EFFECTIVE QUANTITATION OF CEFOTAXIME SODIUM IN BULK AND PHARMACEUTICAL DOSAGE FORMS USING SPECTROSCOPY

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ABSTRACT

A simple, sensitive and accurate UV spectrophotometric method has been developed for the determination of cefotaxime sodium in bulk and pharmaceutical injectable dosage formulation. This method obeys Beer's law in the concentration range of 5-30 µg/mL with correlation coefficient of 0.998 and exhibiting maximum absorption at 238 nm with apparent molar absorptivity of 1.68092×10^3 Lmol^{-1}cm^{-1}. The method is accurate and precise and is extended to pharmaceutical injectable forms and there was no interference from any common pharmaceutical additives and excipients. The results of analysis were validated statistically and by recovery studies.

Keywords: Cefotaxime sodium, Linearity, Precision, Recovery studies, UV spectrophotometry.

INTRODUCTION

Cefotaxime sodium is chemically sodium 7-[2-(2-amino-4-thiazolyl)-2methoxy iminoacetamido]-3-acetoxy methyl-3-cephem-4-carboxylate (Fig 1) with molecular formula $C_{16}H_{16}N_5NaO_7S_2$ and molecular weight 477.4. Liquid chromatographic method of analysis is official in IP, USP and BP. Cefotaxime is third generation broad spectrum cephalosporins for parentral administration and is bactericidal and mainly used in the treatment of various bactericidal infections caused by Gram-positive and Gram-negative microorganisms. Cefotaxime is given by parental injection and it is marketed under various trade names including Eltax-250mg and Axim-1000mg in India[1, 2].
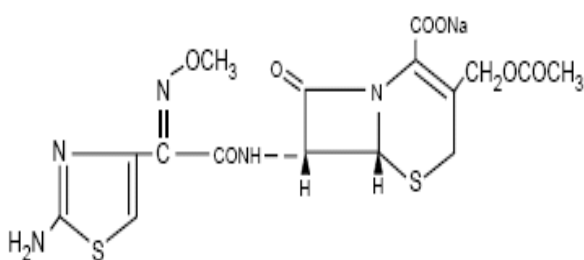

Figure 1: Chemical structure of Cefotaxime sodium

A survey of literature has revealed few UV spectrophometric methods for simultaneous estimation of cefotaxime sodium in pharmaceutical formulation. Few HPLC and HPTLC determinations are available for the estimation of the drug in formulation. There is a need for develop new, simple, economic and rapid method for the estimation of cefotaxime sodium in bulk and injectable forms and can be used for routine analysis[3-7].

MATERIALS AND METHODS

Equipment and reagents

Systronics 2201 double beam UV-Visible spectrophotometer with a matched pair of 10 mm quartz cells are used for experimental purpose. Freshly prepared 0.1N NaoH (Merck-AR grade) is used. The commercially available two brands of parentral preparations containing cefotaxime sodium 1000 mg and 250 mg have procured from local market.

Preparation of standard stock solution

Accurately weighed 100 mg of cefotaxime sodium pure drug taken in separate 100mL volumetric flask and dissolved with 70 mL of 0.1N NaoH and shaken for 30min and then diluted with 0.1N NaoH to get 1 mg/mL standard stock solution.

Construction of calibration curve

Aliquots of standard stock solution were pipetted out and suitably diluted with 0.1N NaoH to get the final concentration of 5-30 µg/mL. The solution was scanned in the spectrum mode from 400 nm - 200 nm wavelength range. Calibration curve was constructed by plotting the absorbance against the concentration and regression equation was computed.

Analysis of formulation

For the estimation of cefotaxime sodium from injection, a portion of the powder equivalent to 100 mg of the drug was accurately weighed and transferred to separate 100 mL volumetric flasks. The drug was dissolved by adding 70 mL of 0.1N NaoH to the volumetric flask with constant stirring for 15-20 min on a magnetic stirrer. Volumes were made up to the mark with 0.1N NaoH. Sample solution of 10 mL transferred to 100 mL volumetric flask and diluted up to the mark with 0.1N NaoH and diluted the

supernatant sample solutions to get the concentration of 5-30 µg/mL of cefotaxime sodium. Evaluation was performed with double beam spectrophotometer for cefotaxime sodium at 238 nm.

Validation of proposed method

Accuracy of the method was determined by the recovery studies in the injectable formulations of the cefotaxime sodium. Recovery studies were carried out by addition of known quantities of standard drug to pre-analyzed sample at three different concentrations. Also the experiment was repeated six times in a day to determine intra-day precision and on six different days to determine inter-day precision. The percentage relative standard deviation was calculated at each concentration level[8, 9].

