UV Spectrophotometric Determination of Cefixime in Bulk and its Dosage Form

Article *in* Journal of Pharmacy Research · November 2012

CITATIONS
9

READS
8,170

5 authors, including:

Suddhasattya Dey
Bengal College of Pharmaceutical Technology
79 PUBLICATIONS **360** CITATIONS
SEE PROFILE

Prasanna Pradhan
Pioneer Pharmacy Degree College
24 PUBLICATIONS **129** CITATIONS
SEE PROFILE

Shreya R Shah
Harbourview Pharmacy
16 PUBLICATIONS **78** CITATIONS
SEE PROFILE

Suddhasattya Dey et al. / Journal of Pharmacy Research 2012,5(12),5419-5422

Research Article
ISSN: 0974-6943

Available online through
www.jpronline.info

UV Spectrophotometric Determination of Cefixime in Bulk and its Dosage Form

[*]Suddhasattya Dey[1], Prasanna Kumar Pradhan[1], U. M. Upadhayay[1], Shreya Shah[1], Kuntal Goswami[1]
[1]Sigma Institute of Pharmacy, Bakrol, Vadodara-390019, Gujarat, India

Received on:12-09-2012; Revised on: 17-10-2012; Accepted on:26-11-2012

ABSTRACT

A novel, simple, accurate, sensitive, reproducible, economical and less time consuming spectroscopic method was developed and validated for determination of cefixime. The solvent used was 0.1N HCL and the absorbance maxima or the λmax was found to be 283.0 nm and 303nm for zero order and first order derivative respectively. This method obeyes Beer's Law for the concentration range of 8–16 µg/ml for cefixime. The proposed method was been validated statistically as per the ICH guidelines for linearity, accuracy, precision, specificity, LOD and LOQ. The method developed and validated successfully for the quantitative analysis of cefixime in bulk and dosage form.

Key words: Cefixime, UV-Spectrophotometric method, validation.

INTRODUCTION

Cefixime is official in British Pharmacopoeia (6R, 7R)-7-[2-(2-amino-4-thiazolyl) glyoxylamido]- 8-oxo-3-vinyl-5-1 –azabicyclo [4.2.0] oct-2- ene-2-carboxylicacid,7-9z)-[o carboxymethyl)-oxime] trihydrate[1].

Formula
$(C_{16}H_{15}N_5O7S_2)$[1]

Mol.Wt
(453.452 g/mol)[1]

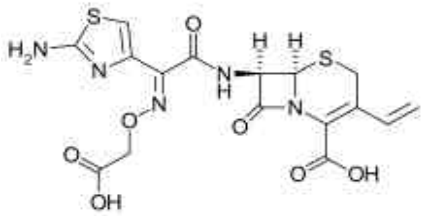

Fig:-1 Structure of Cefixime[1].

It is third generation cephalosporin antibiotic. It is under the category of ß-Lactam Antibiotics/Cell Wall inhibitor. It Acts by inhibiting an enzyme transpeptidase, involved in the building of bacterial cell walls. It is used in lower respiratory tract infections. It is helpful in acute urinary tract infections, biliary tract infections, sinusitis, acute otitis media, peptic ulcer and many more[1-2].

Literature survey reveals that cefixime is estimated in various combine dosage form like- azithromycin[5], ofloxacin[6], moxifloxacin[7],Ornidazole[8] dicloxacillin[9], cefuroxime axitile[10], Cloxacillin[11], ofloxacin[12], ofloxacin[13] by derivative spectroscopy method, spectrophotometric methods, simultaneous equation method and absorption ratio method, TLC densitometric method , RP-HPLC, HPLC, RP-HPLC, RP-HPLC, respectively. As per literature survey, no analytical method has been reported for the estimation of cefixime in pharmaceutical dosage forms. Therefore the present research work, our aim is to develop a novel, simple, accurate, sensitive, reproducible, economical analytical method to estimate cefixime in routine analysis.

MATERIALS AND METHODS

The drug, cefixime is a gift of Cipla Goa branch. The instrument used for the present study was a UV-Vis double beam spectrophotometer (model 2080, Analytical Technological Limited) with 1cm matched pair quartz cell. The solvent used was 0.1N HCl which was of AR grade, purchased from SD Fine Chemicals Limited, India and double distilled water.

***Corresponding author.**
Suddhasattya Dey, M.Pharm,
Sigma Institute of Pharmacy
Bakrol, Vadodara.
Gujarat-390019,India.

