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Development and validation of UV-Spectrophotometric method for determination of Cefuroxime Axetil in bulk and in Formulation

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Abstract

A simple, rapid, accurate and economical UV-spectrophotometric method has been developed for estimation of Cefuroxime axetil from bulk and pharmaceutical formulation. The λ_{max} of Cefuroxime axetil in 0.1N HCL was found to be 281 nm. The drug follows linearity in the concentration range 0.4 - 2 µg/ml with correlation coefficient value 0.998. The proposed method was applied to pharmaceutical formulation and % amount of drug estimated 99.19 % was found in good agreement with the label claim. The accuracy of the method was checked by recovery experiment performed at three different levels i.e., 80%, 100% and 120 %. The % recovery was found to be in the range 98.54%– 99.98%. The low values of % R.S.D. are indicative of the accuracy and reproducibility of the method. The precision of the method was studied as an intra-day, inter-day variations and repeatability. The % R.S.D. value less than 2 indicate that the method is precise. Ruggedness of the proposed method was studied with the help of two analysts. The above method was a rapid and cost-effective quality-control tool for routine analysis of Cefuroxime axetil in bulk and in pharmaceutical dosage form.

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Cefuroxime axetil, UV, validation, quantitative determination.

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1. Introduction:

Cefuroxime is chemically (6R, 7R) – 3 – carbamoyloxymethyl – 7 - [(Z)-2-(2-furyl) – 2 - (methoxyimino) acetamido] – ceph – 3 - em-4-carboxylic acid. Cefuroxime is official in Indian pharmacopoeia and United States of Pharmacopoeia.

It is the first of the series of alpha methoxyiminoacyl substituted cephalosporins that constitute most of the third generation agents available for clinical use. It is active against some beta lactamase strains that are resistant to cefamandole[1,2]. The literature survey revealed that various methods of analysis for cefuroxime alone or in combination with other drugs have been reported, which included, HPLC[3–6], electrokinetic[7], HPTLC[8] and spectrophotometric methods.[9]

Accordingly, the objective of this study was to develop and validate the first order derivative method for the estimation of Cefuroxime axetil in bulk and pharmaceutical formulation as per ICH guidelines [10].

2. Experimental:

2.1 Materials:

Cefuroxime axetil was a gift sample from Torrent Pharmaceutical Limited, Ahmedabad. All chemicals and reagents used were of analytical grade and purchased from Qualigens Fine Chemicals, Mumbai, India.

2.2 Preparation of standard stock solution:

Accurately weighed 10 mg of Cefuroxime axetil was transferred to 100 ml volumetric flask, dissolved in 20 ml 0.1N HCL by shaking manually for 10 min. The volume was adjusted with the same up to the mark to give final strength i.e. 100 µg/ml.

2.3 Selection of wavelength for analysis of Cefuroxime axetil:

Appropriate volume 0.2 ml of standard stock solution of Cefuroxime axetil was transferred into 10 ml volumetric flask, diluted to mark with 0.1N HCL to give concentration of 2µg/ml. The resulting solution was scanned in UV range (200 nm – 400 nm). In spectrum Cefuroxime axetil showed absorbance maximum at 281 nm (Fig. 2).

2.4 Validation of the method:

The method was validated in terms of linearity, accuracy, precision, and ruggedness.

2.4.1 Linearity study:

Different aliquots of Cefuroxime axetil in range 0.04-0.2 ml were transferred into series of 10 ml volumetric flasks and the volume was made up to the mark with 0.1N HCL to get concentrations 0.4, 0.8, 1.2, 1.6 and 2 µg/ml, respectively. The solutions were scanned on spectrophotometer in the UV range 200 - 400 nm. The spectrum was recorded at 281 nm. The calibration plot was constructed as Absorbance vs concentration (Fig. 3).

2.4.2 Accuracy:

To the preanalysed sample solutions, a known amount of standard stock solution was added at different levels i.e. 80%, 100% and 120 %. The solutions were reanalyzed by proposed method.

2.4.3 Precision:

Precision of the method was studied as intra-day and inter-day variations. Intra-day precision was determined by analyzing the 0.8, 1.2 and 1.6 µg/ml of Cefuroxime axetil solutions for three times in the same day. Inter-day precision was determined by analyzing the 0.8, 1.2 and 1.6 µg/ml of Cefuroxime axetil solutions daily for three days over the period of week.

2.4.4 Sensitivity:

The sensitivity of measurements of Cefuroxime axeti lby the use of the proposed method was estimated in terms of the Limit of Quanfication (LOQ) and Limit of Detection (LOD). The LOQ and LOD were calculated using equation LOD = 3.3 x N/B and LOQ = 10 x N/B, where, 'N' is standard deviation of the peak areas of the drugs (n = 3), taken as a measure of noise, and 'B' is the slope of the corresponding calibration curve.

