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Determination of nitrofurazone in some pharmaceutical preparations

M. Shahjahan *, A. Shalaby

Drug Control Authority, P.O. Box 24129, Safat, 13102, Kuwait

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Abstract

A simple, selective and accurate paper chromatographic method for the determination of nitrofurazone in some dosage forms has been described. The method was based on impregnation of the chromatographic paper with pH 4.0 buffer containing 10% (w/v) urea. The percentage recovery of nitrofurazone obtained by the developed method indicated the accuracy of the prescribed method. The analytical results obtained compared favourably with those given for the official methods. © 1998 Elsevier Science B.V. All rights reserved.

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Nitrofurazone, an antibacterial drug, was found to be photolabile; its photolability has been described in a number of recent papers (Shahjahan and Enever, 1996a,b). Official methods of assay for nitrofurazone involve the use of spectrophotometric methods (British Pharmacopoeia, 1993, US Pharmacopeia, 1995), although assay of dosage forms such as nitrofurazone ointment and topical solution necessitate pretreatment using column chromatography to remove interfering materials (US Pharmacopeia, 1995). Several other methods that are available for the analysis of nitrofurazone range from colorimetry (Rao et al., 1979), spectrophotometry (Agrawal and Patel, 1986, Tamer and Omar, 1989), and fluorometry (Taniguchi et al., 1974), through gas chromatography (Ryan et al., 1975) to high-performance liquid chromatography (HPLC) (Sugden et al., 1983). However, none of these methods has reported the simultaneous determination of intact drug in the presence of its decomposition products.

The separation of intact drug from its photodecomposition products by paper chromatography (Shahjahan, 1979) and identification of photolysis products on a reversed-phase HPLC (Quilliam et al., 1987) has been reported. The photoproducts were found to be the *syn* isomer of nitrofurazone

* Corresponding author. Tel.: +965 4801304; fax: +965 4801304.

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and 5-nitro-2-furaldehyde azine which retained the strong absorption band at 370 nm. In addition, a number of polar products with short retention times were observed. Since the nature of the products is not completely known, it seemed dangerous to rely on a direct spectrophotmetric assay of the drug in the presence of decomposition products as these may also absorb light. Therefore, in the present work, it was decided to separate the intact drug from its decomposition products and then carry out a relatively non-specific assay for the drug.

Although an ascending paper chromatographic method (Shahjahan, 1979) separated nitrofurazone from its decomposition products in simple aqueous solution, this procedure was not successful with formulations containing surfactant or polyethylene glycols. Hays and Grady (1971) found that urea precipitated cetyl alcohol and polyethylene glycol from nitrofurazone cream as urea inclusion compounds. Urea solution was also successfully employed as an immobile phase for paper chromatographic determination of oxytetracycline (Sina et al., 1971). Based on these findings, a paper chromatographic method for the determination of nitrofurazone in the presence of its degradation products using impregnation of the chromatographic paper with pH 4.0 buffer containing 10% (w/v) urea was established (Shahjahan and Enever, 1992a) and this method was successfully applied in this investigation to determine nitrofurazone content in its dosage forms.

Nitrofurazone (Human Grade) Batch No. 6B 5017 (m.p. 220–224°C with decomp.) was obtained from S.K.F. Laboratories (UK). Commercial samples were kindly provided by the manufacturer. Polyethylene glycol 1000 was obtained from Koch-Light Laboratories (UK). The non-ionic surfactant used was partially purified samples of Texofor A30 (ABM Chemicals, UK). All solvents and laboratory reagents were of analytical grade and used without further purification. Double-distilled water was obtained from an all-glass distillation unit (QVF, UK).

A measured volume or weight corresponding to 2 mg of nitrofurazone for otic drop, solution and gel preparations were taken and diluted to 10 ml with distilled water. Similarly, samples corresponding to 3 mg of nitrofurazone for ophthalmic ointment or 3.33 mg for suspension were diluted to 20 ml.

