DEVELOPMENT AND VALIDATION OF UV SPECTROSCOPIC METHOD FOR THE ESTIMATION OF CEFIXIME IN BULK AND TABLET DOSAGE FORM

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Abstract:

A novel, simple, accurate and precise Zero order derivative spectroscopic method was developed and validated for the estimation of Cefixime in bulk and pharmaceutical dosage forms. The drug shows maximum absorption at 286nm in 0.05N Sodium Hydroxide solution. The Linearity was found to be in the concentration range of 2-10µg/ml and the correlation coefficient was found to be 0.9993 and it has showed good linearity, reproducibility, precision in this concentration range. The regression equation was found to be Y = 0.0531x-0.0068. The % RSD values were less than 2. The present method was accomplish the validation parameters according to ICH guidelines like accuracy, precision, linearity, range, ruggedness, limit of detection and limit of quantification. The developed method was successfully applied for the quantitative estimation of Cefixime in bulk and pharmaceutical dosage forms.

Keywords: *Cefixime, Zero order derivative spectroscopy, 0.05N Sodium hydroxide, validation, pharmaceutical formulations*

Introduction:

Cefixime is an antibiotic useful for the treatment of bacterial infections[1]. This includes oritis media, strep throat, pneumonia, urinary tract infections, gonorrhea and Lyme disease.It chemically known as(6~{R,7~{R})-7-[[(2~{Z})-2-(2-amino-1,3-thiazol-4-yl)-2-(carboxymethoxyimino)acetyl]amino]-3-ethenyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, is a third generation cephalosporin antibiotic which is effective against a variety of gram-negative bacteria, including *K.* pneumoniae, Escherichia coli (*E.* coli), and *H.* influenzae[2]. It has a molecular formula of $C_{16}H_{15}N_5O_7S_2$and molecular weight of 453.452 g/mol.

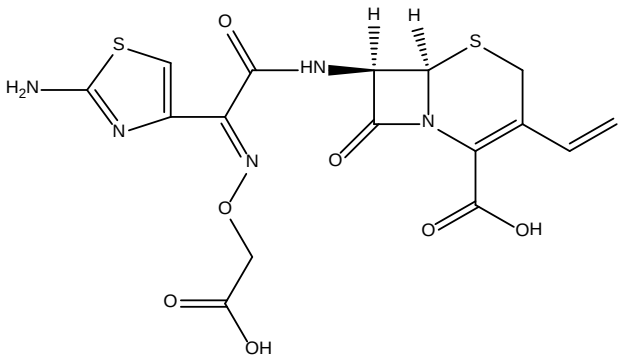

Fig.1: Chemical structure of Cefixime

Literature survey shows that there were few analytical methods have been reported for the determination of Cefixime in pure drug and pharmaceutical dosage forms by using UV spectrophotometric[3-9], HPLC[10-17] and HPTLC so far.

The aim of present work is to develop and validate a novel, rapid, simple, precise and specific Zero order derivative spectrophotometric method for estimation of Cefixime in bulk and tablet dosage form.

Materials and Method

Instrument:

UV-Visible double beam spectrophotometer, SHIMADZU (model UV – 1800) with UV probe software. All weights were taken on analytical balance.

Chemicals:

Cefixime pure form was obtained as gifted sample from pharma industry and its pharmaceutical dosage form Ceftas 10 tablets labelled claim 200mg were purchased from local pharmacy manufactured by Intas LTD.

Solvent:

0.05N Sodium hydroxide (prepared by dissolving 2g in 1000ml of distilled water).

Selection of analytical wavelength:

Appropriate dilutions were prepared for drug from the standard stock solution and using spectrophotometer solution was scanned in the wavelength range of 200-400 nm. The absorption spectra obtained and shows maximum absorbance at 286nm was showing in Fig.2. And Zero order overlain spectra of Cefixime at 286nm were shown in Fig.3.

Preparation of Standard stock solution:

Accurately weigh 100mg of Cefixime was transferred into 100ml volumetric flask and dilute with 0.05N Sodium hydroxide up to the mark. From this pipette out 10ml into 100ml volumetric flask and diluted with 0.05M Sodium hydroxide up to the mark, from this solution pipette out 0.2, 0.4, 0.6, 0.8 and 1.0ml into 10ml individual volumetric flask and add 0.05N Sodium hydroxide up to the mark, this gives 2, 4, 6, 8 and 10µg/ml concentrations.

Preparation of Sample solution:

Twenty tablets of Cefixime marketed formulations were weighed and powdered.100 mg of powdered cefixime equivalent to 20 tablets was transferred into 100ml volumetric flask then it was diluted with 0.05N Sodium hydroxide and made up to mark and the solution was filtered through Whatmans filter paper no.41. From this solution pipetted out 0.6 ml into 10ml volumetric flask and make up the 0.05N Sodium hydroxide, this gives 6µg/ml concentration.

