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International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.4, pp 2177-2181, Oct-Dec 2010

Simultaneous Estimation of Ceftriaxone Sodium and Sulbactam Sodium using Multi-Component Mode of Analysis

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Abstract: A Simple, accurate, precise and economical procedure for simultaneous estimation of Ceftriaxone Sodium and Sulbactam Sodium in combined dry powder for injection dosage form by UV spectrophotometry, using Multi-component mode of analysis. The method is based upon determination of Ceftriaxone Sodium at 251nm and Sulbactam Sodium at 259 nm in 0.1M Sodium hydroxide. Ceftriaxone Sodium and Sulbactam Sodium at their respective λmax shows linearity in the concentration range of 4-20µg/mL and 2-10 µg/mL respectively. The method was validated according to ICH guidelines. Different analytical parameters such as linearity, precision, accuracy, ruggedness and robustness were determined. The results of analysis, formulation given as percentage of label claim were found to be 99.15±0.612 and 98.30±0.601 for Ceftriaxone sodium and Sulbactam sodium respectively. Therefore, the proposed method can be used for the routine analysis of both drugs in quality control laboratories.
Keywords: *Ceftriaxone Sodium, Sulbactam Sodium, Multi-component mode of analysis.*

INTRODUCTION:

Ceftriaxone is (6R,7R)-3[(acetyl-oxy)methyl]-7-[[2Z)-2amino-4-thiazolyl)(methoxy amino)-acetyl]amino]-8-oxo-5-thia-1-azabicyclo[4,2,0]oct-2-ene-2carboxylic acid[1]. Ceftriaxone is a cephalosporin beta-lactam antibiotics used in the treatment of bacterial infections usually caused by susceptible, gram positive organism. These enzymes are involved in cell wall synthesis and cell division[2]. Sulbactam chemically (2R,5R)-3,3-dimethyl-4,47-trioxo-4,6thia-1-azabicyclo[3-2-0]heptane-2-carboxylic acid[3]. It is a competitive, irreversible beta-lactamase inhibitor and has good inhibitor activities against the clinically important plasmid mediated beta-lactamase and most frequently responsible for transferred drug resistance[4]. Both Ceftriaxone and Sulbactam are listed in the USP and the BP. To meet the clinical needs, a new combination was developed and consequently for the quality control of the formulation an analytical method was required.

A literature survey revealed that several methods have been used for determination of Ceftriaxone sodium which includes High performance Thin Layer Chromatography (HPTLC)[5], High performance Liquid Chromatography (HPLC) [6,7] and spectrometry[8,9]. Sulbactam was successfully determined by Capillary Isotachophoresis[10] and colorimetry[11]. However, there is no work was reported for the simultaneous estimation of these drugs by UV spectrophotometry using multi-component mode of analysis. Hence, in the present communication we propose fast, simple, and accurate UV spectrophotometric method, without tedious extraction procedure, was developed for the simultaneous estimation of both drugs in dry powder for injection dosage form by multi-component mode of analysis.

EXPERIMENTAL

Apparatus

A Shimadzu UV-1700 double beam UV-Visible spectrophotometer (Japan) equipped with 10mm matched quartz cells was used in the present study. A shimadzu AX-220 single pan balance was used for weighing purpose.

Chemical and Reagents

Ceftriaxone Sodium and Sulbactam Sodium reference standard of United States of Pharmacopoeia (USP) were bought from Aurobindo chemicals and drugs Ltd, Pondicherry, which was certified to be 98.5% and 99.7% respectively. Double distilled water filtered through 0.45µm filter (MILLI PORE) was used to prepare solution. CETRIAX-S injection (Karnataka Antibiotics and Pharmaceuticals) containing Ceftriaxone sodium and Sulbactam Sodium was obtained from local market. Sodium hydroxide of AR grade, was procured from Merck Ltd, (Mumbai).

Preparation of standard stock solution

The Standard stock solutions of Ceftriaxone Sodium and Sulbactam Sodium was prepared by dissolving 10mg and 5mg in 10ml volumetric flask, dissolved with of Potassium buffer and made up to volume.

