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RESEARCH ARTICLE

Spectrophotometric Method for Degradation Study of Cefixime Trihydrate

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ABSTRACT

Spectrophotometric method for degradation study of cefixime trihydrate was described. The ultra violet spectrum of both acidic and basic degraded product was found to substantial difference from pure drug. The extent of degradation can be calculated by comparing the decrease in absorbance at selective wavelength. The solution which was totally degraded in NaOH did not show any absorbance at 287nm in zero order spectrums. So the decrease in absorbance at 287nm was measure of extent of degradation in NaOH. The percentage degradation for each interval was calculated by comparing the decrease in absorbance with untreated drug solution. In case of acidic degradation there was some interference at 287nm. In first order derivative there was substantial decrease in absorbance at 303nm. So the 303nm was selected for calculation of extent of degradation in acidic condition. The 98.52% of drug is degraded in 0.5hr if heated with 0.1N sodium hydroxide at 80^0c. In 0.01N sodium hydroxide it is somewhat stable and only 54.25% of drug is degraded in 8hr at 80^0c.The degradation is somewhat slower in acidic conditions as 28.08% of drug is degraded if heated with 0.1N hydrochloric acid at 80^0c for 7hr. The 67.42% degradation observed in 1N hydrochloric acid at 80^0c after 7hr. The relative standard deviation (RSD) of both alkaline and acidic degradation was found to be less than 2% which indicate that method is reproducible. The LOD and LOQ for cefixime was found to be 0.028, 0.039 and 0.092, 0.128 µg ml^{-1} at 287nm and 303nm respectively indicates the method is sensitive.

Keywords: Cefixime trihydrate, Spectroscopy, Degradation, First order kinetics.

1. INTRODUCTION

The study of degradation products and impurities is necessary to improve the quality of active ingredient and its dosage forms. Various guidelines and guidance are available for control of impurities and degradation products of API's. The ICH guideline Q1A (R2) emphasizes that the testing of those features which are susceptible to change during storage and are likely to influence quality, safety and efficacy of the drug substance which comes under stability study. The present work based on development of suitable, specific and sensitive analytical method for one of the antibiotic drug. The literature survey has been done for analysis of impurity and degradation product of various antibiotics. Penicillin and Cephalosporin was found to be a ring opening degradation product because of presence of lactam and amide linkage. There are very few reported methods for analysis of degradation product and impurities of Cefixime trihydrate and is selected for the study. Study of extent of drug degradation in the acidic and alkaline medium using suitable analytical method is the part of work.

2. EXPERIMENTAL:

2.1. Apparatus

The instrument used for the present study was PC based Jasco V-530 UV-Visible double beam spectrophotometer with 1 cm matched pair quartz cell and spectral bandwidth of 2 nm.

2.2. Reagents and materials:

Cefixime trihydrate was obtained as a gift sample from Cipla, Vapi, India. Acetonitrile were purchased from Loba

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fine, India. Double distilled water was used throughout the experiment.

2.3. Preparation of standard drug solution:

Standard stock solution containing Cefixime Trihydrate was prepared by dissolving 10 mg of Cefixime Trihydrate in few ml of methanol, sonicated for 10 minutes and then final volume of the solutions was made up to 10 ml with methanol. 1ml of this solution was further diluted up to 10ml with distilled water to get stock solution of 100 µg ml^{-1}.

2.4. Selection of method and wavelength for degradation study:[1]

The zero order UV spectrums of cefixime showed maximum absorbance at 287nm and first order UV spectrum at 303nm. The solution which was totally degraded in NaOH did not show any absorbance at 287nm in zero order spectrums. So the decrease in absorbance at 287nm was measure of extent of degradation in NaOH. In case of HCl degradation there was substantial absorbance at 287nm in zero order spectrums and there was no sharp peak which can measure extent of degradation. But first order spectrum of HCl degraded solution shows sharp peak and substantial decrease in absorbance at 303nm. The overlain zero order spectrum and first order spectrum of cefixime, NaOH degraded and HCl degraded respectively is showed in Fig. No. 1 to Fig. No. 4.