Method validation:

The performedmethod was validated as per the ICH guidelines.

Results and Discussion:

Method: Zero order derivative spectroscopy.

Linearity:

The working standard solution were diluted serially with 0.05N Sodium hydroxide to obtain the range of 2-10µg/ml. a calibration curve for Cefixime was obtained by measuring the absorbance at the λmax of 286 nm and absorbance values are shown in Table.1 and Calibration graph were presented in Fig.3. Statistical parameters like slope, intercept, coefficient of correlation, and Sandell's sensitivity were determined and presented in Table.2.

Precision:

Precision of the method was studied as intra-day precision. Intra-day precision was determined by analysing the 2, 4, 6, 8 and 10µg/ml concentration for three times in same day. Inter-day precision was determined by analysing the same concentration daily for three days.(table-3).

Accuracy:

The accuracy of an analytical method say that closeness of test results obtained by that method to the true value. To assess the accuracy of the developed method, recovery studies were carried out at three level as 50%, 100% and 150%. In which the formulation concentration kept constant and varied pure drug concentration.(table-4).

Ruggedness:

Ruggedness was determined between different analysts. The value of %RSD was found to be less than 2 were shown in Table.5.

Limit of Detection and Limit of Quantitation:

The limit of detection is an individual analytical method is the smallest amount of analyte in a sample which can be reliably by the analytical method. The limit of quantitation is an individual analytical procedure is the smallest amount of analyte in a sample which can be quantitatively determined. LOD and LOQ were calculated using formula.

LOD = 3.3(SD)/S and LOQ = 3(LOD)

LOD and LOQ values of Cefixime were found to be 0.0290µg/ml and 0.0870µg/ml.

Conclusion:

The present analytical method was validated as per ICH guidelines and met the acceptance criteria. It was concluded that the develop analytical method was simple, specific, accurate, economical and sensitive and can be used for routine analysis of Cefixime in bulk drug and in pharmaceutical dosage form.

Tables:

Table.1: Results of calibration curve at 286nm by Zero order Spectroscopy.

SL. NO	**Concentration in µg/ml.**	**Absorbance ± Standard deviation****
1	0	0
2	2	0.093±0.00816
3	4	0.201±0.003651
4	6	0.312±0.00238
5	8	0.424±0.002887
6	10	0.523±0.003958

**Average of six determinations

Table.2: Regression parameters for Cefixime by Zero order spectroscopy.

Regression parameters	**Cefixime**
Range	2-10
λ_{max}(nm)	286
Regression Equation	Y= 0.0531x-0.0068
Slope(b)	0.0531
Intercept(a)	0.0068

Correlation Coefficient $(R)^2$	0.9993
Sandell's Sensitivity	0.0192307692
Limit of detection(µg/ml)	0.290045
Limit of quantification(µg/ml)	0.087013

Table.3: Determination of precision results for Cefixime at 286nm by Zero order derivative spectroscopy.

Concentration (µg/ml)	**Intra-day Absorbance ±SD***	**%RSD****	**Inter-day Absorbance ±SD***	**%RSD****
2	0.093±0.000816	0.877	0.093±0.000816	0.877
4	0.198±0.002449	1.236	0.204±0.001633	0.800
6	0.310±0.001247	0.402	0.313±0.002494	0.796
8	0.422±0.001633	0.386	0.426±0.002449	0.574
10	0.520±0.0017	0.326	0.525±0.00419	0.798

*Average of three determinations, **percentage relative standard deviation.

Table.4: Determination of Accuracy results for Cefixime at 286nm by Zero order derivative spectroscopy.

Spiked levels	**Amount of Sample (µg/ml)**	**Amount of Standard (µg/ml)**	**Amount Recovered**	**%Recovery ±Standard deviation***	**%RSD****
50	6	3	8.97	99.73±0.377212	0.378
100	6	6	11.94	99.51±0.261279	0.262

150	6	9	14.96	99.81±0.220958	0.221

*Average of three determinations, **percentage relative standard deviation.

Table.5: Determination of Ruggedness results for Cefixime at 286nm by Zero order spectroscopy

Absorbance	**Analyst-1**	**Analyst-2**
Mean absorbance	0.312	0.310
Standard deviation*	0.003	0.00152
%RSD**	0.961	0.491

*Average of three determinations, **percentage relative standard deviation.

