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Simultaneous Spectrophotometric Estimation of Cefixime and Azithrhomycin in Tablet Dosage Form.

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Abstract
Accurate, precise, rapid and economical methods were developed for the estimation of Cefixime and azithromycin in tablet dosage form. Method is based on the simultaneous equations and wavelengths selected for analysis were 289.0 nm (λmax of Cefixime) and 254.0 nm (λmax of azithromycin) respectively, in methanol. The linearity was obtained in the concentration range of 5-25µg/ml for both Cefixime and azithromycin. The proposed procedure was successfully applied for the simultaneous determination of both drugs in commercial tablet preparation. The results of the analysis have been validated statistically and by recovery studies.

Key Words
Cefixime, azithromycin, Simultaneous equations.

Introduction
Cefixime (CEF) is an oral third generation cephalosporin antibiotic. Chemically, it is (6*R*, 7R)-7-{[2-(2-amino-1,3-thiazol-4-yl)-2(carboxymethoxy-imino)acetyl]amino}-3-ethenyl-8-oxo-5-thia-1 azabicyclo-[4.2.0]oct-2-ene-2 carboxylic acid, clinically used in the treatment of susceptible infections including gonorrhea, otitis media, pharyngitis, lower respiratory-tract infections such as bronchitis, and urinary-tract infections. Azithromycin is a macrolide antibiotic belonging to the azalide group. Chemically it is (2R, 3S, 4R, 5R, 8R, 10R, 11R, 12S, 13S,14S)-11- ((2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyltetrahydro-2 Hpyran-2-yloxy)-2-ethyl-3,4,10-trihydroxy-13 (2S,4R,5S)-5-hydroxy-4-methoxy-4hyltetrahydro-2H-Pyran-2-yloxy)-3,5,6,8,10,12,14-heptamethyl-1-oxa 6cyclopentade-can-5-one1, used as antibiotic and antibacterial. Both the drugs are marketed as combined dose tablet formulation in the ratio of 200:250 mg CEF: AZI. Literature survey reveals that cefixime can be estimated by spectrophotometrically, HPLC and by HPTLC individually or with other drugs in bulk drugs and in human plasma, while azithromycin can be estimated by spectrophotometrically, HPLC in combination with other drugs. However, there is no analytical method reported for the estimation of CEF and AZI in a combined dosage formulation. Present work describes two methods for simultaneous estimation of CEF and AZI in tablet formulation.

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Materials and Methods
Instrument
A double-beam Jasco-630 UV- Visible spectrophotometer, with spectral bandwidth of 2 nm, wavelength accuracy ± 0.5 nm and a pair of 1-cm matched quartz cells was used to measure absorbance of the resulting solution.

Materials
Standard gift sample of Cefixime provided by Concept Pharmaceuticals Ltd, Aurangabad and Azithromycin by Aristo Pharmaceuticals Pvt. Ltd., Mumbai. Combined dose Cefixime and Azithromycin tablets were purchased from local market. Methanol (AR Grade) was used as solvent, procured from Vijay traders, Shrirampur.
Stock solution Standard stock solutions of CEF (100 µg/ml) and AZI (100 µg/ml) were prepared in methanol and used for the analysis.

Method
Spectral characteristics of CEF and AZI
Solutions of CEF and AZI (5 µg/ml, each), were prepared separately by appropriate dilution of standard stock solution. Both the solutions were scanned in the spectrum mode from 400 nm to 200 nm.

Preparation of calibration curves
Appropriate dilutions of the standard stock solution were done separately to get 5, 10, 15, 20, 25 µg/ml of CEF and AZI, respectively. The absorption spectra of all solutions were recorded between 200-400 nm. The absorbances were measured at 289.0 nm (λmax of CEF),

254.0 nm (λmax of AZI). Beer's lamberts range for CEF and AZI were selected and working calibration curves of both the drugs were plotted separately.

