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

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ABSTRACT

A simple, precise, accurate, economical and reliable UV spectrophotometric method has been developed for the estimation of Cefixime trihydrate in bulk and its tablet dosage form. The drug shows maximum absorption (λmax) at 288 nm in methanol and obeys Beer's law in the concentration range of 2-10 µg/ml with correlation coefficient (R^2=0.999). The accuracy was found to be 98-99%. Limit of detection (LOD) and limit of quantification (LOQ) were found to be 0.042µg/ml and 0.096µg/ml respectively. The relative standard deviation was found to be <2.0%in all cases. The proposed spectrophotometric method was validated as per ICH Q2 (R1) guidelines. Statistical analysis proved that the method is repeatable and specific for the determination of the said drug. The proposed method can be used for the reliable quantification of cefixime trihydrate in bulk form and routine analysis of pharmaceutical formulations.

KEYWORDS

Cefixime trihydrate, UV Spectrophotometer and Method Validation.

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INTRODUCTION

Cefixime is a semi synthetic third generation cephalosporin antibiotic. It inhibits mucopeptide synthesis in the bacterial cell wall. Cefixime tablet is official in United States Pharmacopoeia (USP) and Indian Pharmacopoeia (IP)[1-3].

It is helpful in acute urinary tract infections, biliary tract infections, sinusitis, acute otitis media, peptic ulcer and many more[1,4-6]. Literature survey revealed that CFX has been estimated by spectrophotometric techniques[4-6], HPLC and HPTLC[7,8,9]. The aim of

present study is to develop and validate[10] simple, precise, accurate and sensitive UV Spectrophotometric method for estimation of Cefixime trihydrate in bulk and tablet dosage form.

MATERIAL AND METHODS

Instruments

All spectral and absorbance measurements were made on Shimadzu UV-visible double beam spectrophotometer- 1800 with 1 cm matched quartz cells. For weighing, a calibrated weighing balance (Shimadzu) of 1mg sensitivity was used.

Material

Pure standard Cefixime trihydrate was obtained as a gift sample from Maxkos Pharmaceuticals Pvt.Ltd. Solapur. Cefixime tablet was procured from the local market. Tablet containing Cefixime trihydrate equivalent to Cefixime 200 mg (Cefmax-200) was purchased from the market. Methanol of analytical grade was used as the solvent.

UV Spectroscopic Method

Solvent Selection

Solubility test of Cefixime trihydrate was performed by using various solvents like water, methanol, acetonitrile, 0.1N HCL. However, the drug is freely soluble in methanol. So, for a good result methanol was used as the solvent.

Preparation of Standard Stock Solution

The standard stock solution of Cefixime trihydrate (CFX) was prepared by transferring accurately weighed 10 mg of Cefixime trihydrate separately into 10 ml volumetric flask and dissolved in methanol. Then volume was made up to the mark by using methanol to give a concentration of 1000 µg/ml. From this, 1ml of the solution was transferred to a 10 ml volumetric flask and make up the volume with methanol to give a concentration of 100µg/ml, which was a standard stock solution and it was further diluted with methanol to get concentration of 10 µg/ml of Cefixime trihydrate (CFX).

Determination of absorption maxima

The prepared standard solution (10µg/ml) of CFX was scanned over a wavelength range of 200-400 nm in the UV-VIS spectrophotometer. It was observed that the drug showed maximum absorbance (λmax) at 288nm which was selected as the wavelength for detection.

Procedure for assay of Tablet Dosage Form

Twenty tablets (Cefmax-200) were weighed accurately and powdered. Powder equivalent to 200 mg Cefixime trihydrate was weighed and transferred to a 100 ml volumetric flask, dissolved in methanol and sonicated for 15 min. The volume was then made up to the mark using same solvent. Then it was filtered through 0.45 µ Whatman filter paper to remove some un-dissolved excipients. After filtration, from this filtrate 1 ml was taken and diluted to 10 ml with methanol which gives 200 µg/ml of CFX and further 1 ml was diluted to 10 ml with methanol to get a final concentration of 20µg/ml. Absorbance of this sample solution was recorded at 288 nm.

Method Validation

The developed method was validated as per ICH guidelines for the following parameters:

Linearity

From the 'Std stock CFX'solution (100µg/ml), 0.2, 0.4, 0.6, 0.8, 1 ml were transferred in a series of 10 ml volumetric flasks. The volume was made up to the mark with methanol to obtain conc. of 2, 4, 6, 8, 10µg/ml of CFX.

The absorbances of the spectra were measured at 288nm. The calibration curve was constructed by plotting the Absorbance of CFX v/s Conc. Of CFX and the correlation coefficient (r^2) of least square linear regression for CFX was calculated.