Figures:

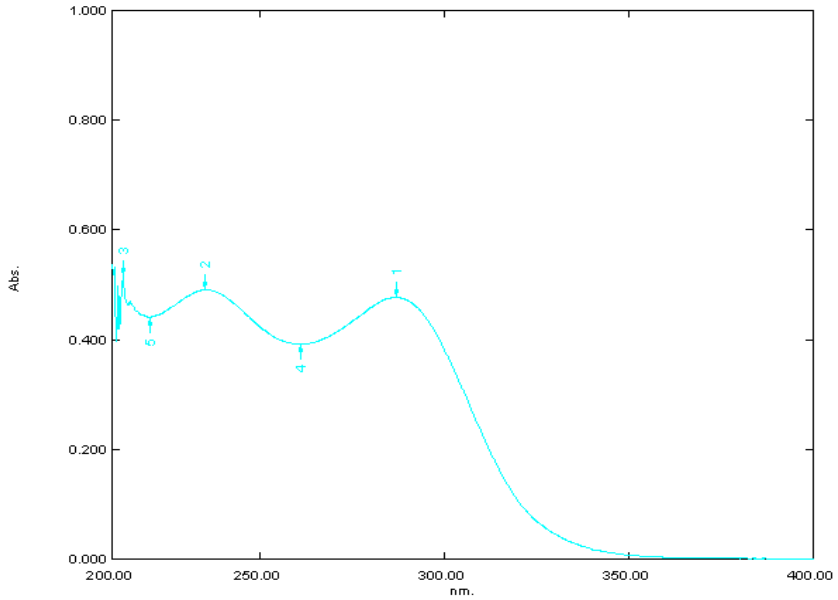

Fig.2: Zero order spectrum of Cefixime at 286nm

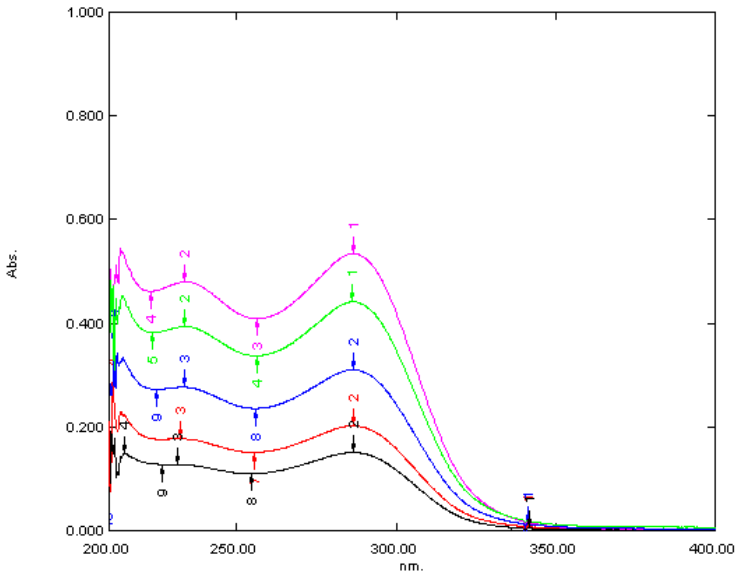

Fig.3: Zero order overlain spectra of Cefixime showing absorbance at 286nm

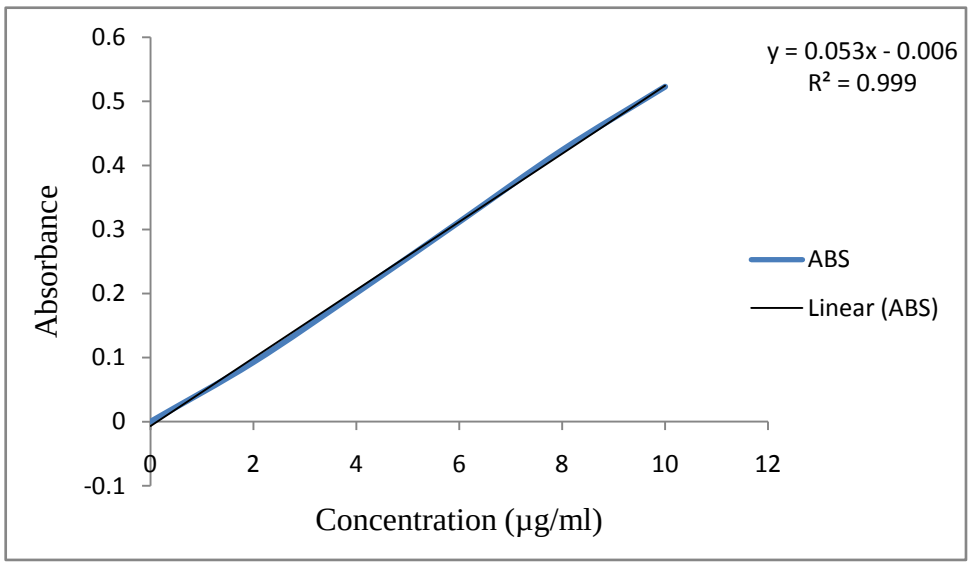

Fig.4: Calibration curve of Cefixime by Zero order spectroscopy

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