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Spectrophotometric Estimation of Ceftazidime in Pure and Pharmaceutical Forms

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Three new, simple, sensitive and economical methods (**I**, **II** and **III**) have been developed for the quantitative estimation of ceftazidime in bulk and its pharmaceutical formulations. Method **I** is based on the oxidation followed by complexation between ceftazidime and 2,2' -bipyridine (2,2'-bpd) in presence of ferric chloride to form a blood red coloured chromogen exhibiting λ_{max} at 520 nm. Method **II** is based on the formation of purple coloured chromogens obtained when drug was diazotised with nitrous acid followed by coupling the resulting diazonium salt with α-naphthol exhibiting λ_{max} 562 nm. Method **III** is based on the formation of coloured Schiff's base obtained when drug reacted with *p*-dimethylaminobezaldehyde to form yellow coloured chromogen exhibiting λ_{max} at 410 nm. These methods obeyed Beer's law in the concentration range at 2-10, 10-50 and 10-50 μg/mL, respectively. The results of analysis for the three methods have been validated statistically and by recovery studies. The results are comparable with those obtained with UV spectorphotometeric method is double distilled water and λ_{max} 239 nm.

Key Words: Ceftazidime, 2,2'-Bipyridine, α-Naphthol, *p*-Diaminobenzaldehyde, Spectrophotometery.

INTRODUCTION

Ceftazidime is chemically (z)-(7R)-7-[2-(2-aminothiazol-4-yl)-2-(1-carboxy-l methoxyimino) acetamido]-3-(1-pyridiniomethyl]-3-cephem-4-carboxylate pentahydrate (Fig. 1)[1,2]. It is a 3rd generation cephalosporin antibiotic characterized by a broad antibacterial spectrum and a resistance to beta-lacttomase-producing organisms in addition to its antimicrobial activity (*streptococci*, *staphylococci*, *pneumococci*[3], *etc.*). Cephalosporins are distributed widely into tissues and body fluids, including pleural, pericardial and synovial fluids. Compared to the previous generation of drugs,

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these are much more effective in treatment of infections caused by gram -ve bacteria but equal to or slightly less in the treatment of gram +ve bacteria. They are much effective in the treatment of *pseudomonas* spp They include bilary tract infections, bone and joint infections, cystic fibrosis, endophthalmitis, infections in immunocopromised patients. Few analytical procedures are available in the literature for the analysis of ceftazidime, *via* high performance liquid chromatography[4-9] charge transfer complex[10] and spectrophotometeric methods[11-17].

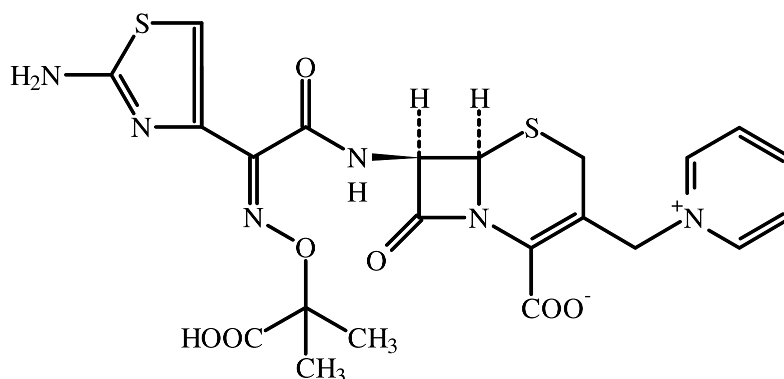

Fig. 1. Ceftazidime

EXPERIMENTAL

Analytical grade chemicals were used. All spectral measurement were made on Elico SL 164 Double Beam, UV-Visible spectrophotometer.

Standard and sample solutions: Ceftazidime (pure or formulation) (*ca.* 100 mg) was accurately weighed and dissolved is 20 mL of double distilled water, transferred to standard 100 mL volumetric flask, the final volume made upto the mark with double distilled water. The final concentration was brought to 100 µg/mL with double distilled water.

Assay

Method I: Aliquots of working standard solution ranging from 0.2-1.0 mL (1.0 mL = 100 µg) were transferred into a series of 10 mL, volumetric flasks. To each 0.2 mL aqueous solution of ferric chloride (0.03 M) and 0.6 mL alcoholic solution of 2,2'-bipyridine (0.03 M) were added, heated on water bath for 5 min and then cooled to room temperature. Then final volume was made upto 10 mL with distilled water. The absorbance of the blood red coloured species was measured at 520 nm against reagent blank. The colour is stable for more than 5 h. The amount of ceftazidime in the sample was computed from calibration curve.

