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Research Article

Estimation of Cefdinir in Bulk Drug Using Area Under Curve Method

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Abstract

A simple, rapid, accurate and economical UV-Spectrophotometric method has been developed for estimation of Cefdinir from bulk and pharmaceutical formulation. The λ_{max} of Cefdinir in phosphate buffer pH7 was found to be 287 nm. The drug follows linearity in the concentration range 3 - 18 µg/ml with correlation coefficient value 0.999. The proposed method was applied to pharmaceutical formulation and % amount of drug estimated 98.00% - 102.00% 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 98.00% - 102.00%. The low values of % RSD 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 was 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 Cefdinir in bulk and in pharmaceutical dosage form.

Keywords: *Cefdinir; UV-Spectrophotometry; Area Under Curve; Validation*

Introduction

Chemically, cefdinir is 8-[2-(2-amino-1,3-thiazol-4-yl)-1-hydroxy-2-nitroso- ethenyl]amino-4 ethenyl-7-oxo-2-thia-6-n azabicyclo[4.2.0]oct-4-ene-5-carboxylic acid (Figure 1) [1]. It is a semi- synthetic, broad-spectrum, third-generation cephalosporin. The molecular formula of Cefdinir is $C_{14}H_{13}N_5O_5S_2$ with a molecular weight of 395.42. It has a broad spectrum of activity, good therapeutic action against susceptible Gram-positive and Gram- negative bacteria as having positive microbial activity, excellent efficacy, convenient dosing and favourable tolerability correlated with other antimicrobial agents [2-5]. A simple, inexpensive, selective, and rugged visible spectrophotometric would be more appropriate for the analysis of copied [6]. The spectrophotometric methods reported in the literature for the analysis of cefdinir are based on UV measurement, derivative spectrophotometric [7]. Hence, our study reports a simple, precise and economical UV- Spectrophotometric method for estimation of Cefdinir in capsule formulation. The method was validated according to ICH guidelines [8].

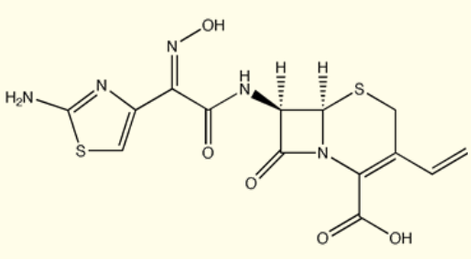

Figure 1: Chemical structure of Cefdinir.

Experimental Work

Material and Method

Cefdinir working standard was obtained as gift sample from Analytical solution. The drug was used without further purification. A capsule formulation containing 300 mg of Cefdinir was purchased from local market. An analytical grade solvent was used for the experiment.

Instrument

A double beam UV-VIS spectrophotometer (UV-2450, Shimadzu, Japan) connected to computer loaded with spectra manager software UV Probe with 10 mm quartz cells was used. The spectra were obtained with the instrumental parameters as follows: wavelength range: 200 - 400 nm; scan speed: medium; sampling interval: 1.0 nm; derivative mode: 1D (first order derivative, dA/dλ); band width (Δλ):10.0 nm; spectral slit width: 1 nm. All weights were taken on electronic balance (Model Shimadzu AUX 120).

Preparation of standard stock and working standard solution

The standard stock solution of Cefdinir was prepared by dissolving accurately weighed 10 mg of the drug in phosphate buffer pH7 and diluted to 100 ml with same solvent to obtain a final concentration of 3 µg/ml.

Method: Area under curve

The AUC (area under curve) method is applicable where there is no sharp peak or when broad spectra are obtained. It involves the calculation of integrated value of absorbance with respect to the wavelength between the two selected wavelengths λ1 and λ2. Area calculation processing item calculates the area bound by the

curve and the horizontal axis. The horizontal axis is selected by entering the wavelength range over which area has to be calculated. This wavelength range is selected on the basis of repeated observation so as to get the linearity between area under curve and concentration. The spectrum obtained of first order derivative was used to calculate AUC. The calibration curve was constructed by plotting concentration (3 - 18 µg/mL) versus AUC.