Determination of Absorptivity Value of CEF and AZI

Appropriate dilutions of the standard stock solution were done to get 20 µg/ml of each CEF and AZI, respectively. The absorbances were measured for CEF and AZI at 289.0 nm (λmax of CEF), 254.0 nm (λmax of AZI). The absorptivity values of the drugs were determined at the selected wavelengths. These absorptivity values are the mean of six determinations.

Application of the proposed method for the determination of CEF and AZI in tablets

Twenty tablets were weighed and average weight was calculated. The tablets were crushed to obtain fine powder. Tablet powder equivalent to 10mg of AZI was transferred to 100.0 ml volumetric flask, methanol added, ultrasonicated for 10 minutes and volume was made-up to the mark with methanol and. The solution was then filtered through a Whatmann filter paper (No. 41). The filtrate was further diluted with methanol to obtain 10µg/ml of AZI and 8 µg/ml of AZI. The concentration of both CEF and AZI were determined by measuring the absorbance of the sample at 289.0 nm, 254.0 nm. Concentration of sample solution was determined by using following equations:

Simultaneous equation method

Equation

A set of two simultaneous equations obtained by using mean absorptivity values are given below,

$$Cx = \frac{A1\ ay2 - A2\ ay1}{ax1ay2 - ax2ay1} \quad \text{..... Eq. (i)}$$

$$Cy = \frac{A1\ ax2 - A2\ ax1}{ay1ax2 - ay2a\ x1} \quad \text{.....Eq. (ii)}$$

Where A1 and A2 are absorbance of the sample at 254.0 nm and 289.0 nm respectively, ax1 and ax2 are the absorptivity values of AZI at 254 nm and 289 nm respectively. Similarly ay1 and ay2 are the absorptivity value of CEF at 254nm and 289nm respectively. Cx is the concentration of CEF and Cy is the concentration of the AZI.

Validation

The method was validated with respect to linearity, LOD, LOQ and accuracy.

Accuracy

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% & 120%). The mean % recovery being 99.16% ± 0.44 for AZI and– 99.21% ± 1.00for CEF.

Linearity

The linearity of measurement was evaluated by analyzing different concentrations of the standard solution of CEF and AZI. For both the methods, the Beer- Lambert's concentration range was found to be from 5-25 µg/ml for both CEF and AZI, respectively.

Results and Discussion

The method discussed in the present work provides a convenient and accurate way for simultaneous analysis of CEF and AZI. In simultaneous equation method, wavelengths selected for analysis were 289.0 nm (λmax of Cefixime) and 254.0 nm (λmax of Azithromycin). In this method linearity for detector response was observed in the concentration range of 5-25 µg/ml for both CEF and AZI. Absorptivity coefficient were calculated for both the drugs at selected wavelengths and substituted in equations for determining concentration of CEF and AZI in tablet sample solution. Percent label claim for CEF and AZI in tablet analysis, by this method was found in the range of 98.54 % to 100.94 %. Low values of LOD and LOQ indicated good sensitivity of proposed method. Accuracy of proposed methods was ascertained by recovery studies. The percent recovery for CEF and AZI, by this method, was found in the range of 99.21 % & 99.16 % respectively (Table No. 3). The proposed method could be employed for routine quality control of Cefixime and Azithromycin in combined dose tablet formulation.

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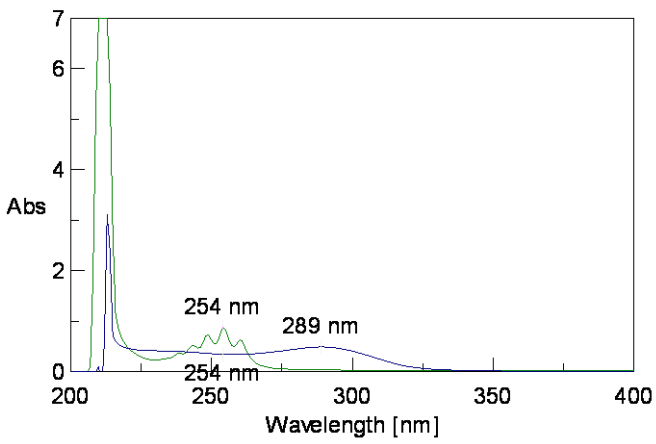

Fig. 1: Overlain Spectra of Cefixime (CEF) and Azithromycin (AZI).