Method II: Aliquots of working standard solution ranging from 1.0-5.0 mL (1 mL = 100 μg) were transferred into a series of 10 mL, volumetric flasks. To each of the above aliquots, conc. hydrochloric (0.2 mL) and 0.5 mL aqueous solution of sodium nitrite (0.1 % w/v) were added and an 0.5 mL aqueous solution of ammonium sulfamate (0.2 % w/v) added followed by 1.0 mL aqueous solution of α-naphthol (0.2 % w/v) in aqueous solution of sodium hydroxide (20 % w/v) in 10 mL, with distilled water. The absorbance of purple coloured species was measured at 562 nm against reagent blank. The colour is stable for more than 5 h. The amount of ceftazidime present in the sample solution was computed from its calibration curve.

Method III: Aliquots of working standard solution ranging from 1.0-5.0 mL (1 mL = 100 μg) were transferred in to a series of 10 mL, volumetric flasks. To each 1.0 mL alcoholic solution of *p*-dimethylaminobenzaldehyde (1.0 % w/v) was added and heated at 60-70ºC for 0.5 h. After cooling, the volume was brought upto 10 mL with ethanol and the absorbance of the yellow coloured species formed was measured at 410 nm against reagent blank which remains stable more than 6 h after final dilution. The amount of ceftazidime in the sample was computed from calibration curve.

The results of the above methods are compared with the results obtained with UV spectrophotometeric method. In UV method, solution of ceftazidime in distilled water either pure or formulation (100 μg/mL), was prepared. Aliquots of ceftazidime ranging from (0.5 2.5 mL) (1 mL = 100 μg) were transferred into series of 10 mL volumetric flasks. The volume was made upto mark with distilled water and the absorbance of the solution was measured at 239 nm against solvent blank. The amount of ceftazidime was computed from its calibration curve.

RESULTS AND DISCUSSION

The optical characteristics such Beer's law, absorption maxima, molar absorptivity, Sandell's sensitivity, percent relative standard deviation (calculated from the eight measurements containing ¾th of the amount of the upper Beer's law limits of the ceftazidime) and per cent range of error (0.05 and 0.01 confidence limits) were calculated for the three methods and the results are summarized in Table-1. The optimum conditions for colour development for method **I**, **II** and **III** 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 it was incorporated in the procedures. The values obtained for the determination of ceftazidime in different injection samples, T_1, T_2 and T_3 by proposed methods are presented in Table-2.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

	Method I	Method II	Method III
λ_{max} (nm)	520	562	410
Beer's law limits (μg/mL) (C)	2-10	10-50	10-50
Molar absorptivity (L mol^{-1} cm^{-1})	6.5212×10^{4}	9.8513×10^{3}	1.2712×10^{4}
Sandell's sensitivity (μg/cm^2 0.001 absorption units)	0.025	0.040	0.035
Regression equation (Y = a + bc)*			
Slope (b)	9.9952×10^{-2}	1.0057×10^{-2}	2.0066×10^{-2}
Intercept (a)	4.8095×10^{-3}	1.5439×10^{-1}	1.0833×10^{-3}
Correlation coefficient (r)	0.9999	0.9999	0.9999
RSD (%)	0.2759	0.5640	0.3142
Range errors**			
Confidence limits with 0.05 level	± 0.0014	± 0.0021	± 0.0015
Confidence limits with 0.01 level	± 0.0020	± 0.0032	± 0.0023

*Y is the absorbance and C is the concentration in μg/mL
**For eight measurements

TABLE-2
EVALUATION OF CEFTAZIDIME IN PHARMACEUTICAL PREPARATIONS

Samples	Labelled amount (mg)	Amount obtained (mg) proposed method*			Reference method	Percentage recover**		
		I	II	III	UV	I	II	III
T_1	100	99.55	99.89	99.78	99.85	99.63 ± 0.34	99.92 ± 0.42	99.69 ± 0.32
T_2	100	99.81	99.94	99.83	99.92	99.98 ± 0.46	99.94 ± 0.38	99.75 ± 0.41
T_3	100	99.74	99.86	99.94	99.79	99.65 ± 0.32	99.78 ± 0.56	99.89 ± 0.51

*Average of eight measurements.
**Mean and standard deviation of eight determinations.

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 percent recoveries are given in Table-2. These studies revealed that the common excipients are usually present in the injection dosage did not interfere at their regularly added levels.

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