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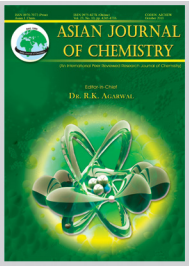

Determination of Cefotaxime in Pharmaceutical Preparations by Visible Spectrophotometry using Methyl Orange and Indigo Carmine Dyes

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A rapid, simple and sensitive validated visible spectrophotometric method has been explained for the assay of cefotaxime in pure form or in pharmaceutical formulations. In this methods, we employed *N*-bromosuccinimide (NBS) as the oxidimetric reagent and methyl orange and indigo carmine as spectrophotometric reagents. Spectrophotometry involves adding a measured exess of *N*-bromosuccinimide to cefotaxime in acid medium followed by determination of residual *N*-bromosuccinimide by reacting with a fixed amount of either methyl orange and measuring the absorbance at 509 nm (method **A**) or indigo carmine and measuring the absorbance at 608 nm (method **B**). In both methods, the amount of *N*-bromosuccinimide reacted corresponds to the amount of cefotaxime. In this methods, the measured absorbance is found to increase linearly with concentration of cefotaxime, which is corroborated by the correlation coefficients of 0.9949 and 0.9935 methyl orange and or indigo carmine, respectively. The system obeys Beer s law for 1.66–10 μg mL^{-1} and 14.89–44.68 μg mL^{-1} for method **A** and method **B**, respectively. The calculated apparent molar absorptivity values are found to be 1.99×10^4 and 5.44×10^3 L $mol\ cm^{-1}$ for method **A** and method **B**, respectively. The limits of detection and quantification are also reported for both spectrophotometric methods. The proposed methods were applied successfully to the determination of cefotaxime in commercial vial.

Key Words: Cefotaxime, Determination, *N*-Bromosuccinimide, Methyl orange, Indigo carmine.

INTRODUCTION

Cephalosporins structurally differ from pencillins by the heterocyclic ring system. They are pencillinase-resistant antibiotics with significant activity against both gram-negative and gram-positive bacteria[1]. Cefotaxime is β-lactam antibiotics that including broad spectrum of antibacterial properties[2,3]. It is the member of the cephalosporin antibiotic class of drugs that have useful as pre-surgery antibiotics. It is also useful for serious infections caused by susceptible strains of micro-organisms in lower respiratory infections, gynaecologic infections, genitourinary infections and central nervous system infections. Side effects of cefotaxime include, fainting, diarrhea, vomiting, headache and difficulty in breathing. In conclusion cefatoxime is cephalosporin of clinical and, hence, analytical interests. For their pharmacological significance coupled with the risk of side effects sometimes expanded in the course of the therapy, we deemed practical to propose novel methods for the determination of this antibiotic for routine quality control of pharmaceutical dosage forms for these. Several methods have been reported in the literature for the quantitative determination of cephalosporins. These include fluorimetric[4], polarographic[5] and isotachophoretic methods[6]. Recently a rapid development of chromatographic determination methods of pharmaceuticals has been observed too[7,8]. Some reported spectrophotometric methods for the determination of these analytes are chloranilic acid[9] paramolybdate anion[10], molybdophosphori acid[9] formation of a complex with Cu(II)[11]. Cefotaxime was also determined in pharmaceuticals preparations[12,13], urine[14-16] and human serum[17].

EXPERIMENTAL

All UV-VIS spectra were recorded A Jasco-V 530 double beam spectrophotometer with mached 10 mm quartz cell. Calibrated glasswares were used throughout the experiment.

All chemicals used were of analytical grade and doubly distilled water was used for dilution of the reagents and samples. Cefotaxime was kindly provided by the Jabber Ebne Hayyan Pharmaceutical Industries Company. Cefotaxime stock solution 10 μg mL^{-1} were prepared by dissolving standard sodium cefotaxime. 0.01 M of *N*-bromosuccinimide solution was prepared by dissolving *ca.* 1.8 g of chemical (Merck) in water with the aid of heat and diluted to 100 mL with water