2.4.5 Repeatability:

Repeatability was determined by analyzing 1.2 µg/ml concentration of Cefuroxime axetil solution for six times.

2.4.6 Ruggedness:

Ruggedness of the proposed method is determined for 1.2 µg/ml concentration of Cefuroxime axetil by analysis of aliquots from homogenous slot by two analysts using same operational and environmental conditions.

2.5 Determination of Cefuroxime axetil in bulk:

Accurately weighed 10 mg of Cefuroxime axetil was transferred into 100 ml volumetric flask containing 20 ml 0.1N HCL and volume was made up to the mark using same. Appropriate volume 0.3 ml of this solution was transferred to 10 ml volumetric flask and volume was adjusted to mark using distilled water. The resulting solution was scanned on spectrophotometer in the UV range 200 - 400 nm. The concentrations of the drug were calculated from linear regression equations.

2.6 Application of proposed method for pharmaceutical formulation:

For analysis of commercial formulation 5 ml of Cefuroxime axetil eye drop solution was taken in 100 ml volumetric flask and the volume was made up to the mark with 0.1N HCL to give 100µg/ml concentration. From this 1 ml was taken and transferred to 10 ml volumetric flask and volume was made up to the mark with distilled water to give 10 µg/ml concentration. It was scanned on spectrophotometer in the UV range 200 - 400 nm. The spectrum was recorded at 281 nm. The concentrations of the drug were calculated from linear regression equation.

3. Results and Discussion:

3.1 Method Validation:

The proposed method was validated as per ICH guidelines. The solutions of the drugs were prepared as per the earlier adopted procedure given in the experiment.

3.1.1 Linearity studies:

The linear regression data for the calibration curves showed good linear relationship over the concentration range 0.4-2.0 µg/ml for Cefuroxime axetil. Linear regression equation was found to be Y = 0.453 X + 0.0285 (r^2 = 0.998). The result is expressed in Table 1.

3.1.2 Accuracy:

The solutions were reanalyzed by proposed method; results of recovery studies are reported in Table 2 which showed that the % amount found was between 98.54% to 99.98% with %R.S.D. >2.

3.1.3 Precision:

The precision of the developed method was expressed in terms of % relative standard deviation (% RSD). These result shows reproducibility of the assay. The % R.S.D. values found to be less than 2, so that indicate this method precise for the determination of both the drugs in formulation (Table 3).

3.1.4 Sensitivity:

The linearity equation was found to be Y = 0.0317 X + 0.0047. The LOQ and LOD for Cefuroxime axetil were found to be 0.038 µg and 0.32 µg, respectively.

3.1.5 Repeatability:

Repeatability was determined by analyzing 1.2 µg/ml concentration of Cefuroxime axetil solution for six times and the % amount found was between 98% to 102% with % R.S.D. less than 2 (Table 4).

3.1.6 Ruggedness:

Peak area was measured for same concentration solutions, six times. The results are in the acceptable range for both the drugs. The results are given in Table 5**.** The result showed that the % R.S.D. was less than 2%

Determination of Cefuroxime axetil in bulk:

The concentrations of the drug were calculated from linear regression equations. The % amount found was between 99.17% to 100.43% (Table 6).

Application of proposed method for pharmaceutical formulation:

The spectrum was recorded at 281 nm. The concentrations of the drug were calculated from linear regression equation. The % amount found was between 98.36% to 101.31% (Table 7).

4. Conclusion:

This UV-spectrophotometric technique is quite simple, accurate, precise, reproducible and sensitive. The UV method has been developed for quantification of Cefuroxime axetil in tablet formulation. The validation procedure confirms that this is an appropriate method for their quantification in the plant material and formulation. It is also used in routine quality control of the raw materials as well as formulations containing this entire compound.

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Table 1: Linearity study of Cefuroxime axetil

Sr. no.	Concentration µg/ml	Absorbance* Mean ± S.D. (n=6)	% R.S.D.
1	0.4	0.149± 0.001	1.21
2	0.8	0.349± 0.002	1.63
3	1.2	0.507± 0.004	1.66
4	1.6	0.688± 0.006	1.83
5	2.0	0.886± 0.004	1.15

* average of five estimations

Table 2: Recovery studies

Pre-analyzed sample solution (µg/ml)	Amount of drug added (µg/ml) (n=3)	Amount recovered* (µg/ml) (n=3)	% Recovery	% R.S.D.
1.2	0	1.19	98.54	1.38
	0.09	1.28	99.98	1.40
	1.2	2.37	98.68	1.44
	1.4	2.56	99.54	1.33