Range

The Range of the analytical method was decided from the interval between upper and lower level of calibration curve by plotting curve.

Accuracy

Recovery study was carried out by the standard addition method by adding a known amount of CFX to the pre-analyzed sample at three different concentration levels that is 80%, 100%, 120% of assay concentration and percent recovery were calculated. 5 ml from 20µg/ml of tablet solution was transferred to 3 different 10 ml volumetric flasks (labelled 80%, 100%, 120%) separately and 8, 10, 12µg/ml standard solution was added respectively and the volume was made up to the

mark with methanol. Absorbances were noted for these samples. Accuracy is reported as % recovery, which was calculated from the expression as equation given below:

% Recovery = Observed value / True value ×100

Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scattering) between a series of measurements obtained from multiple sampling of the same sample under the prescribed conditions. The precision of the method was determined in terms of repeatability and intra-day and inter-day precisions.

The Intraday precision of the developed UV method was determined by analyzing the six samples of same concentration (10µg/ml) for 3 times in a day and the absorbance was noted. From the absorbance result mean, standard deviation and % RSD was calculated.

Inter-day precision was determined similarly, but the analysis being carried out daily, for two consecutive days.

Repeatability

Repeatability of the method was determined by analyzing six samples of same concentrations of the drug (10µg/ml). Absorbance of each was measured.

Robustness

The robustness of the developed method is its capacity to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage. To determine the robustness of the method, the wavelength of analysis was changed and the absorbance was measured. The effect of detection wavelength was studied at ±5 nm.

Ruggedness

Ruggedness was determined by carrying out analysis by two different analysts and the respective absorbance was noted and the results were indicated as % RSD.

Limit of Detection (LOD)

Detection limit was determined based on the standard deviation of absorbance of same concentration that is a standard solution of CFX (10µg/ml) and LOD calculated by equation below:

$LOD = 3.3 \times (SD/S)$

Where, SD- standard deviation; S= slope of the curve

Limit of Quantification

Quantification limit was determined based on the standard deviation of absorbance of same concentration that is standard solution CFX (10µg/ml) and LOQ calculated by following equation:

$LOD = 10\times (SD/S)$

Where, SD= standard deviation; S= slope of Curve.

RESULTS AND DISCUSSION

Linearity

The linearity of this method was determined at ranges from 2-10µg/ml. The regression equation was found to be.

Accuracy

The accuracy of the analytical method for CFX was determined at 80%, 100% and 120% levels of standard solution. Absorbance was measured at 288 nm. Results were expressed in terms of % recoveries.

Precision

The precision (measurement of intra-day, inter-day, repeatability) results showed good reproducibility with the relative standard deviation (% RSD) below 2.0 %. This indicated that method was highly precise.

Preliminary Analysis of Cefixime trihydrate

Preliminary analysis of Cefixime trihydrate such as description, solubility was performed.

UV- Spectrophotometry for Cefixime trihydrate

CFX being UV absorbing has been successfully employed for its quantitative determination by UV Spectrophotometric method. Being soluble in methanol, stock solutions and working standards were prepared in methanol. The maximum wavelength of absorption of drug was determined by taking scan of the drug solution in the UV region (200-400 nm). The correlation of the standard curve for the drug was 0.999. The accuracy was found to be 98-99%. The proposed method showed absorption maxima at 288 nm and obeyed Beer's law in the concentration range of 2-10µg/ml. The limit of detection (LOD) was found to be 0.042µg/ml and limit of quantification (LOQ) to be

0.096µg/ml respectively. All statistical data prove validity of the proposed method, which can be applied for routine analysis of Cefixime trihydrate.

Assay of Tablet formulation

Amount of drug present in tablet formulation was calculated using equation *y= 0.046x+0.112* at 288 nm. Amount of Cefixime trihydrate was found to be 104.5 % of label claim. This method can be employed for routine analysis of Cefixime trihydrate.

Summary and conclusion

Summary of UV Spectrophotometric Method for Cefixime trihydrate.

