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VALIDATED SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF CEFUROXIME AXETIL IN BULK DRUG AND TABLETS

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ABSTRACT: Two simple spectrophotometric methods have been developed for the determination of Cefuroxime Axetil in bulk drug and its tablet formulation. Method I is a simple UV spectrophotometric method. In this method the simple UV spectrum of Cefuroxime Axetil in 0.1 N HCl was obtained which exhibits absorption maxima (λ max) at 281 nm. Calibration curve was prepared by plotting the absorbance vs. concentration. The quantitative determination of the drug was carried out at 281 nm and the linearity range was found to be 2 to 30 µg/ml. Method II is the 1st derivative spectrophotometric method. In this method the simple UV spectrum of Cefuroxime Axetil in 0.1 N NaOH was obtained and derivatised to 1st order. Maxima occur at 266 nm and minima at 300 nm. A calibration curve was prepared by plotting the absorbance difference between maxima and minima vs. concentration. The linearity range was found to be 4 – 30 µg/ml. All the proposed methods were extensively validated. The proposed methods were successfully applied to the assay of Cefuroxime Axetil in pure and tablet dosage form. No interference was found from tablet excipients at the selected wavelengths and assay conditions. There was no significant difference between the performance of the proposed methods regarding the mean values and standard deviations.
KEYWORDS: Cefuroxime axetil, UV spectrophotometry, I[st] derivative spectrophotometry

INTRODUCTION

Cefuroxime is a second-generation cephalosporin. Cefuroxime axetil is an ester prodrug of cefuroxime, which is rendered more lipophilic by esterification of carboxyl group of the molecule by the racemic 1-acetoxyethyl bromide, thus enhancing absorption. The absorbed ester is hydrolyzed in the intestinal mucosa and in portal circulation. Products of hydrolysis are active cefuroxime, acetaldehyde and acetic acid. Cefuroxime is chemically (1RS)-1-[(acetyl) oxy] ethyl-(6R, 7R)-3-(carbamoyloxy) methyl]-7-[(Z-2-furan-2yl)-2-(methoxy imino) acetyl) amino]-8-oxo-5-thia-1-aza bicyclo- (4,2,0)-oct-2-ene-2-carboxylate[1-2]. Literature survey revealed that few HPLC methods were reported for the estimation of cefuroxime axetil in the biological fluids[3] HPTLC method was also reported for the simultaneous estimation of cefuroxime axetil and probenecid[4]. Derivative spectrophotometry is an analytical technique for the enhancement of sensitivity and specificity in qualitative and quantitative analysis of various compounds including pharmaceuticals. The main purpose of the present study was to establish a relatively simple, single - step, sensitive, validated and inexpensive spectrophotometric method for the determination of cefuroxime axetil in pure form and in pharmaceutical dosage form, since most of the previous methods have been found to be relatively complicated and expensive

EXPERIMENTAL MATERIAL AND METHODS

Schimadzu UV 1601 spectrophotometer with 1 cm matched quartz cell were used for the absorbance measurements. The solutions of 0.1 N HCl and 0.1 N NaOH were prepared in double distilled water.

Stock standard solution of Cefuroxime axetil (1 mg/ml) was prepared in methanol. Working standard solution (100 µg/ml) was prepared by appropriate dilutions of stock solutions in methanol.For selection of the analytical wavelengths, from the stock solutions working solution of Cefuroxime Axetil 10 µg/ml were prepared separately in 0.1 N HCl & 0.1 N NaOH for method I and method II. respectively The UV and derivative spectra of solutions were recorded in the scanning range of 400-200 nm. Method I is a simple UV spectrophotometric method. In this method the simple UV spectrum of Cefuroxime Axetil in 0.1 N HCl was obtained which exhibits absorption maxima (λ max) at 281 nm. Aliquots of working solution of Cefuroxime Axetil (0.2-3 ml) were transferred into a series of 10 ml volumetric flasks and volume was made up to the mark with 0.1 N HCL.The absorbances of the resulting solutions were measured at 281 nm against 0.1 N HCL as blank. Calibration curve was prepared by plotting absorbance versus concentration. The calibration curve was linear in concentration range of 2 – 30 µg/ml (fig. 3).