UV Method Development[3]

Solubility Test

Solubility test for the drug cefixime was performed by using various solvents. The solvents include water, methanol, ethanol, acetonitrile, 0.1N hydrochloric acid (0.1N HCl), 0.1N sodium hydroxide (0.1N NaOH) and chloroform.

Determination of λmax

Preparation of Stock Solution

Standard stock solution of cefixime was prepared by dissolving 10mg of cefixime in 10ml of 0.1N HCl which gives 1000µg/ml. One ml of this stock solution was taken and was diluted up to 10ml by using 0.1N HCl (solvent) to produce a concentration of 100µg/ml solution.

Preparation of Working Solution

From the above stock solution 1ml was transferred into 10ml volumetric flask and volume was made up to the mark with 0.1N HCL to make 10µg/ml. Then the sample was scanned with UV-Vis Spectrophotometer in the range 400-200nm against 0.1N HCl as blank and the wavelength corresponding to maximum absorbance was noted at 283nm and 303nm for zero order & first order derivative respectively [fig.2, 3 & 4].

Preparation of Calibration Curve

From the above stock solution (100µg/ml) further dilution were made and the volume was make up to 10ml using 0.1N HCl to produce 8µg/ml, 10µg/ml,12µg/ml,14µg/ml and 16µg/ml solutions respectively. Then the construction of calibration curve was showed a straight line [in fig.5 (a) & (b)]. The correlation coefficient was found to be 0.999 & 0.999 for zero order and first order derivative respectively.

Method Validation[3]

Validation is a process of establishing documented evidence, which provides a high degree of assurance that a specific activity will consistently produce a desired result or product meeting its predetermined specifications and quality characteristics[3].

The validation for UV method development was performed using parameters like Linearity, Accuracy, Precision, Robustness, Ruggedness, and Limit of detection (LOD), Limit of quantification (LOQ)[3].

Linearity

The samples were scanned in UV-VIS Spectrophotometer against 0.1N HCl as blank. It was found that the selected drug shows linearity between the ranges of 8-16µg/ml (Table .no.1 - 3).

Table 1. Summary of Validation.

PARAMETER	RESULT (Zero order derivative at 283nm)	RESULT (1st derivative Absorbance at 303nm)
Range	8-16µg/ml	8-16µg/ml
Linear regression equation	Y=0.037x+0.011	Y=0.001x+0.00006
Linearity indicated by correlation coefficient	0.999	0.999
Precision indicated by %RSD	0.86% ± 0.0041	0.647 ± 0.00009
Limit of Detection	1.91µg/ml	0.001105µg/ml
Limit of Quantification	5.79µg/ml	0.00335µg/ml
Robustness indicated by %RSD	0.48% ± 0.0001	0.59% ± 0.00007
Accuracy indicated by % recovery	99.69-100.49%	99.28-102.4%
Specificity indicated by % recovery	100.21% ± 1.21	102.82% ± 0.19
Assay	101.47% ± 0.68	102.60% ± 0.69

Illustrations: Tables
Validation: Table for Linearity.

Table 2. Linearity.

Concentration (µg/ml)	0º Devt. Abs (283nm)	1st Devt. Abs (303nm)
8	0.3184	0.0100
10	0.3893	0.0123
12	0.4644	0.0148
14	0.5398	0.0174
16	0.6224	0.0199

Table 3. Optical characteristics.

Optical characteristics	0? Devt Abs (283nm)	1st Devt Abs(303nm)
Beer's Law limit (µg/mL)	8-16 µg/ml	8-16 µg/ml
Molar extinction coefficient ($l\,mole^{-1}\ c.m^{-1}$)	172	-
Correlation coefficient	0.999	0.999
Regression equation (Y*)	0.037x + 0.011	0.001x + 0.00006
Slope (a)	0.037	0.001
Intercept (b)	0.011	0.00006

Accuracy

Recovery study was performed at 80%, 100% and 120% levels in triplicate. The recovery results showed that the proposed method has an acceptable level of accuracy for cefixime which is from 80% - 120% of test concentration is form 99.69-100.49% (Table no. 4).

Table 4. Accuracy.

No.of preparations	Concentration (µg/lml) Formulation	Pure Drug	0º order Devt *%Recovery	%RSD	1º order Devt *%Recovery	%RSD
80%	10	8	99.69	0.069	99.28	0.187
100%	10	10	100.49	0.007	100.84	0.009
120%	10	12	99.83	0.1	102.4	0.097

Precision

Precision of the method was demonstrated by intraday and interday variation studies. In intraday variation study 6 different solutions of same concentration 12µg/ml were analyzed 3 three times in a day and the absorbance is noted. From the absorbance result mean, standard deviation and %RSD was calculated (Table no. 5).