TABLE-1
RESULTS OF ANALYSIS OF CEFOTAXIME VIAL AND EVALUATION OF ACCURACY AND PRECISION METHODS

Method	Sample taken ($\mu g\ mL^{-1}$)	Sample found ($\mu g\ mL^{-1}$)	Recovery (%)	RSD (%)	SD	$X \pm t_{n-1}S/\sqrt{n}$
Method **A**	2	1.87	93.50	1.64	0.001	0.074 ± 0.0015
	4	3.95	98.80	1.23	0.002	0.172 ± 0.0026
	6	6.02	100.4	0.64	0.002	0.264 ± 0.0021
	8	7.95	99.38	1.72	0.006	0.346 ± 0.0076
	10	9.54	95.40	0.44	0.002	0.393 ± 0.0021
Method **B**	15	12.60	84.00	1.71	0.004	0.214 ± 0.0004
	25	22.50	90.00	0.52	0.002	0.333 ± 0.0021
	30	27.90	93.00	0.35	0.001	0.421 ± 0.0018
	35	28.70	82.00	0.53	0.003	0.520 ± 0.0033
	44	43.12	98.00	0.28	0.002	0.582 ± 0.0019

and standardized. With dilution appropriately to get 90 and 340 $\mu g\ mL^{-1}$ *N*-bromosuccinimide for use in spectrophotometric method **A** and method **B**, respectively. Indigo carmine 200 $\mu g\ mL^{-1}$ was prepared by dissolving 0.01 g in distilled water. Methyl orange 50 $\mu g\ mL^{-1}$ was prepared by dissolving 0.0025 g in distilled water.

Spectrophotometry method A: In each of series of 10 mL calibrated flasks were placed (0.5, 1, 2, 3, 3.5, 4, 4.5, 5, 5.5, 6 mL) of standard 10 $\mu g\ mL^{-1}$ cefotaxime solution and the total volume was adjusted to 6 mL with water. To each flask was added 1.5 mL of 1 M hydrochloric acid followed by 1 mL of *N*-bromosuccinimide solution (90 $\mu g\ mL^{-1}$). The flasks were stoppered and let stand for 20 min with occasional shaking. At last, 1 mL of 50 $\mu g\ mL^{-1}$ methyl orange solution was added to each flask volume diluted to the mark with water, mixed well and absorbance measured at 608 nm against a water blank after 5 min.

Spectrophotometry method B: Different aliquots (0.5, 1, 2, 3, 3.5, 4, 4.5, 5, 5.5, 6 mL) of standard (50 $\mu g\ mL^{-1}$) cefotaxime solution were accurately measured into a series of 10 mL calibrated flasks by means of a microburette and the total volume was adjusted to 2 mL by adding water. 1 mL of 1 M hydrochloric acid was added to each flask followed by 1 mL *N*-bromosuccinimide solution (340 $\mu g\ mL^{-1}$). The flasks were stoppered and let stand for 20 min with occasional shaking. At last, 1 mL of 200 $\mu g\ mL^{-1}$ indigo carmine dye solution was added to each flask, this was diluted to the mark with water, mixed well and absorbance *versus* concentration of drug or regression equation was derived using the calibration curve data.

Standard curves were constructed by plotting the observed absorbency readings *versus* concentrations of cefotaxime in $\mu g\ mL^{-1}$ of the solution. Plots show high correlation coefficient with good linearity.

We determined the precision and accuracy of the proposed methods, solution containing five concentrations of cefotaxime and were tested by carrying out the determination of eight replicates of pure and vial samples of the drug, whose concentration was within Beer's law range. The linearity, slope and the intercepts were calculated using the regression equation. Values of the standard deviation, recovery, confidence interval, relative standard deviation were calculated (Table-1). The limit of detection and limit of quantification were also evaluated.

A linear correlation was found between absorbance at λ_{max} and concentration of cefotaxime in the ranges given in Table-2. The results obtained such as Beer's law range, molar absorptivity and were statistically compared with other visible spectrophotometry method (Table-3).