Method II is the 1st derivative spectrophotometric method. In this method the simple UV spectrum of Cefuroxime Axetil in 0.1 N NaOH was obtained and derivatised to 1st order. Maxima occur at 266 nm and minima at 300 nm Aliquot of working solutions of Cefuroxime Axetil (0.4 – 3) ml were transferred into series of 10 ml volumetric flask. These solutions were diluted with 0.1 N NaOH up to the mark and first derivative spectra were obtained which shows absorbance maxima at 266 nm and minima at 300 nm. A first derivative spectrum of Cefuroxime Axetil is shown in figure 2. A calibration curve was prepared by plotting the absorbance difference between maxima and minima vs. concentration. The calibration curve was linear in concentration range of 4 – 30 µg/ml (fig. 4).Under the experimental conditions described the graph obtained for UV and 1st derivative spectrophotomety showed linear relationship. Regression analysis using the method of least squares was made for slope, intercept and correlation coefficient value. The results are presented in table 1.

ANALYSIS OF TABLET FORMULATIONS

The proposed methods were successfully applied for the determination of Cefuroxime Axetil in tablet dosage form.

Twenty tablets were weighed & crushed to fine powder. Powder equivalent to average weight of the tablet was weighed and dissolved in 30 ml methanol by sonication. The solution was then filtered through Whatman No. 41 filter paper to remove insoluble matter. The filtrate was collected in 50 ml volumetric flask and diluted up to the mark with methanol. Further this solution was suitably diluted to obtain concentration of 100µg/ml with methanol. From this solution appropriate dilution were made to obtain concentration of 10µg/ml. For method I dilution was done with 0.1 N HCl and for method II with 0.1 N NaOH. The absorbance of the solutions was measured and the amount of Cefuroxime Axetil was computed from the calibration curves. The results of analysis of marketed tablets formulation by both methods are shown in Table 2.

TABLE 1: Optical characteristics and data for calibration curves for determination of cefuroxime axetil

Sr.No.	Parameters	Simple UV Method	First derivative Method
1	Absorption maxima	281nm	266 nm
2	Absorption minima	-	300 nm
3	Beer's Law limit	2-30 µg/ml	4-30 µg/ml
4	Molar absorptivity (lit/mole/cm)	2.2×10^4	3.8×10^2
5	Slope (b)	4.4×10^{-2}	8.57×10^{-4}
6	Intercept (a)	7.14×10^{-3}	1.14×10^{-3}
7	Correlation coefficient (r)	0.999	0.99

TABLE 2: Result of analysis of tablet formulation

Sample	Parameter	% Drug Found		% Recovery	
		Method I	Method II	Method I	Method II
ALTACEF Tablet	Mean	100.0167	99.20333	99.95	99.33667
	SD	0.61403	0.063509	0.43589	0.257164

Method I is the simple UV method and Method II is the first derivative method. Values for percentage drug found and percentage recovery are mean of three estimations. SD is standard deviation.

VALIDATION

The developed methods were validated [5-9] in terms of linearity, precesion, accuracy, ruggedness parameters. For recovery studies known amount of pure drug was added to the previously analyzed tablets Accuracy was ascertained on the basis of recovery studies. Precision was studied by analyzing three replicates of sample solutions and concentrations were calculated. Ruggedness was established by carrying out experiment at different conditions like intra-day, inter-day and by different analyst. The recovery studies were carried out at different concentrations by spiking a known concentration of standard drug to the pre-analyzed sample and contents were reanalyzed by proposed methods. The assay values were in good agreement with the corresponding labeled claim. The recovery studies justified accuracy of the proposed methods

RESULT AND DISCUSSION

The proposed methods were successfully used to estimate Cefuroxime Axetil in marketed tablet formulation. Both the methods were validated statistically as per ICH/USP16 uidelines for parameters like accuracy, precision, ruggedness, specificity, linearity and range. The assay values were in good agreement with the corresponding labeled claim. The recovery studies show accuracy of the method.

CONCLUSION

On observing the assay results and validation parameters, both these methods were found to be accurate, precise and specific. Hence, the methods can be employed for quality control and routine analysis of Cefuroxime Axetil in pharmaceutical formulations.