*average of three estimates

Table 3: Precision studies

Component	Concentration (µg/ml)	Intra-day precision* (n=3)		Inter-day Precision* (n=3)	
		Conc. found	% R.S.D.	Conc. found	% R.S.D.
Cefuroxime axetil	0.8	0.0795	1.47	0.0792	1.43
	1.2	1.190	0.54	1.194	0.61
	1.6	1.595	1.24	1.590	1.13

*average of three estimates

Table 4: Repeatability studies

Component	Amount taken (µg/ml) (n=6)	Amount found* (%)	%R.S.D.
Cefuroxime axetil	1.2	99.63 ± 0.38	0.64

*average of six estimations

Table 5: Ruggedness studies

Component	Amount taken (µg/ml) (n=3)	Amount Found (%) *	
		Analyst I ±S.D.	Analyst II ±S.D.
Cefuroxime axetil	1.2	99.04 ± 1.3	98.90 ± 0.95

*average of six estimations

Table 6: Analysis of Cefuroxime axetil in bulk

Concentration (µg/ml)	Amount found (µg)	Amount found (%)
10	9.94737	99.18
	9.97368	99.56
	9.97368	99.56
	9.71053	99.17
	9.97368	99.56
	10.02632	100.43
Mean ± S.D.	9.93 ± 0.102	98.90 ± 1.71
% R.S.D.	1.73	1.73

Table 7: Analysis of formulation

Conc. (µg/ml)	Amount found (µg)	Amount found (%)
10	9.89474	98.44
	9.97368	99.56
	9.84211	98.36
	9.97368	99.56
	9.94737	99.12
	10.07895	101.31
Mean ± S.D.	9.95 ± 0.08	99.19 ± 1.34
% R.S.D.	1.35	1.35

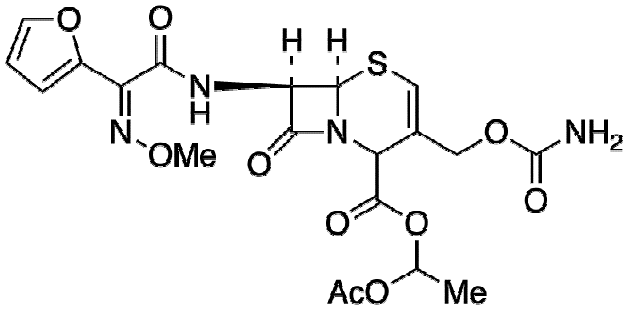

Figure 1. Chemical structure of Cefuroxime axetil

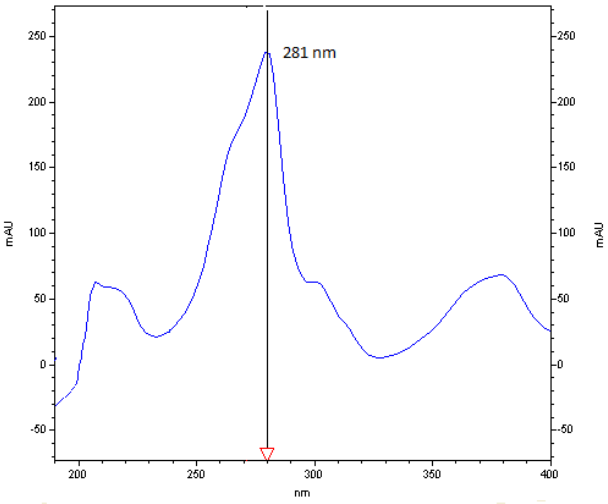

Figure 2: UV Spectrum of Cefuroxime axetilat 281 nm

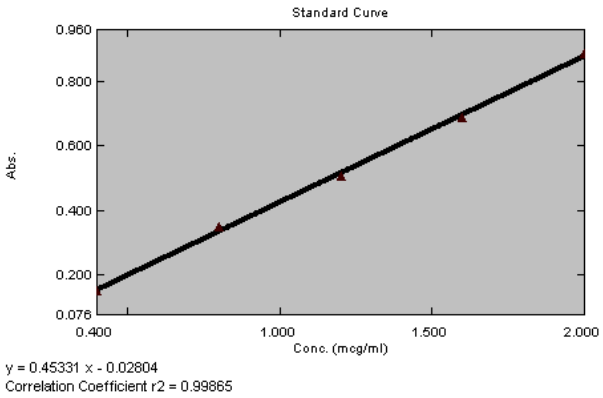

Figure 3: Calibration curve of Cefuroxime axetilat 281 n

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