Table No.1: Result of analysis of tablet dosage form

S.No	Drug	Label Claim (mg / tab.)	Amount found (mg)	% Drug found
1	CFX	200	209	104.5%

Table No.2: Linearity of Cefixime trihydrate

S.No	Conc.(µg/ml)	Absorbance
1	2	0.210
2	4	0.293
3	6	0.390
4	8	0.485
5	10	0.580
Regression equation: *Y=0.046X+0.112*		
R^2= 0.999		

Table No.3: Result for Accuracy

S.No	Drug	Amount present(µg/ml)	Level of addition (%)	Amount of standard drug added (µg/ml)	Amount Recovered (µg/ml	%Recovery
1	CFX	10	80	8	17.8	98.8
		10	100	10	19.2	96
		10	120	12	21.8	99.09

Intra-day Precision

Table No.4: Intra-day Precision

S.No	CFX	
	Concentration (µg/ml)	Absorbance
1	10	0.589
2	10	0.588
3	10	0.588
4	10	0.587
5	10	0.586
6	10	0.589
7	% RSD	0.18

Inter-day Precision

Table No.5: Inter-day Precision

S.No	CFX	
	Concentration (µg/ml)	Absorbance
1	10	0.588
2	10	0.589
3	10	0.590
4	10	0.591
5	10	0.589
6	10	0.588
7	% RSD	0.186

Repeatability

Table No.6: Repeatability Study

S.No	CFX	
	Concentration (µg/ml)	Absorbance
1	10	0.588
2	10	0.589
3	10	0.590
4	10	0.591
5	10	0.590
6	10	0.588
7	% RSD	0.193

Limit of Detection

Table No.7: For Limit of Detection

LOD (µg/ml)	Conc.
CFX	0.042µg/ml

Limit of Quantification

Table No.8: For Limit of Quantification

LOQ (µg/ml)	Conc.
CFX	0.096µg/ml

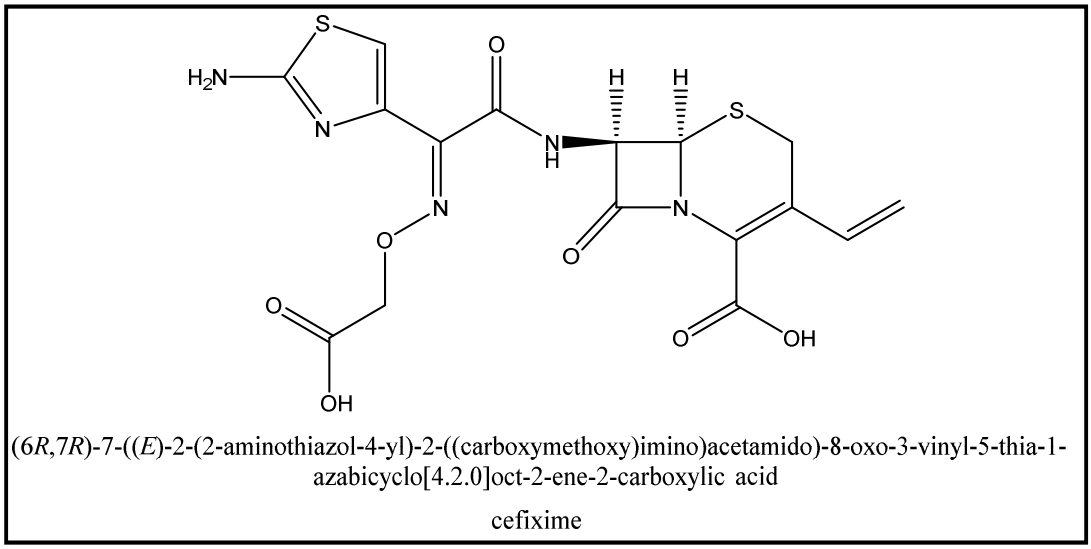
Robustness and Ruggedness

Table No.9: Result for Robustness and Ruggedness

S.No	Method	Condition	Conc.(µg/ml)	Abs.	%RSD
1	Robustness	Wavelength= 286nm	10	0.565	0.26
		Wavelength= 290	10	0.567	
		Wavelength=287	10	0.568	
2	Ruggedness	Analyst 1	10	0.583	0.262
		Analyst 2	10	0.585	
		Analyst 3	10	0.582	

Table No.10: For Summary

S.No	Parameters	CFX
1	Beer's Law limit (µg/ml)	2-10
2	Absorption maxima (nm)	288
3	Standard regression equation	*y= 0.046x + 0.112*
4	Correlation coefficient (R^2)	0.999
5	Accuracy	98.8-99.09%
6	Precision (% RSD) Repeatability	0.193
7	LOD (µg/ml)	0.042
8	LOQ (µg/ml)	0.096
9	Robustness (%RSD)	0.26
10	Ruggedness(%RSD)	0.262
11	Assay (%)	104.5



