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DEVELOPMENT AND VALIDATION OF UV SPECTROPHOTOMETRIC METHOD FOR QUANTITATIVE ESTIMATION OF CEFTAROLINE FOSAMIL IN BULK AND INJECTION FORM

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ABSTRACT

Two simple, sensitive, specific, spectrophotometric methods have been developed for the determination of ceftaroline fosamil in bulk and Injection forms. The λmax of ceftaroline fosamil was found to be 245.2 nm in distilled water. The zero order UV Spectrophotometric method exhibits high sensitivity, with linearity and obeys beer's law in the range of 2 – 10 µg/mL. The limit of detection and quantification were found to be 0.231 µg/mL and 0.7019 µg/mL respectively. While area under curve for zero order spectrum of ceftaroline fosamil was measured from 235 – 255 nm which obeys Beer's law in the concentration range of 2 – 10 µg/mL. These methods were fully validated according to ICH guidelines. The LOD and LOQ were found to be 0.223µg/mL and 0.669 µg/m, respectivelyL. Hence it could be concluded that the proposed methods would be suitable for the analysis of ceftaroline fosamil in bulk and pharmaceutical preparations.

Keywords: Ceftaroline fosamil, UV – Spectorphotometric methods, Validation.

INTRODUCTION

Ceftaroline fosamil [1], belongs to a class of V generation of broad-spectrum cephalosporin exhibiting bactericidal activity against Gram-positive organisms, including methicillin-resistant Staphylococcus aureus (MRSA) and multidrug-resistant Streptococcus pneumoniae, as well as common Gram-negative pathogens. Ceftaroline has also demonstrated in vitro bactericidal activity against etiologic pathogens frequently associated with complicated skin and skin structure infections.

OBJECTIVES

Analysis plays an important role in the formulation development of any drug molecule. A suitable and validated method has to be available for the analysis of drugs in bulk, in drug delivery systems, in dissolution studies (in vitro), and in biological samples (in vivo). If such a suitable method for a specific need is not available, then it becomes essential to develop a simple, sensitive, accurate, precise and reproducible method for the estimation of drug samples. The literature survey reveals that study of Comparative Pharmacokinetics of Ceftaroline in Rats, Rabbits, and Monkeys [2] and pathogens [3-9] following a Single Intravenous or Intramuscular Injection. More over U.V, H.P.L.C & H.P.T.L.C methods have not been reported for estimation of Ceftaroline fosamil in bulk and pharmaceutical formulation. Thus the present study was undertaken to develop and validate a simple, sensitive, accurate, precise, and reproducible UV method for Ceftaroline fosamil as per ICH guidelines [10-12].

EXPERIMENTAL WORK

MATERIALS & METHODS

Ceftaroline fosamil pure drug was procured from Facta Farmaceutici S.P.A. St. Louis. The pure drug obtained was having 99.9% w/w assay value, and was used without further purification. An Elico SL 244 Double Beam UV/Visible spectrophotometer with 1cm matched

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quartz cells was used for all spectral and absorbance measurements. All chemicals and reagents used were of analytical grade and solutions were prepared with double distilled water. Ceftaroline fosamil is available as powder for injection under the brand name Teflaro containing 400 mg.

Preparation of the standard stock solution

A standard drug solution of ceftaroline fosamil was prepared by dissolving 100 mg of ceftaroline fosamil in sufficient amount of distilled water and this was transferred into a 100 ml volumetric flask to obtain a stock solution of 1.0 mg/mL.

Preparation of the working solution

From the above stock solution, 10ml was transferred into a 100ml volumetric flask and the volume was made up to the mark with distilled water to prepare a concentration of 100 µg/mL.

Analysis of marketed formulations

The proposed method was applied to analyze the commercially available ceftaroline fosamil injections. Ceftaroline sample solution was prepared by adding the distilled water into a vial and the contents were dissolved in distilled water, then the volume was brought up to 20 ml by using the same solvent. Filtered through 0.45µ whatt man filter paper. The solution was diluted suitably with distilled water to get a final concentration within the calibration range. This was subsequently analyzed using a double beam UV-VIS spectrophotometer against distilled water as a blank. The drug content of the sample was calculated by using regression analysis.

Zero order Spectrophotometry

The working standard solution was further diluted and scanned in the range of 200-400 nm using distilled water as blank to obtain zero order U.V-Spectra of ceftaroline fosamil .The peak was observed at 245.2 nm which was used as an analytical wavelength for measurement of absorbance. The calibration curve was obtained by plotting absorbance at 245.2 nm against the concentration of ceftaroline fosamil. Beer's-lamberts' law was obeyed in the concentration range of 2-10 µg/ml. The concentration of sample solution was determined using regression equation.