Table 5. Precision: Repeatability.

Concentrations (µg/ml)	0º Order Devt. Abs.	1st Devt. Abs.	0º Order Devt. Statistical Analysis	1st Derivative Statistical Analysis
12	0.4726	0.0152	Mean = 0.4733	Mean = 0.01518
12	0.4748	0.0152		
12	0.4665	0.0150		
12	0.4744	0.0152	SD = 0.004111	SD = 0.000098
12	0.4744	0.0152	%RSD = 0.8686	%RSD=0.64755
12	0.4772	0.0153		

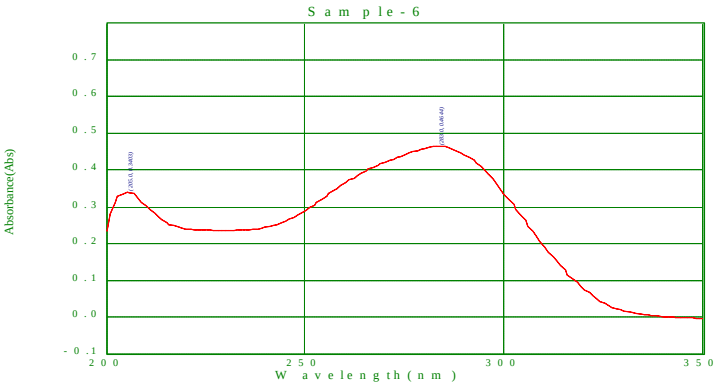

Fig:-2 lmax of Cefixime at 283nm (12µg/ml).

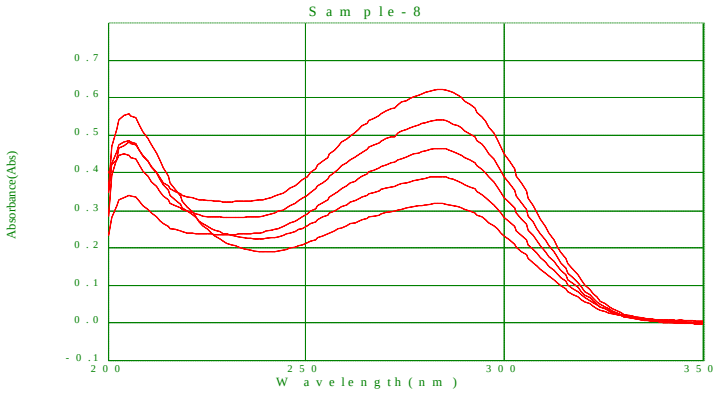

Fig:-3 Linearity curve (8-16 µg/ml).

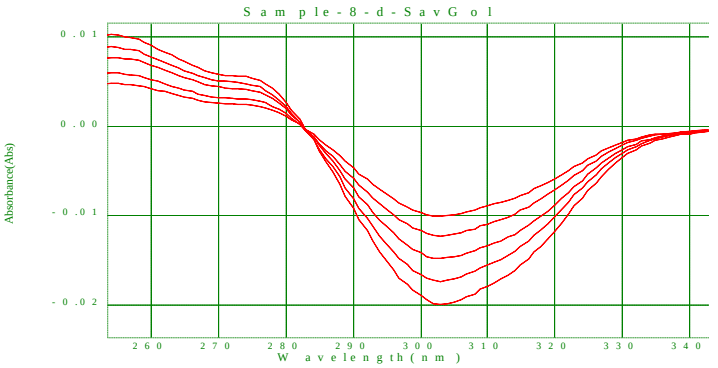

Fig:-4 lmax of Cefixime at -303nm for 1st order derivative.

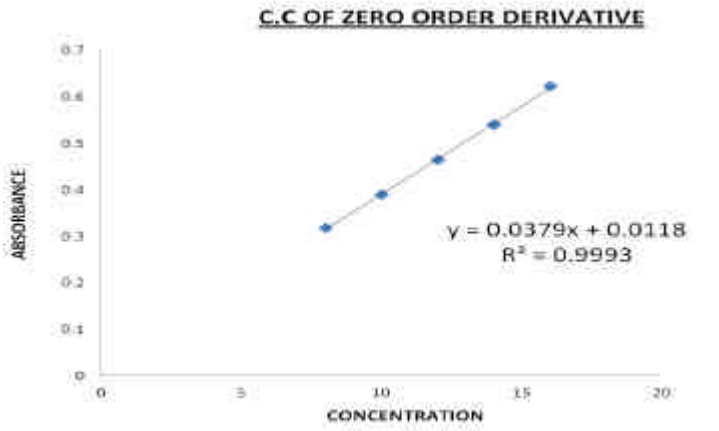

Fig:-5(a) Calibration curve of Cefixime at 283nm (0º derivative).