2.5. Linearity study of drug at selected wavelength:

In to a series of 10 ml volumetric flasks, 0.4 to 1.4 ml of drug stock solution (100 µg/ml) was pipette and final volume of the solutions was made up to 10 ml with water. These solutions were scanned at 200-400nm and the absorbance at 287nm was measured and plotted against concentration which is shown in Fig. No.05. The same spectrums were converted in to first order derivative and the absorbance at 303 nm was measured and plotted against concentration which is shown in Fig. No. 06.

2.6. Forced Degradation Study: 2, 3, 4

2.6.1 Alkaline degradation study:

The alkaline degradation was done against 0.1N sodium hydroxide and 0.01N sodium hydroxide.

Procedure:

Accurately weighed 50mg of Cefixime Trihydrate was dissolved in 5ml of 0.1N sodium hydroxide and 0.01N sodium hydroxide respectively in 50ml of volumetric flask and volume made up to 50ml with water. These solutions were placed in 100ml of two necked round bottom flask and reflux at 80^0c in the thermostatically controlled heating mental. Initially 1ml of the solution was withdrawn for study and then it was exposed to reflux. The 0.1ml solution was withdrawn at the interval of 0.5hr up to 8hr. It was then diluted up to 10ml with water and measures the absorbance of a solution at 287nm. The extent of degradation was calculated by comparing the concentration remaining after each interval of degradation.

2.6.2 Acidic degradation study:

The acidic degradation was done against 0.1N hydrochloric acid and 1N hydrochloric acid.

Procedure:

Accurately weighed 50mg of Cefixime Trihydrate was dissolved in 5ml of 0.1N hydrochloric acid and 1N hydrochloric acid respectively in 50ml of volumetric flask and volume made up to 50ml with water. These solutions were placed in 100ml of two necked round bottom flask for reflux at 80^0c in the thermostatically controlled heating mental. Initially 1ml of the solution was withdrawn for study and then it was exposed to reflux. The 0.1ml solution was withdrawn at the interval of 1hr up to 7hr. It was then diluted up to 10ml with water and measures the absorbance of a solution at 303nm by first order derivative. The extent of degradation was calculated by comparing the concentration remaining after each interval of degradation.

2.7. Method validation: 5,6,7,8

The method was validated according to ICH Q2B guidelines for validation of analytical procedures in order to determine the linearity, sensitivity, precision and accuracy for the analyte . Results are shown in Table No. 01 to 06**.**

Recovery studies:

Accuracy of analysis was determined by performing recovery studies by spiking different concentrations of pure drug in the preanalyzed tablet sample. Results of recovery studies indicated that the method is rapid, accurate and reproducible shown in Table. No. 7.

