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Spectrophotometric Determination of Cefotaxime Sodium

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Three simple and sensitive visible spectrophotometric methods (A, B and C) have developed for the quantitative estimation of cefotaxime sodium in bulk drug and pharmaceutical preparations. Method A is based on the diazotization of cefotaxime sodium with nitrous acid and coupling with 2-naphthol to form red coloured chromogen with absorption maximum at 534 nm and Beer's law is obeyed in the concentration range of 20–100 μg/mL. Methods B and C are based on diazotization of cefotaxime sodium with nitrous acid and its coupling with phlorogucinol and resorcinol to form orange yellow and red coloured chromogen with absorption maxima at 464 and 513.5 nm, respectively. Beer's law is obeyed in the concentration range of 20–100 μg/mL and 10–50 μg/mL, respectively. The results obtained with the proposed methods are in good agreement with labelled amounts when marketed pharmaceutical preparations are analyzed. The results of analysis for the three methods have been validated statistically and by recovery studies. The results are compared with those obtained with UV spectrophotometric method at 234 nm.

Key Words: **Spectrophotometry, Cefotaxime sodium.**

INTRODUCTION

Cefotaximesodium[1–6] is chemically, sodium(7R)-7-[(Z)-2-(2-aminothiozol-4-yl)-2-(methoxyimino)acetamido]cephalosporinate. It is broad spectrum cephalosporin for parentral administration. It is used in respiratory, urinary, bone and soft tissue infections. It also recommended in meningitis and gonorrhea. It is official in U.S.P., China and Japan Pharmacopoeia. Some spectrophotometric methods are reported for its quantitative estimation. The present work deals with the development of three simple and sensitive visible spectrophotometric methods for the quantitative estimation of cefotaxime sodium in bulk drug and pharmaceutical preparations (injectables).

Method A is based on the diazotization of cefotaxime sodium with nitrous acid ($NaNO_2$/HCl) and coupling with 2-naphthol to form red coloured chromogen with absorption maximum at 534 nm and obeyed Beer's law in the concentration range of 20–100 μg/mL. Methods B and C are based on the diazotization of cefotaxime sodium with nitrous acid and its coupling with phloroglucinol and resorcinol to

form orange yellow and red coloured chromogens with absorption maxima at 464 and 513.5 nm, respectively. Beer's law is obeyed in the concentration ranges of 20–100 and 10–50 μg/mL, respectively.

EXPERIMENTAL

All chemicals used are of A.R. grade from S.D. Fine-Chemicals, Mumbai. A Shimadzu UV/vis double beam spectrophotometer (Model 1601) with 1 cm matched quartz cells was used for all spectral measurements.

Working standard of drug solution

About 100 mg of cefotaxime sodium was weighed accurately and dissolved in 30 mL of distilled water in a 100 mL volumetric flask and diluted up to the mark with distilled water (1 mg/mL). 10 mL of this solution was diluted up to 100 mL in volumetric flask with water to get final concentration 100 μg/mL.

Sample preparation

One brand of commercial injectable was analyzed by the proposed methods. Contents of five vials each containing 1 g of cefotaxime sodium were mixed thoroughly and volume equivalent to 100 mg of drug was pipetted out in to a 30 mL water in to 100 mL volumetric flask and the volume was made up to the mark with water (1 mg/mL). 10 mL of this solution was diluted to 100 mL in a volumetric flask to get final concentration 100 μg/mL with water.

Assay

Method A: Aliquots of cefotaxime sodium ranging from 0.2–1.0 mL (1 mL = 1 mg) were transferred into a series of 10 mL volumetric flasks. To each flask, 1 mL of $NaNO_2$ (0.1%) (w/v) and 1 mL of HCl (0.5 M) were added. After 5 min, 1 mL of 2-naphthol (0.5%) (w/v) was added. After 2 min, 1 mL of NaOH (2%) (w/v) was added. The volume was made upto the mark with distilled water. The absorbance of the violet coloured chromogen was measured at 534 nm against reagent blank. The coloured chromogen was stable for more than 1 h. The amount of cefotaxime sodium present in the sample was computed from calibration curve.