Diluted sample (0.2 ml) was spotted along a 15 cm horizontal line on Whatman No. 4 chromatographic paper, previously impregnated with 10% (w/v) urea in McIlvaine's pH 4.0 buffer. These chromatograms were then partially dried in air, and while still damp were subjected to ascending development in a chromatographic jar containing 100 ml of ethyl acetate–n-butanol–benzene (3:2:1) saturated with urea. The chromatographic jar was covered with aluminium foil to protect the chromatograms from light. When the solvent front reached about 20 cm above the starting line, the chromatograms were removed and dried in air (about 1 h in a fume-cabinet covered with aluminium foil). Similarly, a reference chromatogram spotted with 0.2 ml of standard nitrofurazone solution containing an identical concentration and a blank paper without nitrofurazone were also run. The yellow horizontal area of nitrofurazone (R_f 0.79) was cut from the chromatogram and divided into squares of approximately 5 mm dimension. The equivalent area was removed from a blank paper. The subdivided areas from each chromatograms were extracted with 10 ml of water–ethanol (1:2) mixture by shaking for 1 min in a glass vial (30 ml capacity) and then standing for another minute. The eluate was then centrifuged at 4000 rpm for 10 min. The concentration of nitrofurazone present in the eluate was determined spectrophotometrically by recording the absorbance at 372 nm and referring to the standard run. The whole chromatographic assay was carried out under subdued light. Each potency reported represents the average of three determinations.

Five different concentrations of standard solution were made from a solution containing 0.25 mg/ml of nitrofurazone in surfactant (0.1 M), polyethylene glycol (0.25 M) and aqueous solution. Aliquots of 2, 4, 6 and 8 ml were taken and diluted to 10 ml with appropriate solvent. Chromatograms of 0.2 ml samples were made and the mean UV detector response of the eluate at 372 nm wavelength was determined for a dilution series of three formulations in the range of 25–

Table 1
Comparative analytical results of the proposed and official method for nitrofurazone assay in some pharmaceutical preparations

Name of dosage form	Concentration of active agent	Equivalent of active agent taken (mg)	Proposed method		USP method	
			mg found	Recovery (%)	mg found	Recovery (%)
Furacin, ophthalmic ointment (Eaton)	1%	3.00	2.897 ± 0.0208	96.57 ± 0.69	2.917 ± 0.0351 ($t = 0.848$)	97.23 ± 1.17
Furacin, otic solution (Eaton)	0.2%	2.00	1.987 ± 0.0251	99.35 ± 1.26	1.977 ± 0.0351 ($t = 0.401$)	98.85 ± 1.76
Furacin, solution (Eaton)	0.2%	2.00	2.027 ± 0.0416	101.35 ± 2.08	1.997 ± 0.0321 ($t = 0.990$)	99.85 ± 1.61
Furoxone, suspension (Eaton)	3.33 mg per 5 ml	3.33	3.387 ± 0.0306	101.71 ± 0.92	3.333 ± 0.0306 ($t = 2.157$)	100.09 ± 0.92
Nifucin, gel (Germed)	0.2%	2.00	1.973 ± 0.0115	98.65 ± 0.58	1.963 ± 0.0153 ($t = 0.909$)	98.15 ± 0.77

Tabulated value of $t_{0.5}(2) = 4.303$.

125% of the target drug concentration. A graphical representation of these results shows that the relationship between the concentration given above and their detector responses is linear for all three formulations; all points lie in a straight line, and the correlation coefficients, r, are greater than 0.999 for all the formulations. Since it was observed that, although the calibration curves did not vary with the formulations used, minor differences occurred due to the composition of the solvent system and the quality of the chromatographic paper due to variation between batches, it was decided to run a reference chromatogram spotted with a known concentration of nitrofurazone with every quantitative evaluation. The working linear range obtained from the response factor plot lie within 98–102% of the response factor for the standard preparation, thus permitting the use of single point standardization.

Results of analysis for nitrofurazone in some pharmaceutical preparations by the proposed method and official USP method are given in Table 1. The percentage recovery of nitrofurazone from the chromatogram was found to range from 95.9% to 102.6%, which suggested that the accuracy of the quantitative determination of the drug by the prescribed method was adequate for its application in pharmaceutical preparations. As evident from the statistical analysis of the results using Student's t-test, there is no significant difference between the two methods as regards the accuracy and precision. The results showed agreement with those given with the official method, being within $\pm 2\%$.

The effect of urea can be explained on the basis that it increased the solubility of nitrofurazone whilst precipitating the surfactant and polyethylene glycol near the starting line of the chromatogram. Urea did not form a complex with the drug nor did it interfere with the subsequent UV assay of the eluted spot (Shahjahan and Enever, 1992b).

The commonly used excipients (polyethylene glycol, surfactant, etc.) were found to offer no positive interference by the proposed method, thus making the method more reliable and suitable for routine analysis of nitrofurazone in these dosage forms. It is precise and stability-indicating, offering distinct advantages over the compendial spectrophotometric assay.

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