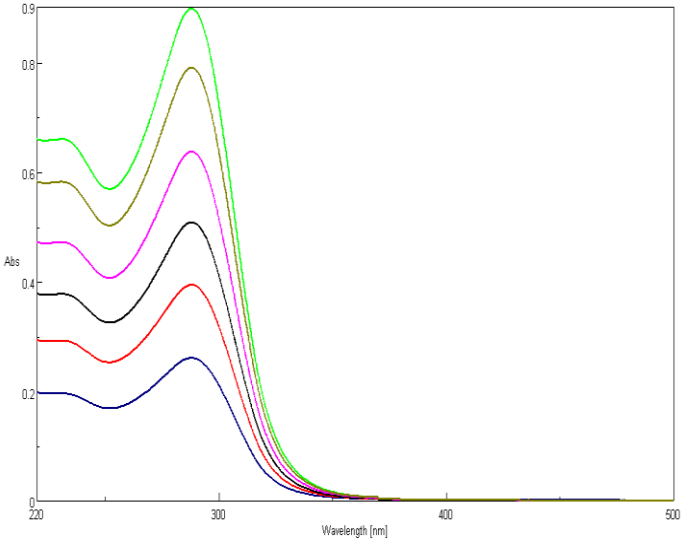

Fig. No. 1. Overlain zero order spectra of Cefixime

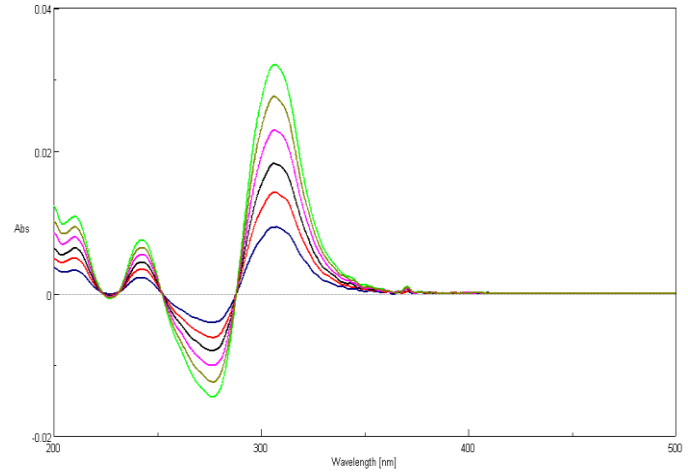

Fig. No. 2. Overlain first order spectra of Cefixime

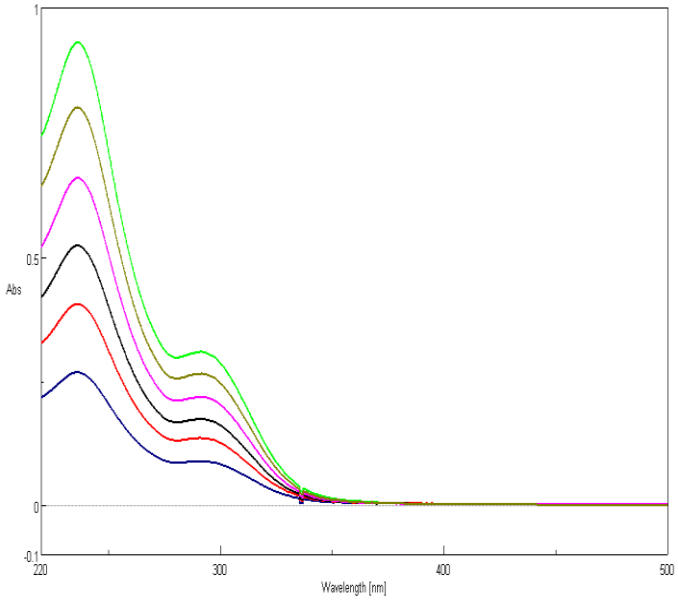

Fig. 3. Overlain first order spectra of alkaline degradation

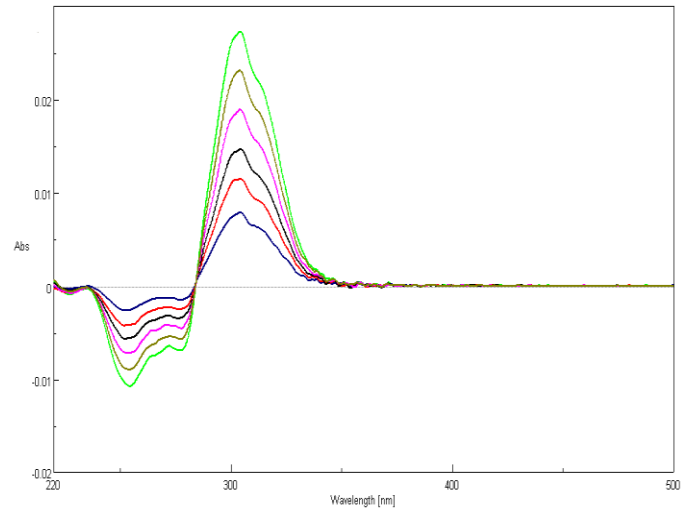

Fig. No. 4. Overlain first order spectra of acid degradation

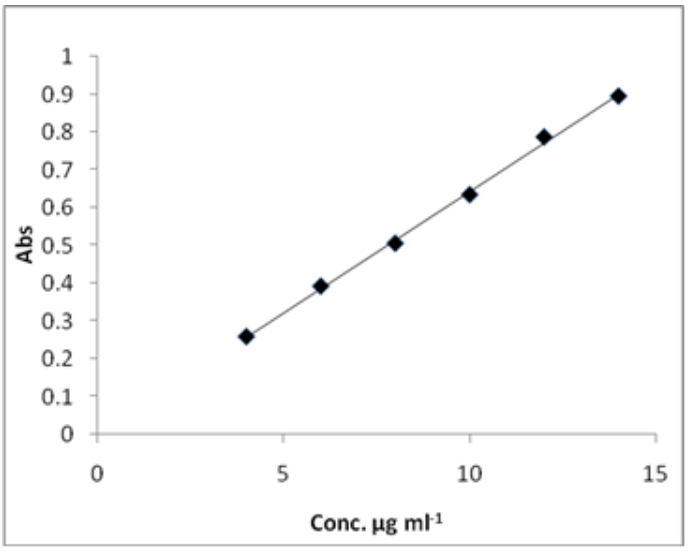

Fig No. 5: Linearity of Cefixime at 287 nm

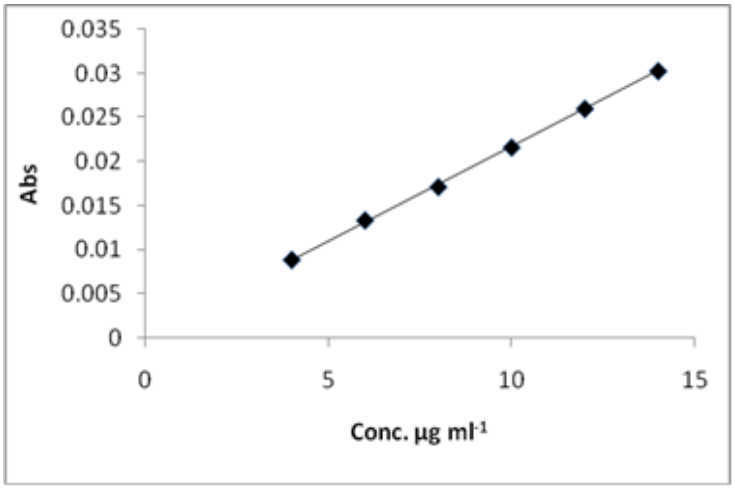

Fig. 6. Calibration plot of Cefixime at 303nm

Sr. No.	Concentration (µg ml^{-1})	Absorbance
1.	4	0.2598
2.	6	0.3933
3.	8	0.5065
4.	10	0.6355
5.	12	0.7881
6.	14	0.8962
Regression Equation Data For Cefixime, Y = A + B*C		
Slope (B)	0.06422	
Intercept (A)	0.00192	
Correlation coefficient	0.99920	

Table 1: Linearity of Cefixime at 287 nm
Where C is the concentration in µg ml^{-1} and Y is the absorbance

Sr. No.	Concentration (µg ml^{-1})	Absorbance
1.	4	0.0088
2.	6	0.0133
3.	8	0.0171
4.	10	0.0216
5.	12	0.0260
6.	14	0.0303

Regression Equation Data For Cefixime, Y = A + B*C	
Slope (B)	0.002144
Intercept (A)	0.000218
Correlation coefficient	0.99979

Table No. 2: Linearity of Cefixime at 303 nm (first order derivative)
Where C is the concentration in µg ml^{-1} and Y is the absorbance.