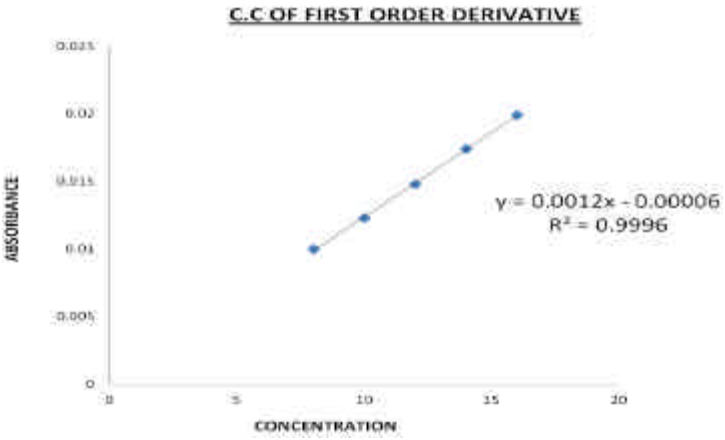

Fig:-5(b) Calibration curve of Cefixime-at 303nm (1st derivative).

In the interday variation studies, solution of same concentration 12µg/ml were analyzed three times for the three consecutive days and the absorbance result mean, standard deviation and %RSD was calculated and given in (Table no.6)

Table 6. Intra-Inter assay Precision.

PRECISION	SAMPLE NO.	CONC (µg/ml)	0º Order Devt. S.D	AVERAGE %RSD	1st Order Devt. S.D	AVERAGE %RSD
INTRA DAY	1	12	0.00097		0.0001	
	2	12	0.000706	0.2370	0.0001	0.6463
	3	12	0.00085		0.0005	
INTER DAY	1	12	0.0087	1.877%	0.00015	0.4707%
	2	12	0.0095		0.00018	
	3	12	0.015		0.0025	

Specificity

10mg of cefixime was spiked with 50% (5mg), 100% (10mg), and 150% (15mg) of excipient (Magnesium Stearate) and the sample was analysed for % recovery of cefixime (Table no.7).

Table 7. Test for Specificity.

Sample No.	Excipient Conc. (%)	Cefixime Input (mg)	0º Order Devt. Recovered (µg)	*Recovered (%)	1st Order Devt. Recovered (µg)	*Recovered (%)	0º Order Devt. S.D	%RSD	1st Order Devt. S.D	% RSD
1	50%	10	11.89		12.31					
2	100%	10	11.99	100.21%	12.33	102.82%	1.21	1.21	0.19139	0.18613
3	150%	10	12.8		12.36					

Robustness

Robustness of the method was determined by carrying out the analysis under different temperature condition i.e. at room temperature and at 180c. The respective absorbances of 12µg/ml were noted and the result was indicated as %RSD (Table no.8).

Table No. 8: Test for Robustness & Ruggedness.

METHOD	CONDITION	CONC (µg/ml)	0º Order Devt. SD	%RSD	1st Order Devt. SD	%RSD
Robustness	Analyst-1	12	0.000083	1.2970	0.0000983	0.6478
	Analyst-2	12	0.000121	1.8710	0.00007527	0.4862
Ruggedness	Room Temperature	12	0.000121	1.8710	0.00007527	0.4862
	Temp. 18ºC	12	0.000122	1.8345	0.00117	0.00012

Ruggedness

Ruggedness of the method was determined by carrying out the analysis by different analyst and the respective absorbance of 12µg/ml was noted. The result was indicated as %RSD(Table no.8).

Limit of Detection (LOD)

LOD was determined by preparing solutions of lower concentrations from Linearity range (8µg/ml). (Table no.1).Equation shown below[4].

LOD = 3.3 × S.D / Slope

Limit of Quantification (LOQ)

The LOQ was calculated using the formula involving standard deviation of response and slope of calibration curve (Table no.1).

Equation shown below[4]

LOQ = 10 × S.D / Slope

Assay: Table No. 9: Analysis of Cefixime by proposed method.

