected buffer.

Portions of 5.0 ml of the nasal drop were transferred into a 100-ml volumetric flask and diluted to the volume with the selected buffer.

Voltammograms were recorded as in the pure nitrofurazone.

Recovery Experiments

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

RESULTS AND DISCUSSION

The pH of supporting electrolyte strongly influences the voltammetric response of nitrofurazone at the rotating platinum electrode. The effect of pH on the reduction curves was investigated by recording voltammograms

of $6 \cdot 10^{-4}$ nitrofurazone.

Figure 1 shows some typical voltammetric curves of nitrofurazone obtained at four pH values. At pH 4 with acetate buffer, the nitrofurazone wave and background current were not separated and thus were not useful for analysis. Current-potential curves of this drug exhibited only a single wave in the pH range 6-8,5. At approximately pH 12 we observed two reproducible and well- defined waves for the reduction of nitrofurazone with half-wave potentials of -0,53 and -0,71 Vs SCE. The half-wave potentials of the first wave were found to be almost pH independent.

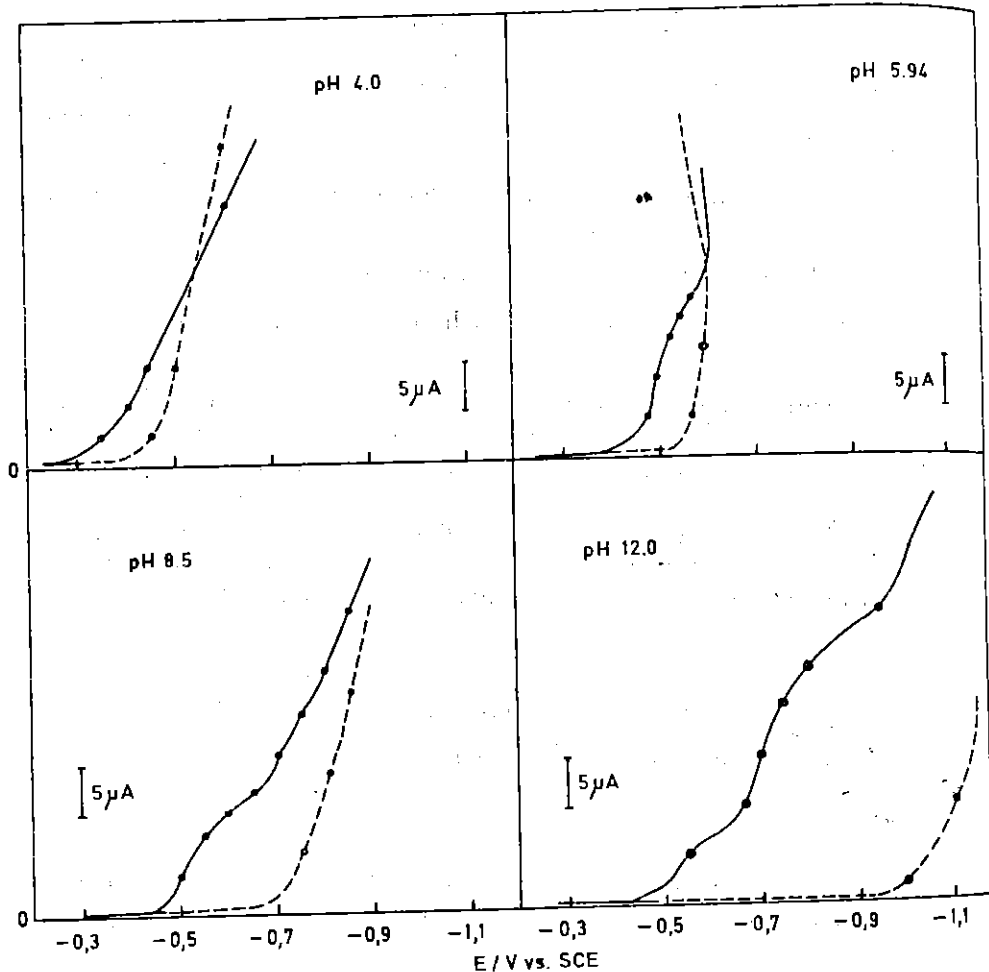


Figure 1 : Reduction of nitrofurazone ($6 \cdot 10^{-4}$ M) in various buffers.

Scan rate, 5 mVs^{-1} .

Solutions : (————), nitrofurazone;

(-----), buffer only.

From a quantitative point of view, the second cathodic wave obtained at pH 12 was well suited for the determination of nitrofurazone. The current-potential scans run in 0,2 M sodium hydroxide also gave a limiting current. However, when the lack of stability of nitrofurazone in Britton-Robinson buffer was compared with in sodium hydroxide solution it was found that the limiting current decreased 5.7% in 60 min and 19 % in 20 min, respectively. Thus, regarding to the conclusions drawn from these data the Britton-Robinson buffer pH 12 were used as supporting electrolyte in the analysis if test solutions were assayed within a few minutes of preparation.

Reduction curves showed that the limiting current varied a linear manner with the concentration between 10^{-4} and 10^{-3} M which corresponds to 19,81 and 198,14 μgml^{-1} . The results of a linear regression analysis are given in Table 1. When the results were compared with USP method where the recommended assay is by spectrophotometry (9) it was seen that the values obtained for the pure drug by both methods were in close agreement. Table 2 gives the assay results for the two dosage forms investigated. The recoveries which were 98,8 % for nasal drops and 98,0% for soluble ointments, indicate the high accuracy and reproducibility of the proposed voltammetric method.

