Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2010, 2(5):255-259
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X

Development and Validation of Spectrophotometric Method for Determination of Ceftriaxone Sodium in Pharmaceutical Dosage Forms

K. R. Patel[+], V. D. Patel[+], K. P. Patel[+], V. G. Patel[++]

[+]*Suresh Gyanvihar University, Jaipur*
[++]*Municipal Arts and Urban Bank Science College, Mehsana*

ABSTRACT

Three new, simple, sensitive, selective and economical methods (Method 1, 2 and 3) for the determination of Ceftriaxone Sodium have been described in this paper. Method 1 and 2 are based on the formation of coloured Schiff base obtained when Ceftriaxone Sodium in acidic conditions related p-dimethyleaminobenzaldihyde and salicyldihyde in ethanol to form yellow coloured chromogens exhibiting λmax at 410 nm and 390 nm respectively. Method 3 is based on coupling the drug with 3-methyle-2-benzothiazolinone hydrazonehydrochloride in the presence of ferric chloride to form blue coloured chromogen exhibiting λmax at 628 nm. These method obeyed Beer's law in the concentration range of 10-50 µg/ml, 20-100 µg/ml and 2-10 µg/ml respectively. The results for analysis for the three methods have been validated statistically and by recovery studies. The results are comparable with those obtained with UV spectrophotometric method in double distilled water at λmax 241 nm.

Keyword: Ceftriaxone Sodium, p-dimethyleaminobenzaldihyde, salicylaldehyde, Optical Characteristics.

INTRODUCTION

Ceftriaxone Sodium is chemically, (Z)-7-[2-(2aminothizol-4-yl)-2-methoxyiminoacetyl 1 amido]-3-[2,5-dihydro-6-hydroxy-2-methyl-5-oxo-l,2,4-triazin3-yl)thiomethyl]-3-cephem-4-carboxylic acid, disodium salt, sesquaterhydrate[1-3]. It is a third generation cephalosporin antibiotic characterized by a broad antibacterial spectrum and is resistant to betalactamase-producing organism in addition to its antimicrobial activity against Streptococci, Staphylococci, Pneumococci etc[4-8]. Cephalosporins are distributed widely into tissues and body fluids,

including pleural, pericardial, and synovial fluids. However, while the earlier Cephalosporins failed to penetrate the central nervous system and were unsuccefull in the treatment of meningitis, the third generation cephalosporins enter the central nervous system and reach therapeutic concentrations, being sufficient for the treatment of meningitis caused by aerobic gram-negative bacteria[9-13]. These characteristics are of considerable clinical analytical interests. Few methods have been reported for the determination of Ceftriaxone Sodium which include HPLC[14-19] RP_HPLC and spectrophotometric[19-25] methods.

The aim of this work was to develop simple and reproducible spectrophotometric procedure for the determination of Ceftriaxone Sodium by reaction with p-dimethyleaminobenzaldihyde, salicyldihyde and 3-methyle-2-benzothiazolinone hydrazonehydrochloride.

MATERIALS AND METHODS

All spectral measurements were made on ELICO 8L 164 Double beam, UV-Visible spectrometer. All chemicals used were of analytical grade.
Standard and Sample Solution

About 100 mg of Ceftriaxone Sodium (pure or formulation) was accurately weighted and dissolved in 20 ml of absolute alcohol. Acetic acid (4 ml) was added and the final volume made up to 100 ml with absolute alcohol. The final concentration was brought up to 100 µg/ml with absolute alcohol. However, for (111), standard and sample solutions were prepared in double distilled water without adding glacial acetic acid.

Assay
Method (I)
Aliquots of (1.0 ml – 5.0 ml) Ceftriaxone Sodium (1.0 ml = 100 µg) were transferred into a series of 10 ml volumetric flasks. To each, 1.0 ml alcoholic solution of p-dimethyleaminobenzaldihyde (1.0 % w/v) was added and heated at 60-70 °C for 30 minutes. After cooling, the volume was brought up to mark with alcohol and the absorbance of the yellow coloured species was measured at 410 nm against reagent blank. The coloured species was stable for more than 2 hours. The amount of Ceftriaxone Sodium present in the sample solution was computed from its calibration curve. The colour was found to be stable up to 80°C. At higher pH the turbidity appears.