Tablet	Company Name	Labeled claim (mg)	Amount found (mg)	% Label claim (± S.D) (n=3)
HIFEN-200DT	Hetero Healthcare Ltd	200	202.94	100.75 ± 0.68

Assay of Cefixime Tablet (HYFEN-200DT)

A quantity of powder equivalent to 50mg of cefixime was taken in a 50ml volumetric flask and it was dissolved and diluted up to the mark with the 0.1N HCL. The resultant solution was ultra-sonicated for 45 minutes. The solution was then filtered using Whatmann filter paper No.40. From the filtrate, appropriate dilutions were made in 0.1N HCl to obtain the desired concentration (12µg/ml). This solution was then analysed in UV and the result was indicated by % purity given in Table 1.

RESULTS AND DISCUSSION

The developed method was found to be precise as the %RSD values for intra-day and inter-day were found to be less than 2%. Good recoveries (99.69-100.49% & 99.28-102.4% for zero order and 1st order derivative respectively) of the drug were obtained at each added concentration, indicating that the method was accurate. The method was also found to be specific indicated by the % recoveries ranging from 98.2% to 101.2%. The LOD and LOQ were found to be in sub-microgram level indicating the sensitivity of the method. The method was also found to be robust and rugged as indicated by the %RSD values which are less than 2%. The results of Assay show that the amount of drug was in good agreement with the label claim of the formulation as indicated by % recovery (101.47% & 102.60% for zero order and 1st order derivative respectively). Summary of validation parameters of proposed spectrophotometric method is shown in Table no.1

REFERENCES

1. http://www.drugbank.ca/drugs/DB00218.
2. http://www.medlineindia.com/cefixime, retrieved on 25/12/2009
3. ICH, Q2 (R1) validation of analytical procedures: text and methodology, International conference on harmonization; Nov.1996.
4. Beckett AH and Stenlake JB: UV-visible Spectrophotometry Practical Pharmaceutical Chemistry, C.B.S.Publishers, Delhi, 4th edition **2001**, Part-II: 285-297.

5. Vishal Shah and Hasumati Raj,Development and Validation of Derivative Spectroscopy Method For Simultaneous Estimation Of cefixime trihydrate and azithromycin dehydrate in Combined dosage Form, IJPSR (2012), Vol. 3, Issue 06.
6. Ashok Kumar, Lalit Kishore, Anroop Nair, Navpreet Kaur, Estimation of cefixime and ofloxacin in its pharmaceutical dosage form by spectrophotometric methods, Journal of Pharmacy Research 2011,4(6),1864-1866.
7. Ronak K. Patel, Rajesh R. Parmer, Vishnu M. Patel, Dushyant A. Shah , Method Development and Validation Of Cefixime and Moxifloxacin In Pharmaceutical Dosage Form by UV spectrophotometric method, IJPRBS, 2012: Volume1 (2):81-93.
8. Devika G.S, M. Sudhakar1and J. Venkateshwara Rao, Validated TLC Densitometric method for the quantification of Cefixime Trihydrate and Ornidazole in bulk drug and in tablet dosage form, Scholars Research Library Der Pharma Chemica, 2010, 2(6): 97-10.
9. K.Kathiresan, R.Murugan, M. Shahul Hameed, K.Gokula inimai and Taranath kanyadhara Analytical method development and validation of cefixime and dicloxacillin tablet by RP-HPLC ,Rasayan J. Chem , Vol.2, No.3 (2009), 588-592 .
10. K. Azhagesh Raj, Divya Yada, Deepthi Yada, C. Prabu, S. Manikantan DPLC etermination of cefixime trihydrate and cefuroxime axetile in bulk drug and pharmaceutical dosage forms by HPLC .
11. Ajit R. Wankhede, Prashant Y. Mali, Vikram Karne, Anubha R. Khale, C. S. Magdum, Development and Validation of RP-HPLC Method For Simultaneous Estimation of Cefixime and Cloxacillin in Tablet Dosage Form, International Journal of Pharmaceutical & Biological Archives 2010; 1(2): 317 – 320.
12. Kapil S. Khandagle, Santosh V. Gandhi, Padmanbh B. Deshpande, and Nilesh V. Gaikwad, A Simple and Sensitive RP-HPLC method for simultaneous estimation of cefixime and ofloxacin in combined tablet dosage form International Journal of Pharmacy and Pharmaceutical Sciences,ISSN- 0975-1491 Vol 3, Issue 1, 2011.
13. K. S. Khandagle, S. V. Gandhi, P. B. Deshpande, A. N. Kale, P. R. Deshmukh, High Performance Thin Layer Chromatographic determination of Cefixime and Ofloxacin in combined tablet dosage form J. Chem. Pharm. Res., 2010, 2(5): 92-96.

Source of support: Nil, Conflict of interest: None Declared