Preparation of Synthetic mixture of Ceftriaxone and Sulbactam

The eight mixed standard solutions with concentration of Ceftriaxone Sodium and Sulbactam Sodium in the ratio of 4:2, 6:3, 8:4, 10:5, 12:6, 14:7, 16:8, 18:9(µg/mL) were prepared in 0.1M Sodium hydroxide. All the mixed standard solution were scanned over the range of 200-300nm, in multi-component mode; using two sampling wavelength 251 and 259nm.The spectral data from these scan were used to determine the concentration of these drugs in combined powder for injection dosage form.

Procedure for analysis

Marketed powdered injection formulation (Cetriax-S) containing 1g of Ceftriaxone Sodium and 0.5g of Sulbactam Sodium were analyzed by this method. Weighed accurately 15mg from the sample container. Diluted with 0.1M Sodium hydroxide, finally to get the concentration 10 µg/mL and 5µg/mL of Ceftriaxone sodium and Sulbactam sodium. The sample was analyzed in triplicate by multi-component mode of analysis. 0.1M Sodium hydroxide was used as blank. The concentrations of each component was obtained by the spectral data of the sample solution with reference to that of the mixed standard. Results of analysis are shown in table-1.

Validation of the method

The following validation parameters; linearity, range, accuracy, precision and specificity were studied. The accuracy of the method was ascertained by carrying out recovery studies using standard addition method. The recovery study was performed to determine if there was any positive or negative interference from excipients present in the formulation. The precision of an analytical method is expressed as standard deviation or relative standard deviation of series of measurements. It was ascertained by replicate estimation of drug by the proposed method. Test for ruggedness was carried out by repeating the procedure under difference conditions i.e. on different days, and by different analysts.

Table I: Result of analysis and statistical data

DRUG	Ceftriaxone				Sulbactam			
	Label Claim gm/vial	Amount found* ± SD gm/vial	% assay	%RSD	Label Claim gm/vial	Amount found* ± SD (mg/vial)	% assay	%RSD
Cetriax-S inj 1.5g	1.0	0.998 ± 0.027	99.80	0.020	0.500	0.498± 0.06	99.70	0.062

*Results are mean of six readings

Table 2: Summary of optical characteristics of Ceftriaxone sodium and sulbactam sodium

Parameters	Data	
	CEFTRIAXONE	**SULBACTAM**
Absorption maximum	251nm	259nm
Beer's law limit (µg/mL)	4-20µg/mL	2-10µg/mL
Correlation coefficient (r^2)	0.9998	0.9999
Regression equation (y=mx+c)	0.1082X + 0.0081	0.1061X + 0.0071
Slope (m)	0.1082X	0.1061X
Intercept (C)	0.0081	0.0071
Limit of detectioin (µg/mL)	0.5	0.25
Limit of Quantitation (µg/mL)	1.5	2.5

*Average of six determinations.