Time interval	Degradation in 0.1N NaOH		Degradation in 0.01N NaOH	
	%*	R.S.D.	%*	R.S.D.
Initial	9.74	1.28	1.98	0.54
0.5hr	98.52	1.84	9.62	0.53
1.0hr	-	-	16.74	0.71
1.5hr	-	-	23.91	1.04
2.0hr	-	-	30.97	1.22
3.0hr	-	-	37.57	1.29
5.0hr	-	-	44.34	0.68
8.0hr	-	-	54.25	0.92

TableNo. 3: Degradation of Cefixime Trihydrate in NaOH

Time interval	Degradation in 0.1N HCl		Degradation in 1N HCl	
	%*	R.S.D.	%*	R.S.D.
Initial	1.54	0.71	2.11	1.41
1hr	4.01	0.73	12.06	1.8
2hr	7.4	1.82	23.52	1.18
3hr	11.11	1.56	33.78	1.42
4hr	15.12	1.13	39.96	1.56
5hr	17.43	1.71	49.92	1.38
6hr	24.07	1.82	59.57	1.7
7hr	28.08	2.06	67.42	1.38

TableNo.4:Degradation of CefiximeTrihydrate in HCl

Parameter	At 287nm	At 303nm
LOD µg ml^{-1}	0.028	0.039
LOQ µg ml^{-1}	0.092	0.128

Table No. 5: Sensitivity of method

Analyte	% Concentration estimated* (Mean ± S.D.)	R.S.D.
Cefixime	99.72 ± 0.89	0.89

Table No. 6: Results of analysis of laboratory samples
***Average of six determinations; S.D.,**
standard deviation; R.S.D., relative standard deviation

Analyte	% Concentration estimated* (Mean ± S.D.)	R.S.D.
Cefixime	99.45 ± 1.31	1.31

Table No. 7: Results of recovery study
***Average of nine determinations; S.D.,**
Standard deviation; R.S.D., relative standard deviation

3. RESULTS AND DISCUSSION:

The ultra violet spectrum of both acidic and basic degraded product was found to substantial difference from pure drug. The extent of degradation can be calculated by comparing the decrease in absorbance at selective wavelength. The solution which was totally degraded in NaOH did not show any absorbance at 287nm in zero order spectrums. So the decrease in absorbance at 287nm was measure of extent of degradation in NaOH. The percentage degradation for each interval was calculated by comparing the decrease in absorbance with untreated drug solution.

In case of acidic degradation there was some interference at 287nm. Hence it was converted in to first order derivative. In first order derivative there was substantial decrease in absorbance at 303nm. So the 303nm was selected for calculation of extent of degradation in acidic condition.

In the basic degradation study found that cefixime is more sensitive to alkaline hydrolysis. The 98.52% of drug is degraded in 0.5hr if heated with 0.1N sodium hydroxide at 80^{0}c. In 0.01N sodium hydroxide it is somewhat stable and only 54.25% of drug is degraded in 8hr at 80^{0}c.The degradation is somewhat slower in acidic conditions as 28.08% of drug is degraded if heated with 0.1N hydrochloric acid at 80^{0}c for 7hr. The 67.42% degradation observed in 1N hydrochloric acid at 80^{0}c after 7hr.

The relative standard deviation (RSD) of both alkaline and acidic degradation was found to be less than 2% which indicate that method is reproducible. The LOD and LOQ for cefixime was found to be 0.028, 0.039 and 0.092, 0.128 µg ml^{-1} at 287nm and 303nm respectively indicates the method is sensitive.

4. CONCLUSION:

The proposed spectrophotometric method for degradation study of cefixime trihydrate was quite accurate, precise,yield reproducible result and rugged.Moreover the method is economic, simple and rapid,hence can be employed for routine analysis in quality control laboratories.

5. ACKNOWLEDGEMENTS:

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Conflict of Interest: None Declared