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Fig 1: Normal Spectra for varying concentrations i.e. 2,4,6,8,10,20and 30 µg/ml inN HCl depicted in graph from bottom to top respectively

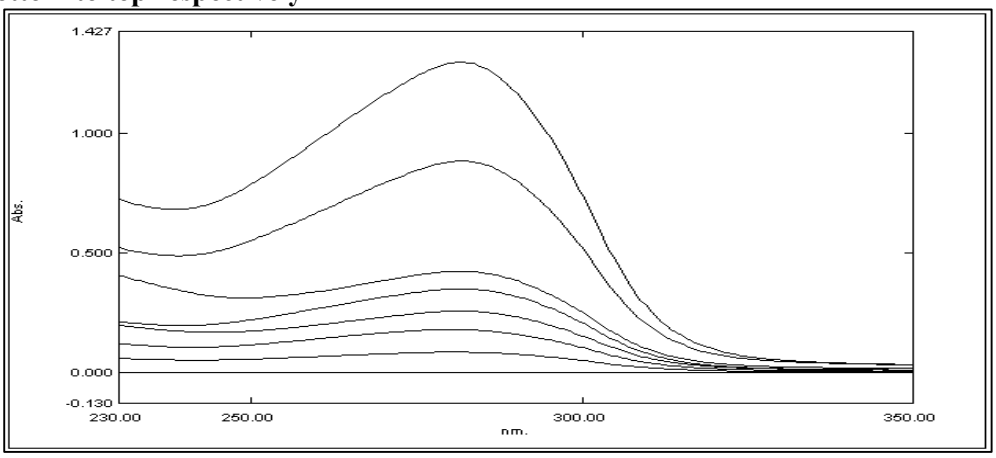

Fig 2: I[st] derivative overlain Spectra for varying concentrations i.e. 4,6,8,10,20,30 µg/ml of Cefuroxime Axetil in 0.1 N NaOH

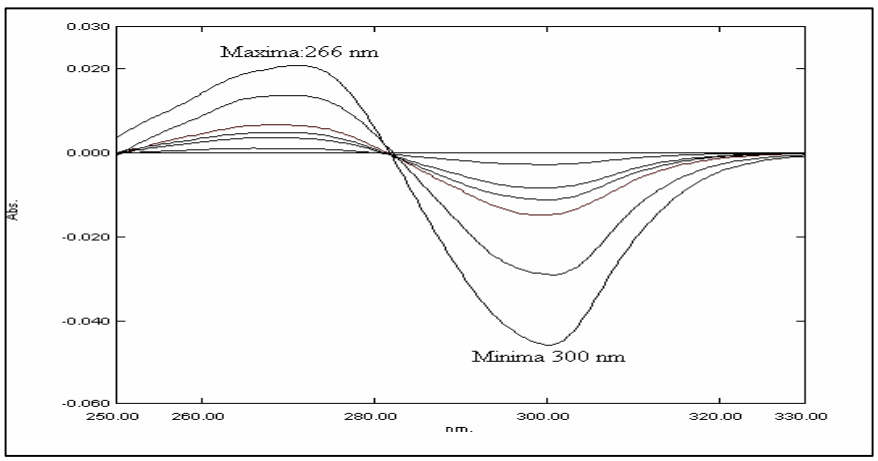

Fig 3: Cefuroxime Axetil absorbance plot in 0.1 N HCl

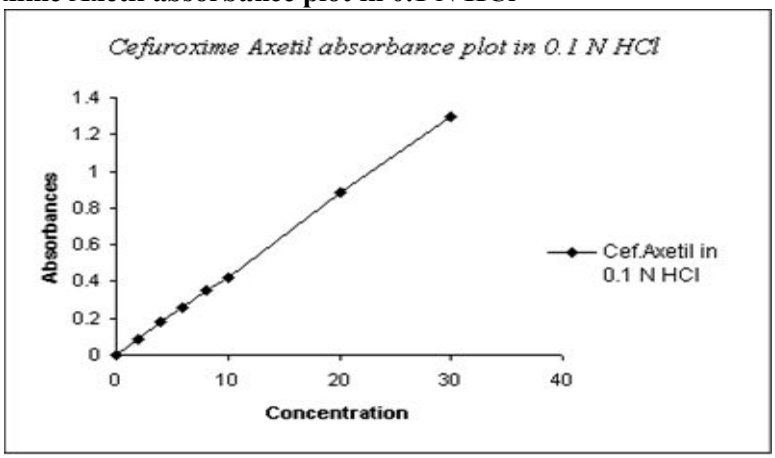

Fig.4: Cefuroxime Axetil Maxima-Minima absorbance plot in 0.1 N NaOH

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