AUC Spectrophotometry

In this method, zero order UV- Spectra were obtained and Area Under the Curve (AUC) between the range 235-255 nm were measured using UV – Probe, calibration curve was obtained by plotting AUC between 235-255 nm against the concentration of ceftaroline fosamil. Beer-lamberts' law was obeyed in the concentration range of 2-10 µg/ml. The concentration of sample solution was determined by using regression equation.

Method Validation

Validation is a process of establishing documented evidence, which provides a high degree assurance that a specific activity will consistently produce a desired result, or a product meeting its predetermined specifications and quality characteristics. The method was validated for different parameters like Linearity, Accuracy, Precision, Specificity, Robustness, Ruggedness, Limit of Detection (LOD) and Limit of Quantification (LOQ).

Linearity

Various aliquots were prepared from the stock solution (100µg/mL) ranging from 2 – 10 µg/mL and the resulting solutions were analyzed with the help of a UV-VIS Spectrophotometer using distilled water as blank.

Accuracy

The accuracy of the method was determined by preparing solutions of different concentrations, i.e 80, 100, 120% of specification limit in triplicate as per ICH guide lines. The recovery studies were carried out by spiking a known quantity of ceftaroline fosamil into a previously analyzed sample.

Precision

The precision of the method was demonstrated by intra-day and inter-day variation studies. In the inter-day variation study, 5.0 µg/mL of solution was prepared and analyzed thrice, for three consecutive days, and the absorbance was recorded. In the intra-day variation study, three different solutions of the same concentration (5.0 µg/mL) was prepared and analyzed thrice a day (morning, afternoon, and evening). The results were indicated by % RSD.

Limit of Detection & Limit of quantification

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample, which can be detected, but not necessarily to quantify as an exact value. The LOQ is the concentration that can be quantify reliably with a specified level of accuracy and precision. The LOD & LOQ were calculated using the formula involving the standard deviation of response and the slope of the calibration curve.

$$\mathbf{LOD = Cd \times Syx / b \text{ and } LOQ = Cq \times Syx / b}$$

Where Cd and Cq are the coefficients for LOD and LOQ. Syx is the residual Variance of the Regression, and b is the Slope. Calculation was performed by using values of Cd and Cq of 3.3 and 10.

RESULTS AND DISCUSSIONS

Ceftaroline fosamil shows the absorbance maxima at 245.2 nm (Fig.2). The proposed method obeyed beer's law in the concentration range of 2-10 µg/mL with distilled water (Fig.3). The % assay of ceftaroline fosamil was calculated in injection form and the results were mentioned in Table 1. The optical characteristics and the data concerning the proposed methods were represented in Table 2. The recovery studies were carried out for the developed method by the addition of standard drug solution of ceftaroline fosamil to pre-analyzed solution. The recovery studies were satisfactory and the percentage of drug recovered was in the range of 99.99-100.02%, which showed that there was no interference from excipients. The precision of the method expressed as % RSD of intraday and interday validation is given in Table 2. It was successfully applied for determination of drugs in their newly formulated pharmaceutical formulations.