Validation of the Method

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

Linearity study

Different aliquots of Cefdinir in range 0.3 - 1.8 ml were transferred into series of 10 ml volumetric flasks and the volume was made up to the mark with buffer to get concentrations 3, 6, 9, 12, 15 and 18 µg/ml, respectively. The solutions were scanned on spectrophotometer in the UV range 200 - 400 nm. The two wavelengths 270 and 299 nm was selected for the determination of Area Under Curve (AUC). The calibration plot was constructed as Area Under Curve vs. concentration.

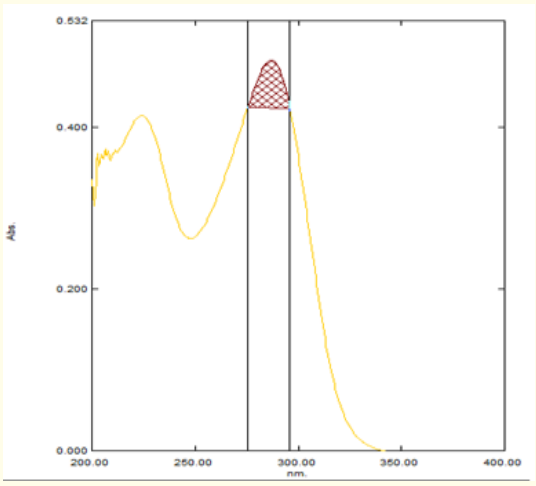

Figure 2: Area under curve spectrum of Cefdinir in Phosphate buffer pH 7 (270 - 299 nm).

Accuracy (% Recovery)

To the pre analyzed 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.

Precision

Precision of the method was studied as intraday and inter-day variations. Intra-day precision was determined by analyzing the 9, 12 and 15 µg/ml of Cefdinir solutions for three times in the same day. Inter-day precision was determined by analyzing the 9, 12 and 15 µg/ml of Cefdinir solutions daily for three days over the period of week.

LOD and LOQ (Sensitivity)

The sensitivity of measurements of Cefdinir by the use of the proposed method was estimated in terms of the Limit of Quantification (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.

Repeatability

Repeatability was determined by analyzing 9 µg/ml concentration of Cefdinir solution for six times.

Ruggedness

Ruggedness of the proposed method is determined for 9 µg/ml concentration of Cefdinir by analysis of dilution from homogenous slot by two analysts using same operational and environmental conditions.

Determination of Cefdinir in Bulk

Accurately weighed 10 mg of Cefdinir was transferred to a 100 ml volumetric flask and 50 ml phosphate buffer pH7 was added. After ultrasonic vibration for 15 minutes, the mixture was diluted up to mark with same solvent. The whole solution filtered using whatman filter paper no. 42. From filtrate correct dilution was taken in such a way that the final concentration is 9 µg/ml. The concentrations of the drug were calculated from linear regression equations. The resulting solution was scanned on a spectrophotometer in the UV range 200 - 400 nm. The spectrum was recorded at 287 nm.

Application of Proposed Method for Pharmaceutical Formulation

For analysis of commercial formulation 10 mg of Cefdinir capsule was transferred to a 100 ml volumetric flask and 50 ml phosphate buffer pH 7 was added. After ultrasonic vibration for 15 minutes, the mixture was diluted up to mark with water. The

whole solution filtered using whatman filter paper no. 42. From filtrate correct dilution was taken in such a way that the final concentration is 9 µg/ml. The concentrations of the drug were calculated from linear regression equations. The resulting solution was scanned on a spectrophotometer in the UV range 200 - 400 nm. The spectrum was recorded at 287 nm.

Results and Discussion

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.

Linearity studies: The linear regression data for the calibration curves showed good linear relationship over the concentration range 3 - 18 µg/ml for Cefdinir (Figure 3). Linear regression equation was found to be Y = 0.053x -0.002 (r^2 = 0.998). The result is expressed in table 1.