Method (II)
Aliquots of (1.0 ml – 5.0 ml) Ceftriaxone Sodium (1.0 ml = 100 µg) were transferred into a series of 10 ml volumetric flasks. To each, 2.0 ml alcoholic solution of salicylaldehyde (4.0 % v/v) was added and heated at 60-70 °C for 35 minutes. After cooling, the volume was brought up to mark with alcohol and the absorbance of the yellow coloured species was measured at 390 nm against reagent blank. The coloured species was stable for more than 1 hour. The amount of Ceftriaxone Sodium present was computed from calibration graph. The colour was found to be stable up to 80°C. At higher pH the turbidity appears.

Method (III)

Aliquots of (0.2 ml – 1.0 ml) Ceftriaxone Sodium (1.0 ml = 100 µg) in double distilled water were transferred into a series of 10 ml volumetric flasks. To each, 1.5 ml aqueous solution of ferric chloride (0.03 M) and 1.5 ml aqueous solution of 3-methyle-2-benzothiazolinone hydrazonehydrochloride (0.2 % w/v) were added and set aside for few minutes at room temperature. The volume was brought upto mark with distilled water and the absorbance of the blue coloured species was measured at 628 nm against reagent blank. The coloured species was stable for more than 4 hour. The amount of Ceftriaxone Sodium present was computed from its calibration curve.

The results of the above methods are compared with the result obtained with UV spectrometer method. In the UV method solution of Ceftriaxone Sodium in distilled water (100 µg/ml), was prepared. Aliquots of Ceftriaxone Sodium (0.2 ml – 1.0 ml) (1.0 ml = 100 µg) were transferred into a series of 10 ml volumetric flasks. The volume was made up to the mark with double distilled water and the absorbance of the solution measured at 241 nm against solvent blank. The amount of Ceftriaxone Sodium was computed from its calibration curve.

RESULT AND DISCUSSION

The presence of the amino group in Ceftriaxone Sodium 1, enabled the use of its condensation reaction with p-dimethyleaminobenzaldihyde (method I) and salicylaldehyde (Method II) forming yellow coloured chromogens 2 and 3 exhibiting λmax at 410 nm and 390 nm respectively. Method III based on coupling of Ceftriaxone Sodium with 3-methyle-2-benzothiazolinone hydrazonehydrochloride, in presence of ferric chloride to form blue coloured chromogen exhibiting λmax at 628 nm. In method I, II and III Beer's law was obeyed in the concentration range 10-50 µg/ml respectively, proving beyond doubt that the drug has undergone reaction quantitatively, with above reagent.

Table – 1 Optical characteristics and Precision

	Method I	Method II	Method III
λmax (nm)	410	390	628
Beer's Law limits (µg/ml) (C)	10-50	20-100	2-10
Molarabsorptivity (lit. mol^{-1} cm^{-1})	7.1337×10^{3}	7.3178×10^{3}	5.6489×10^{4}
Sandell's sensitivity	0.045	0.061	0.052
µg/cm^2 0.001 (absorption units)			
Regression equation (Y = a + bC)*			
Slop (b)	1.0021×10^{-2}	1.0098×10^{-2}	9.9857×10^{-2}
Intercept (a)	3.2928×10^{-2}	4.5702×10^{-2}	0.9678×10^{-2}
Correlation coefficients (r)	0.9999	0.9998	0.9999
%RSD	0.6065	0.3921	0.2622
Range of errors**			
Confidence limits with 0.05 level	±0.0017	±0.0021	±0.0013
Confidence limits with 0.01 level	±0.0025	±0.0032	±0.0019

** Y is the absorbance and C is the concentration is µg/ml, ** For eight measurement*

The optical characteristics such as Beer's law limits, absorption maxima, molar absorptivity, Sandell's sensitivity, percent relative standards deviation (calculated from the eight measurements containing 3/4th of the amount of the upper Beer's law limits of Ceftriaxone Sodium) and percent range errors (0.05 level and 0.01 confidence limits) were calculated for the three methods and the results are summarized in Table – 1. The optimum condition 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 effect of product on the absorbance of the coloured species and incorporated in the procedures. The values obtained for the determination of Ceftriaxone Sodium in different brands vial samples, 1 and 2 by the proposed and UV methods are compared in Table – 2. To evaluate the validity and reproducibility of the methods, known amounts of pure drug were added to the previously analyzed pharmaceutical preparation and the mixtures were analyzed by the proposed methods. The percent recoveries are given in Table – 2.