(6*R*,7*R*)-7-((*E*)-2-(2-aminothiazol-4-yl)-2-((carboxymethoxy)imino)acetamido)-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid

cefixime

Figure No.1: Structure of Cefixime

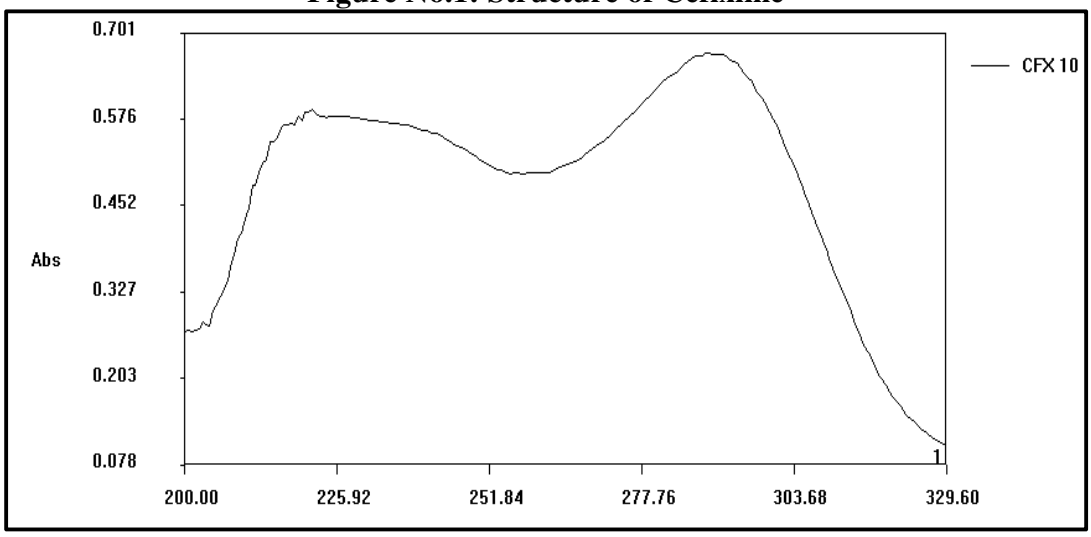


Figure No.2: Absorption maxima of CFX at 288nm

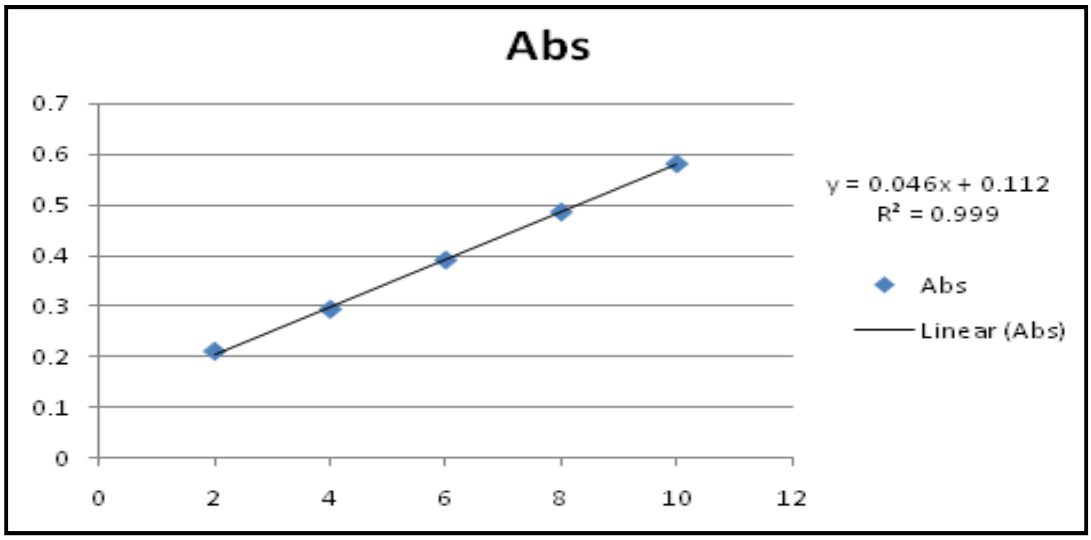


Figure No.3: Linearity of CFX

CONCLUSION

The UV-Spectrophotometric method was developed and it was found to be simple, accurate, precise, highly sensitive, reproducible and inexpensive. The proposed method was found suitable for determination of Cefixime trihydrate in API and its dosage form without any interference from the excipients. This method can be effectively applied for the routine analysis of Cefixime trihydrate in API. Its advantages are the low cost of reagents, speed and simplicity of sample treatment, satisfactory precision and accuracy.

ABBREVIATIONS

UV-Ultra Violet
API- Active Pharmaceutical Ingredient
CFX- Cefixime trihydrate
LOD- Limit of Detection
LOQ- Limit of Quantification

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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