Concentration µg/mL	Absorbance[a] mean± SD (n = 6)	% RSD
3	0.1662 ± 0.0008	0.5034
6	0.3118 ± 0.0041	1.3106
9	0.4818 ± 0.0087	1.8058
12	0.6482 ± 0.0011	0.1690
15	0.7998 ± 0.0086	1.0697
18	0.9768 ± 0.0033	0.3426

Table 1: Linearity study of Cefdinir.
(n = no. of estimations)

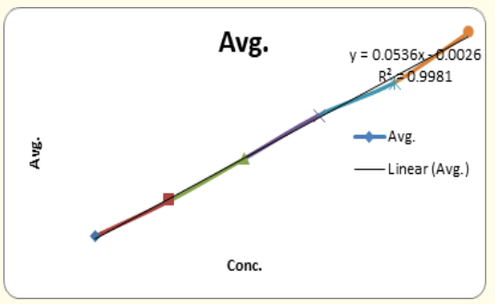

Figure 3: Calibration curve of Cefdinir.

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 98.00% to 102.00% with % R.S.D. > 2.

Drug	Initial amount (µg/mL)	Amount added (µg/mL)	Amount recovered (µg/mL, n = 3)	% Recovered	% RSD
Cefdinir	9	7.2	7.3760	102.8450	0.5005
	9	9	8.9542	99.4807	0.1007
	9	10.8	11.0219	100.0544	0.7504

Table 2: Recovery studies.
(n= no. of estimations)

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).

Component	Conc. (µg/mL)	Intra -day Precision[a] (n = 3)		Inter -day Precision[a] (n = 3)	
		Amt. found	% RSD	Amt. found	% RSD
Cefdinir	9	8.9214	0.1420	9.0409	1.0010
	12	11.9986	0.1670	12.2884	1.1062
	15	14.9071	0.1721	15.0528	1.3169

Table 3: Results of Precision studies.
[a]Average of three estimation

Sensitivity: The linearity equation was found to be Y = 0.053x - 0.002 (r^2 = 0.998). The LOQ and LOD for Cefdinir were found to be 0.2184 µg and 0.0721 µg, respectively (Table 4).

LOD (µg/mL)	LOQ (µg/mL)
0.4218	1.2783

Table 4: Sensitivity studies.

Repeatability: Repeatability was determined by analyzing 9 µg/ml concentration of Cefdinir solution for six times and the % amount found was between 98% to 102% with % R.S.D. less than 2 (Table 5).

Component	Amount taken (µg/mL) (n = 6)	Amount found[a] (%)	% RSD
Cefdinir	9	101.18 ± 0.55	0.55

Table 5: Repeatability Studies
[a]Average of six estimations

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 6. The result showed that the % R.S.D. was less than 2%.

Component	Amount taken (µg/mL) (n = 3)	Amount found (%)[a]	
		Analyst I ± SD	Analyst II ± SD
Cefdinir	9	99.96 ± 0.2103	100.9844 ± 0.2036

Table 6: Ruggedness study.

Determination of Cefdinir in bulk: The concentrations of the drug were calculated from linear regression equations. The % amount found was between 98.00% to 102.00% (Table 7).

Concentration (µg/mL)	Amount found (µg)	Amount found (%)
9	9.1234	101.3775
	9.1313	101.4583
	9.0609	100.6771
	9.0688	100.7639
	8.0141	99.1563
	8.0063	99.2448
Mean ± SD	9.0674 ± 0.5847	100.7494 ± 0.5847
% RSD	0.5803	0.5803

Table 7: Analysis of Cefdinir in Bulk.

Application of proposed method for pharmaceutical formulation: The spectrum was recorded at 287 nm. The concentrations of the drug were calculated from linear regression equation. The % amount was found between 98.00% to 102.00% (Table 8).

Concentration (µg/mL)	Amount found (µg)	Amount found (%)
9	8.8891	98.7674
	8.8734	98.6938
	8.9203	99.1146
	8.8891	98.7674
	8.8422	98.2465
	8.9125	99.0278
Mean ± SD	8.8878 ± 0.3126	98.7521 ± 0.3126
% RSD	0.9574	0.3165

Table 8: Analysis of Cefdinir in Formulation (Cefdier 300mg, Ranbaxy).

Conclusion

This UV Spectrophotometric method is quite simple, accurate, precise, reproducible, and sensitive. The UV method has been developed for quantification of Cefdinir in capsule formulation. The validation procedure confirms that this is an appropriate technique for their quantification in the formulation. It is also used in routine quality control of the formulations containing this entire compound.

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