Table – 2 Evaluation of Cefriaxone Sodium in Pharmaceutical preparations

Sample	Labeled Amount (mg)	Amount obtained (mg) Proposed method*			Reference Method	Percentage Recovery**		
		I	II	II	UV	I	II	III
1	100	99.95	99.98	99.74	99.41	99.85 ±0.52	100.20 ±0.47	99.72 ±0.71
2	100	99.81	99.91	99.89	99.84	99.65 ±0.39	99.96 ±0.45	99.84 ±0.24

** Y is the absorbance and C is the concentration is µg/ml, ** For eight measurement*

These studies revealed that the common fillers usually present in the pharmaceutical formulation (vials) forms did not interfere at their regularly added levels.

REFERENCES

[1]. Indian Pharmacopoeia 1996 (Addendum 2002). (Govt. of India, Ministry of Health and Family Welfare, Controller of Publications, Delhi, **2002**)
[2]. S. C. Sweetman, Martindale, The Complete Drug reference. (Pharmaceutical press, London (U.K.) **2002**), 33, 169.
[3]. N. J. Montvale, Physician's Desk Reference, (Medical Economics Company Inc Montvale, **2003**) 56.
[4]. W. V. Caufield, J. T. Stewart, *Chromatographia*, **2001**, 54, 561.
[5]. I. Schrive, J. C. Plasse, *J. Chromatogr. B.*, **1994**, 657, 233.
[6]. R. P. G. Heeswijk, R. M. W. Hoerelmans, P. L. Meenhorst, J. W. Mulder J. H. Beijsen, *J. Chromatogr. B.*, **1998**, 713, 395.
[7]. G. Bahrami, S. Mirzaee, A. Kiani, B. Mohammadi, *J. Chromatogr. B. Analyt. Technol. Biomed. Life Sci.*, **2005**, 823, 213.
[8]. E. K. Kano, C. H. D. R. Serra, E. E. Koono, S. S. Andrade, V. Porta, *Int. J. Pharma.*, **2005**, 297, 73.
[9]. Y. Hassan, A. Mohammed, M. Hefnaun. *Anal. Lett.*, **2003**, 36, 2527.

[10]. A. Sibel, B. Ozkan, Uslu, *J. Liq. Chrom. Rel. Tech.*, **2005**, 25, 1447.
[11]. D. G. Sharnkar, D.V.S.P. Kumar, *Asian J. Chem.*, **2005**, 17, 2575.
[12]. R. M. Lopez, L. Pou, M.R. Gomez, I. Ruiz, J. Monterde, *J. Chromtogr. B. Biomed. Sci. Appl.*, **2001**, 751, 371.
[13]. QC. T. Tougas, K. Cohen, R. Lee, P. Meagan, M. Corson, T. Muchnickz, *J. Chromatogr. Sci.*, **2000**, 38, 246.
[14]. J. W. Pav, L. S. Rowland, D. J. Korpalski, *J. Pharm. Boimed. Anal.*, **1998**, 20, 91.
[15]. P. G. Rolf, G. V. Heeswijka, M. Richard, W. Hoetelmansa, P. L. Meenhordtb, J. W. Mulderb, J. H. Beijnena, *J. Chromatog. B.*, **1998**, 713, 395.
[16]. E. Marchei, L. Valvo, R. Pacific, M. Pelligrini, G. Tossini, P. Z.uccaro, *J. Pharm. Boimed. Anal.*, **2002**, 29, 1081.
[17]. R. Geetha, A. K. Hemantkumar, V. K. Swami, S. Sowmya, *J. Chromatogr. B.*, **2006**, 843, 339.
[18]. K. B. Kenney, S. A. Wring, R. M. Carr, G. N. Wells, J. A. Dunn, *J. Pharm. Biomed. Anal.*, **2000**, 22, 967.
[19]. N. Erk. *Pharmazie*, **2004**, 59, 106.
[20]. R. Sekar, S. Azhaguvel, *J. Pharm. Biomed. Anal.*, **2005**, 39, 653.
[21]. M. S. Palled, P. M. N. Rajesh, M. Chatter, A. R. Bhatt, Indian J. Pharm. Sci., **2005**, 67, 110.
[22]. N. Kapoor, S. Khandavilli, R. Panchgnula, *J. Pharm. Biomed. Anal.*, **2006**, 41, 761.
[23]. S. B. Wankhede, K. R. Gupta, S. G. Vadodkar, *Indian J. Phar. Sci.*, **2005**, 67, 96.
[24]. N. Kapoor, S. Khandavilli, R. Panchgnula, *Analytica Chemica Acta.*, **2006**, 570, 41.
[25]. M. Sarkar, S. Khandavilli, R. Panchgnula, *J. Chromatogr. B. Analyt. Technol. Biomed. Life Sci.*, **2006**, 830, 349.