Method B: Aliquots of cefotaxime sodium ranging from 0.2–1.0 mL (1 mL = 1 mg) were transferred into a series of 10 mL volumetric flasks. To each flask 1 mL of $NaNO_2$ (0.1%) (w/v) and 1 mL of HCl (0.5 M) were added. After 5 min, 1 mL of phloroglucinol (1%) (w/v) was added. The volume was made up to the mark with water. The absorbance of orange yellow coloured chromogen was measured at 464 nm against reagent blank. The colour was stable for more than 2 h. The amount of cefotaxime sodium present in the sample was computed from calibration curve.

Method C: Aliqouts of cefotaxime sodium ranging from 0.1–0.5 mL (1 mL = 1 mg) were transferred into a series of 10 mL volumetric flasks. To each 1 mL of $NaNO_2$ (0.1%) (w/v) and 1 mL of HCl (0.5 M) were added. After 5 min, 1 mL of resorcinol (0.5%) (w/v) was added and after 2 min, 1 mL of NaOH (2%) (w/v) was added. The volumes were made up to the mark with distilled water. The absorbance of the red coloured chromogen was measured at 513.5 nm against

reagent blank. The colour was stable for more than 1 h. The amount of cefotaxime sodium present in the sample was computed form calibration curve.

The results of the above methods are compared with results obtained with UV method where cefotaxime sodium exihibits absorption maximum at 234 nm in distilled water and Beer's law is obeyed in the concentration range of 10–50 μg/mL. In UV method, solution of cefotaxime sodium either pure or formulation (100 μg/mL) was prepared as mentioned above. Aliquots of cefotaxime sodium ranging from 1–5 mL (1 mL = 100 μg) were transferred into a series of 10 mL volumetric flasks. The volumes were made up to the mark with water. The absorbance of the solutions was measured at 234 nm against solvent blank. The amount of cefotaxime sodium present in the sample was computed from calibration curve.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in Table-1. The regression analysis using method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentrations and the results are summarised in Table-1. The per cent relative standard deviation and per cent range of error (0.05 and 0.01 level of confidence limits) calculated from the eight measurements, 3/4 of the upper Beer's law limits of cefotaxime sodium are given in Table-1. The results showed that these methods have reasonable precision. The results obtained with the proposed methods for pharmaceutical preparations (Table-2) confirm the suitability of the methods for pharmaceutical preparations (injectables).

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

	Method A	Method B	Method C
λ_{max} (nm)	534	464	513.5
Beer's law limits (μg/mL)(C)	20–100	20–100	10–50
Molar absorptivity (L mol^{-1} cm^{-1})	6.123×10^3	2.532×10^3	7.493×10^3
Sandell's sensitivity (μg/mL–0.001 absorbance unit)	0.037	0.046	0.029
Regression equation (Y*)			
Slope (b)	0.0082	0.0083	0.0111
Intercept (a)	0.2749	0.0534	0.1424
Correlation coefficient (r)	0.9995	0.9999	0.9996
%RSD	0.6300	1.6430	1.0246
Range of errors**			
Confidence limits with 0.05 level	0.00406	0.00604	0.00403
Confidence limits with 0.01 level	0.00599	0.00894	0.00597

*Y = bC + a, where C is the concentration of cefotaxime sodium in μg/mL and Y is the absorbance at the respective λ_{max}.
**For eight measurements.

TABLE-2

Sample* (Injectable)	Labelled Amount (mg)	Amount obtained* (g)				Percentage Recovery**		
		Proposed methods			UV method			
		A	B	C		A	B	C
I_1	1000	1.04	0.993	1.07	0.998	99.82 ± 0.01	98.76 ± 0.04	100.32 ± 0.07
I_2	500	499	498	499		98.42 ± 0.01	101.36 ± 0.06	99.34 ± 0.03
I_3	250	248	248	249		99.12 ± 0.03	99.86 ± 0.01	98.66 ± 0.01

*Average of five determinations.
**Mean ± Standard for eight measurements.
(100 mg of cefotaxime sodium was added and recovered).

The optimum conditions for colour development for Method A, B and C have been established by varying the parameters one at a time and keeping the other parameters fixed and observing the effects of product on the absorbance of the coloured species and incorporated in the procedures. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical preparations and the mixtures were analyzed by the proposed methods. The per cent recoveries are given in Table-2. Interference studies revealed that the additives like antioxidants, preservatives and solubilisers that are usually present in injectables did not interfere at their regularly added levels. The proposed visible spectrophotometric methods are simple, sensitive, selective, accurate, precise and economical and can be used for the routine estimation of cefotaxime sodium in bulk drug and its pharmaceutical preparations (injectables).

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