TABLE-2
ANALYTICAL AND REGRESSION PARAMETERS OF SPECTROPHOTOMETRIC METHODS

Parameter	Method **A**	Method **B**
λ_{max} (nm)	509	608
Beer's law limits ($\mu g\ mL^{-1}$)	1.66-10	14.89-44.68
Sandell sensitivity ($\mu g\ mL^{-2}$)	0.022	0.065
Limit of detection ($\mu g\ mL^{-1}$)	0.137	0.87
Limit of quantification ($\mu g\ mL^{-1}$)	0.416	2.63
Molar absorptivity ($L\ mol^{-1}\ cm^{-1}$)	1.99×10^4	5.44×10^3
Regression equation		
Intercept (b)	0.0172	0.114
Slop (a)	0.0408	0.0973
Correlation coefficient (r)	0.9949	0.9935

RESULTS AND DISCUSSION

The proposed spectrophotometric methods are indirect and are based on the determination of the residual *N*-bromosuccinimide after allowing the reaction between cefotaxime and a measured amount of *N*-bromosuccinimide to be complete. The residual *N*-bromosuccinimide was determined by reacting it with a fixed amount of either methyl orange or indigo carmine dye. The methods make use of bleaching action of *N*-bromo-

TABLE-3
COMPARISON OF THE REPORTED VISIBLE SPECTROPHOTOMETRY METHOD WITH THE PRESENT METHOD

Reagent	Method	Analyst	Beer's law	Molar absorptivity	λ_{max} (nm)	Ref
Leuco crystal violet	Spectrophotometry	Cefotaxime	0.4-4.8	8.4×10^4	588	18
Variamine blue	Spectrophotometry	Cefotaxime	0.5-5.8	1.07×10^5	556	19
Thionin	Spectrophotometry	Cefotaxime	0.5-6.4	7.21×10^4	600	–
Ethylene blue	Spectrophotometry	Cefotaxime	0.5-7.0	–	–	20
1,2 napthaquinon e-4-sulfonic acid	Spectrophotometry	Cefotaxime	20-140	2.71×10^3	475	21

succinimide on the dye, the decolouration being caused by the oxidative destruction of the dyes. Cefotaxime when added in increasing concentrations to a fixed concentration of *N*-bromosuccinimide, consumes the latter proportionally and there take places a simultaneous fall in the concentration of *N*-bromosuccinimide. When a fixed concentration of dye is added to decreasing concentrations of *N*-bromosuccinimide, a concomitant increase in the concentration of dye results. Consequently, a proportional increase in the absorbance at the respective max is observed with increasing concentration of cefotaxime (Figs. 1 and 2).

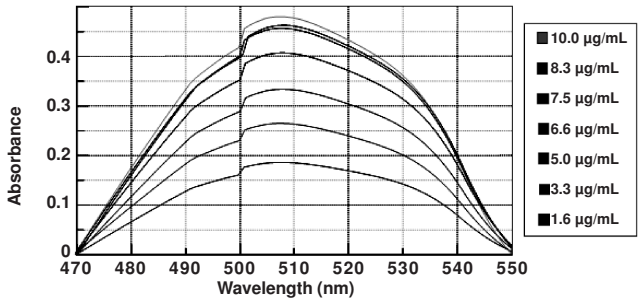

Fig.1. Absorption spectra of methyl orange in different concentration

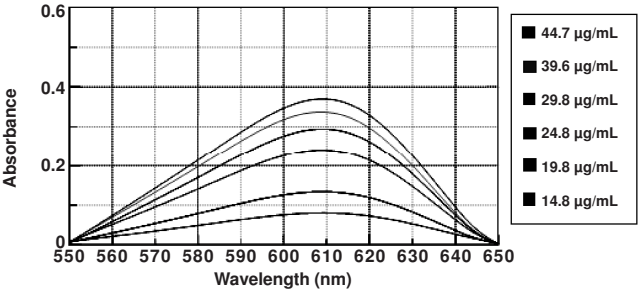

Fig. 2. Absorption spectra of indigo carmine in different concentration

Conclusion

Cefotaxime has been assayed in dosage forms using visible spectrophotometry. Time, cost and efficiency are the essential considerations in the pharmaceutical industry. Undoubtedly, HPLC is the most widely used technique in routine analysis, but it involves an expensive instrumental set up. Hence, spectrophotometric method was developed as viable alternatives to HPLC methods. the proposed methods demonstrate that *N*-bromosuccinimide in combination with methyl orange or indigo carmine could be used for the analysis of cefotaxime in bulk drug and in vial on a small scale.

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