Fig 1. Structure of Ceftaroline fosamil

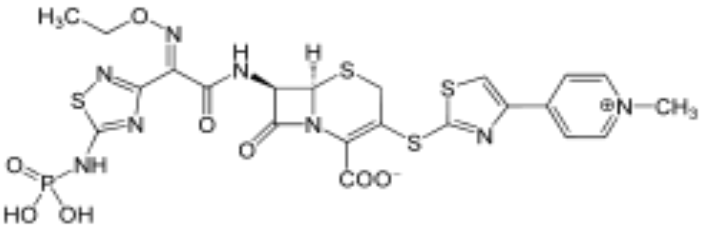

Fig 2. UV absorption spectrum of Ceftaroline fosamil

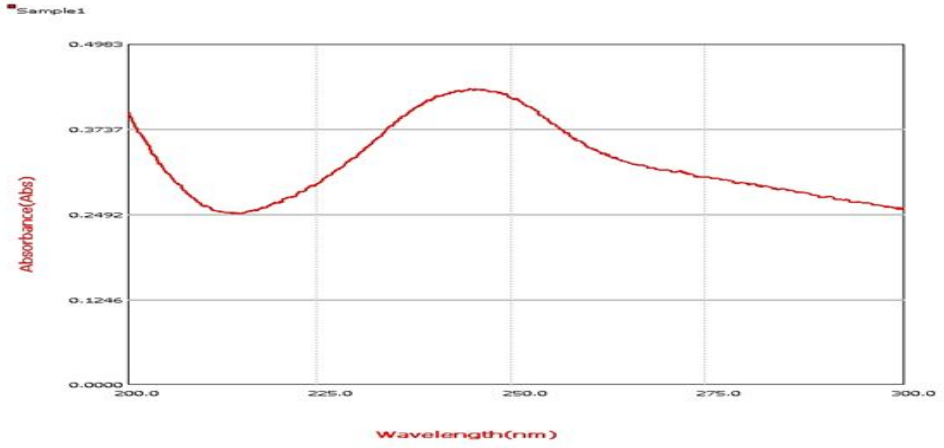

Fig 3. Calibration curve of Ceftaroline fosamil

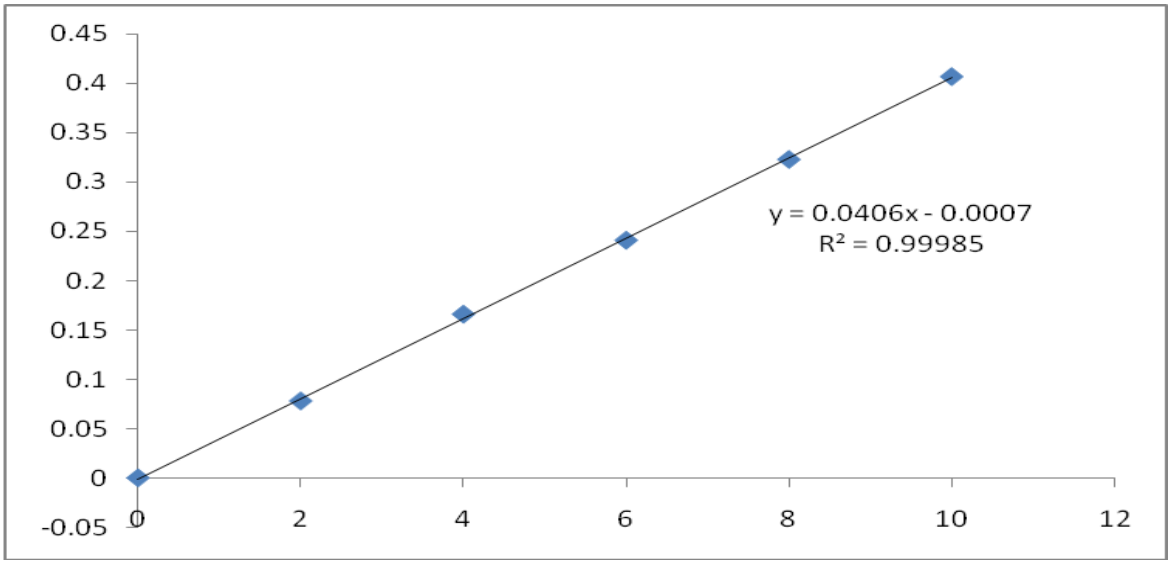

Table 1. Assay and Recovery of Ceftaroline fosamil in Injections

Drug name	Label Claimed (mg)	Amount found*		%Recovery*	
		Zero- order Method	AUC Method	Zero- order Method	AUC Method
Ceftarolinefosamil Injection	400	399.99	399.96	99.99±0.38	99.99±0.45

*****Average of six determinations

Table 2. Validation parameters

Parameter	Zero Order method	AUC method
Absorption maxima λ max (nm)	245.2nm	235-255nm
Beer's law limits (µg/mL)	2-10 µg/mL	2-10 µg/mL
Regression equation* Y= mx+c	Y= 0.0406 x - 0.0007	0.0905,-0.0014
Correlation coefficient	0.99985	0.9999
Sand ell's sensitivity (mg/cm^2/0.001 absorbance unit)	0.024778	0.012468
Molar absorptivity ($lit.mol^{-1}cm^{-1}$)	2.7×10^4	2.3×10^4
LOD	0.231 µg/mL	0.223 µg/mL
LOQ	0.7019µg/mL	0.669 µg/mL
%RSD Intraday Precision Interday Precision	 0.3119 0.4823	 0.1532 0.2315

*****Average of six determinations

CONCLUSION

Described in the manuscript is UV-Spectrophotometric method for the determination of ceftaroline fosamil in bulk and its injection form by using distilled water as the solvent. The statistical analysis of the results showed that all the proposed procedures had good precision and accuracy. The results of analysis revealed that the proposed method was suitable for the analysis with virtually no interference of the usual additives present in pharmaceutical formulations. This method can be adopted for routine quality control of ceftaroline fosamil in bulk and pharmaceutical preparations.

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