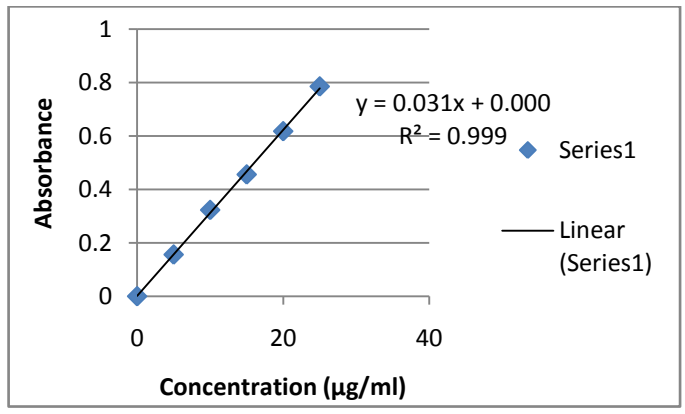

Fig 2: Calibration curve of Azithromycin at 254 nm.

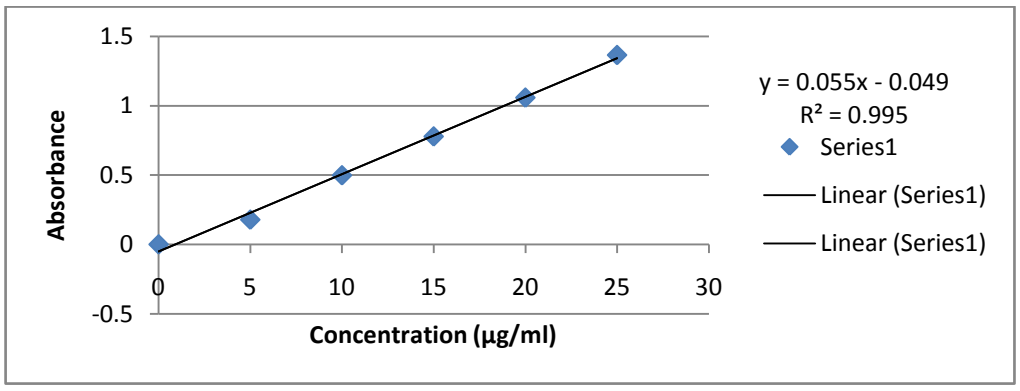

Fig 3: Calibration curve of Cefixime at 289 nm.

Table 1: Analysis of tablet formulation.

Drug	**Label claim (mg/ tab.)**	**Amount found (mg)**	**%Drug found ±SD**	**Standard Error**
AZI	250	248.29	99.31 ± 0.35	0.14
CEF	200	199.39	99.69 ± 0.20	0.085

Table 2: Validation parameter.

Sr. No.	**Parameter**	**Results**	
		Azithromycin	**Cefixime**
1.	Absorption maxima (λ max)	254 nm	289nm
2.	Linearity range (µg/ml)	5 to 25	5 to 25
3.	Standard regression equation	Y=0.031x+0.00	Y=0.055x-0.049
4.	Correlation coefficient (r^2)	0.999	0.995
5.	Accuracy (%Recovery ± S.D.)	99.16 ± 0.44	99.21 ± 1.00
6.	LOD (µg/ml)	0.35	1.06
7.	LOQ (µg/ml)	0.34	1.05

Table 3: Accuracy by percentage recovery method.

Sr. No.	**Tablet Formulation (µg/ml)**	**Level of addition (%)**	**% estimated (mean ± SD)**	
			Azithromycin	**Cefixime**
1.	5	80	99.58 ± 0.56	99.36 ± 0.97
2.	5	100	99.02 ± 0.36	98.99 ± 1.01
3.	5	120	98.90 ± 0.42	99.28 ± 1.04

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