Figure 1: UV spectrum of Ceftriaxone sodium and Sulbactam sodium

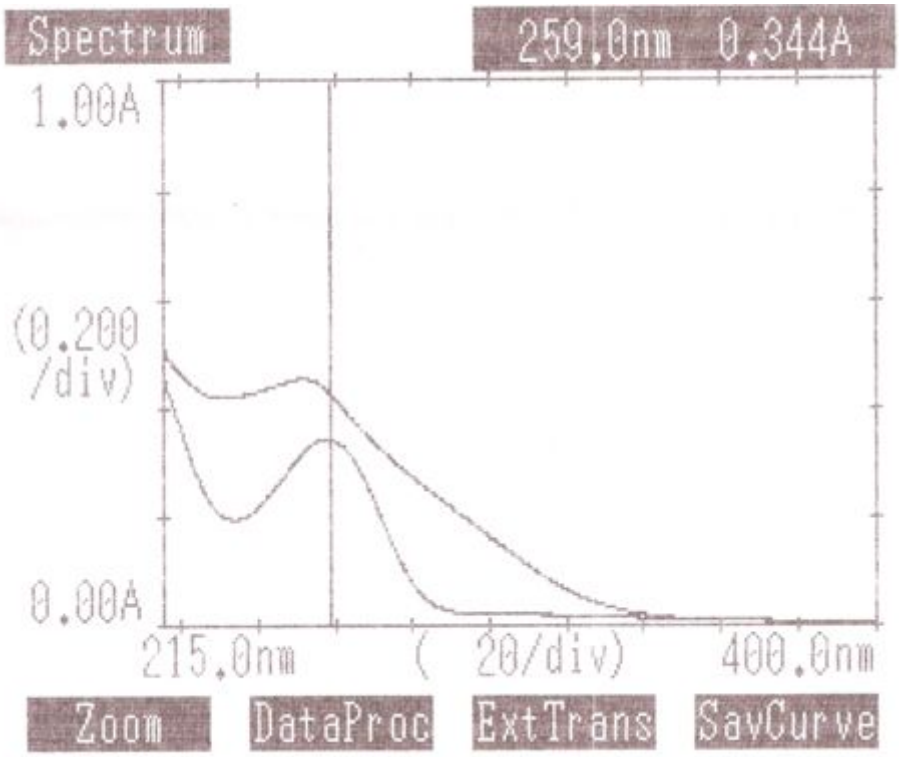
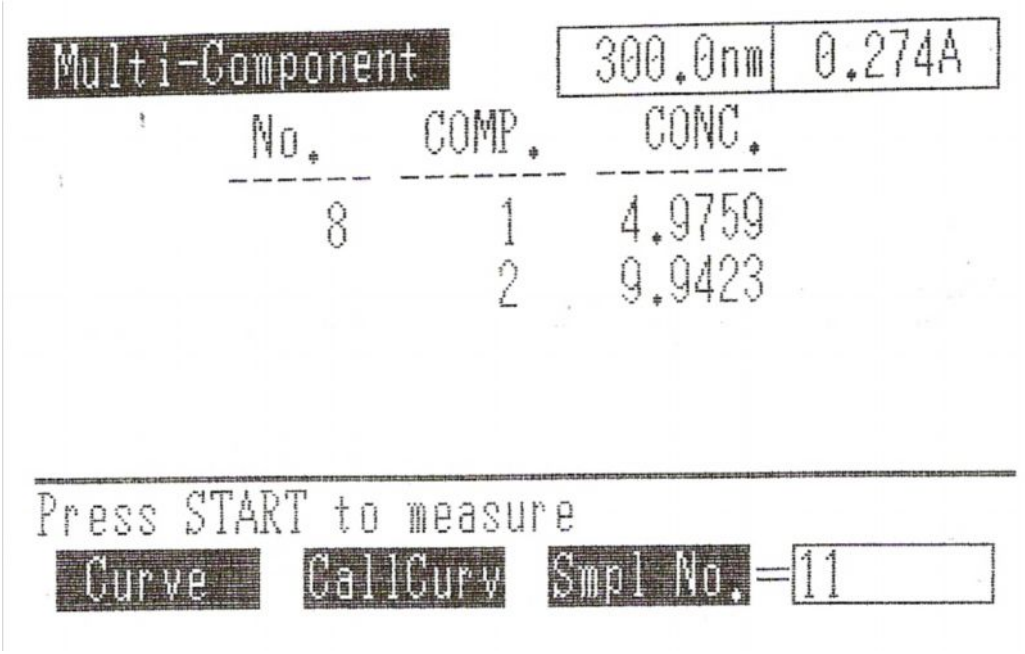


Figure 2: Assay report of ceftriaxone sodium and sulbactam sodium by multi-component mode of analysis



RESULTS AND DISCUSSION

In 0.1M Sodium hydroxide, Ceftriaxone Sodium and Sulbactam Sodium, showed absorbance maxima at 251 and 259nm, respectively. The proposed method for simultaneous estimation of Ceftriaxone Sodium and Sulbactam Sodium in powder for injection dosage form was validated as per the ICH guidelines. The linearity was observed in the concentration range of 4-20 µg/mL for Ceftriaxone and 2-20 µg/mL for Sulbactam with regression co-efficient 0.9989 and 0.9991 respectively. Amount of drugs estimated by the proposed method was in good agreement with the label claim. The accuracy of the method was assessed by recovery experiments. The precision of the method was studied as repeatability, intra-day and inter-day variations; the %RSD less than 2, indicates proposed method is precise. The results did not show any statistical difference between operators (%RSD less than 2) suggesting the method developed was rugged. Recovery was close to 100% for both drugs.

CONCLUSION

The present study comprises a UV spectroscopic, multi-component mode of analysis for the simultaneous determination of Ceftriaxone Sodium and Sulbactam Sodium in injection dosage form. From the study of validation parameters, it was observed that the method is specific, accurate, precise, reproducible and rugged. The proposed method could be applied to routine analysis in quality control laboratories.

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