<div style="text-align:center">RESULTS AND DISCUSSION</div>

Under the experimental conditions described, the λ max was obtained at 238 nm (Fig 2) and the calibration curve (Fig 3) was constructed the absorbance against concentration. Beer's law is obeyed over the concentration range of 5-30 µg/mL, using regression analysis the linear equation $Y=0.034X+0.001$ with correlation coefficient of $R^2=0.998$. The sandell's sensitivity and molar absorptivity were found to be 0.02932 µg/cm^2/0.001 and 1.68092×10^3 Lmol^{-1}cm^{-1} respectively.
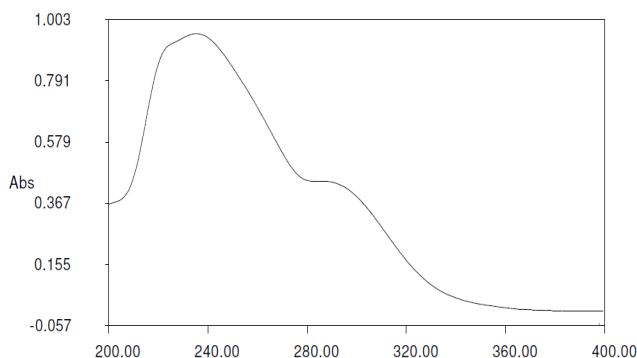

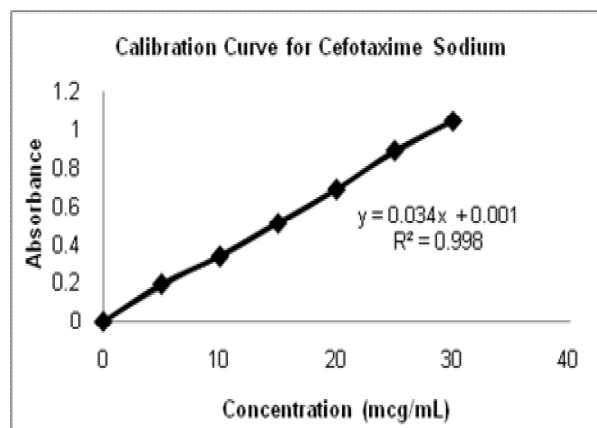**Figure 2:** λ max graph for Cefotaxime sodium pure drug

Figure 3: Calibration curve for Cefotaxime Sodium

The detection limit or LOD is the lowest amount of an analyte in a sample that can be detected, but not necessarily quantified, under the stated experimental conditions. Based on the standard deviation of the response of Y-intercept and slope, the detection limit may be expressed as DL=3.3 σ/S. The limit of detection for cefotaxime sodium was found to be 0.194 µg/mL Quantitation limit or LOQ is the lowest amount of analyte in a sample that can be determined with acceptable precision and accuracy under the stated experimental conditions. Based on the standard deviation of the response of Y-intercept and slope, the quantization limit may be expressed as QL=10 σ/S. The limit of quantization for cefotaxime sodium was found to be 0.588 µg/mL as shown in Table 1.

Table 1: Optical Parameters for cefotaxime sodium

Parameters	Data
λ-Max	228nm
Linearity	5-30 µg/ml
Regression equation	Y=0.034X+0.001
Correlation coefficient	$R^2=0.998$
Slope	0.034
Intercept	0.001
LOD	0.194 µg/mL
LOQ	0.588 µg/mL
Sandell's sensitivity	0.02932 µg/cm^2/0.001
Molar absorptivity	1.68092×10^3 Lmol^{-1}cm^{-1}

Table 2: Results of analysis of cefotaxime sodium in pharmaceutical formulation

S.No	Drug	Amount found* (mg/inj)	% content*	S.D*	% RSD*	S.E*	95% CI	
							Lower	Upper
1.	Brand A (250 mg)	250.12	100.04	0.495	0.198	0.2023	249.60	250.65
2.	Brand B (1000 mg)	1000.1	100.02	1.124	0.112	0.4591	998.91	1001.3

*(n=6), S.D=Standard Deviation, %RSD=Percentage relative Standard Deviation, S.E=Standard Error, C.I=Confidence Interval.

Table 3: Validation data for precision study

S.No	Formulation	Intraday Precision		Interday Precision	
		% Content*	% RSD	% Content*	% RSD
1.	Brand A (250 mg)	99.87	0.90	99.68	1.05
2.	Brand B (1000 mg)	100.21	1.02	100.71	1.02

*(n=6)

Table 4: Data for Recovery studies

S.No	Formulation	% Level of standard drug added	% Recovery	Mean % recovery	% RSD
1.	Brand A (250 mg)	20 % 40 % 60 %	101.50 100.75 100.50	100.91	0.515
2.	Brand B (1000 mg)	20 % 40 % 60 %	101.30 100.62 100.18	100.70	0.560

The proposed method is based upon direct estimation of cefotaxime sodium in injectable preparation at 238 nm. The mean percentage content of drug was found to be within the limit which is determined by taking average of six readings (Table 2).

The developed method was validated as per ICH guidelines for repeatability, intermediate precision and recovery studies. The precision of the method was checked in terms of Inter-day and Intra-day, where methods were repeated on six different days and also repeated on six different time periods in same day. The results were given in Table 3 and shows % RSD of less than 2 % at each level clearly indicated that the method is precise enough for the analysis of the drug.

The accuracy of the method was proved by performing recovery studies in the commercially available formulations (Table 4). Values greater than 98 % indicates that proposed method is accurate for the analysis of drug and there is no interference from the excipients present in the formulations.

CONCLUSION

In the above developed method, there was no additional extraction or separation procedure to extract the active ingredient from the formulation. The error in quantifications can be decreased by the elimination of this procedure. Hence, the developed method is, simple, accurate and economical for the routine estimation of cefotaxime sodium in bulk drug and its pharmaceutical dosage form (dry powder for injection).

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