Concentration /M	Limiting current/ μA^*
1×10^{-4}	6.6
2×10^{-4}	11.6
4×10^{-4}	19.6
6×10^{-4}	28.0
8×10^{-4}	36.0
1×10^{-3}	44.2
Correlation coefficient.....	0.9997
Slope.....	4.14×10^4
y-Intercept.....	2.94

Table 1 : Results of the linear regression analysis of concentration-limiting current relationships at -0,9 V. (*The limiting currents were obtained by subtracting the background current at -0,9 V).

Formulation*	Labelled claim/ mg	Amount** found/mg	Recovery [†] , %	Standard deviation
Nasal Drop	30	28,7	98,8	0,35
Ointment	112	102,9	98,0	2,56

* Ointment (56 g) and nasal drop (15 ml) formulations containing 0.2 % of nitrofurazone

** Each value is the mean of five determinations.

[†] Experiments performed separately by adding known amounts of nitrofurazone

Table 2: Assay of nitrofurazone formulations by voltammetry at rotating platinum electrode.

CONCLUSIONS

The results obtained have shown that the method proposed in this study which is applied to nasal drops and soluble ointments, is simple, sensitive and rapid.

ACKNOWLEDGEMENT

The author is indebted to Eczacıbaşı İlaç Sanayi ve Ticaret A.Ş., İstanbul, who kindly provided pure nitrofurazone.

REFERENCES:

1. Fabregas, J.L., Casassas, E., (1979) "Spectrophotometric determination of nitrofurazone with phloroglucinol". *Anal. Chim. Acta*, 107, 401-404.
2. Baidarovtseva, M. A. Guseva, L.N. (1977) "Colorimetric determination of furacilin in drugs for children", *Farmatsii*, 14, 164-169.
3. Rao, G.R., Raghuvver, S., Murty, S.S.N., Bajrangrao, B., (1979) "Colorimetric determination of nitrofurazone". *Indian Drugs*, 17 (2), 50-51.
4. Cieri, U.R., (1978) "Quantitative thin layer and chromatographic determination of furazolidone and nitrofurazone in animal feeds", *J. Assoc. Off. Anal. Chem.*, 61 (1), 92-95.
5. Ritchie, A.R., Clear, M.H., Solly, S.R.B., (1977) "Improved gas-liquid chromatographic method for determining nitrofurazone drug residues in animal tissues". *N.Z.J. Sci.* 20 (2), 225-229.
6. Cieri, U.R., (1979) "High-pressure liquid chromatographic detection and estimation of furazolidone and nitrofurazone in animal feeds". *J. Assoc. Off. Anal. Chem.*, 62 (1), 168-170.
7. Vilim, A.B., MacIntosh, A.I., (1979) "High-pressure liquid chromatographic determination of nitrofurazone in milk". *J. Assoc. Off. Anal. Chem.*, 62(1), 19-22.
8. Thorpe, V.A., (1980) "Sample preparation of carbadox, furazolidone, nitrofurazone, and ethopabate in medicated feeds for high-pressure liquid chromatography". *J. Assoc. Off. Anal. Chem.* 63(5), 981-984
9. The United States Pharmacopoeia, (1990), Mack Printing Company, Easton, Pa, 950-951.
10. British Pharmacopoeia, (1988), Her Majesty's Stationery Office, London, 392-393.
11. Kemula, W. and Zawadowska, J. (1975) "Investigation in the reduction mechanism of nitrofurazone by cyclic voltammetry. II" *Bulletin de l'Academie Polonaise*

des Sciences, xxiii (3), 275-282.

12. Morales, A., Richter, P., Toral, M.I., (1987) " Voltammetric behaviour of nitrofurazone, furazolidone and other nitro derivatives of biological importance". *Analyst*, 112,965-970
13. Stradins, J.P., Hiller, S.A., Gavars, R.A., Reihmanis, G.O., Baumane, L.H., (1971) " Electrochemical properties and biological activity of nitrofurans ". *Experientia* , supply. 18, 607-617.
14. Queralto, A. and Ortega, M., (1972) "Estudio polarografica de derivados del 2-nitrofurano en presencia de polivinilpirrolidona y de alcohol polivinilico". *Galenica Acta*, 25(3) 3-20.
15. Mishra, A.K., Gode, K. D., (1985)" Electrochemical reduction of nitrofurazone and its determination in pharmaceutical dosage forms by d.c. polarography ". *Analyst*, 110, 1373-1376.
16. Moralias, A., Richter, P., Toral, M.I., (1987) " Polarographic determination of nitrofurazone and furazolidone in pharmaceutical formulations and urine ". *Analyst*, 112 , 971-973.
17. Şentürk, Z. and Biryol, I., "Investigation of the reduction mechanism of nitrofurazone by voltammetry ". *Commun. Fac. Sci. Univ. Ankara* (in press).
18. Kolthoff, I. M. and Tanaka, N., (1954) " Rotated and stationary platinum wire electrodes ". *Anal. Chem.*, 26(4), 632-636.
19. Brun, A. and Rosset, R., (1974) "Etude electrochimique de l'oxydation de la dihydroxy-3,4 phenylalanine". *Electroanal. Chem. and Interfacial Electrochem.*, 49, 286-300.
20. Bishop, E. and Hussein, W., (1984) "Electroanalytical studies of phenothiazine neuroleptics at gold platinum electrodes". *Analyst*, 109, 229-234.
21. Bishop, E. and Hussein, w., (1984) "Anodic voltammetry of dopamine, noradrenaline and related compounds at rotating disc electrodes of platinum and gold". *Ibid*, 627-632.