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DEVELOPMENT OF ANALYTICAL METHOD FOR SIMULTANEOUS ESTIMATION OF CEFIXIME AND LINEZOLID IN TABLET DOSAGE FORM

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ABSTRACT:
A simple, accurate, precise and sensitive UV spectrophotometric method is developed for the simultaneous estimation of Cefixime and Linezolid in tablet dosage form. The method is based on the First order derivative method. In first order derivative method, the quantification was achieved by 247.6 nm (zero crossing point of linezolid) and 236.6 nm (zero crossing point of cefixime) over the concentration range of 2-30 µg/ml respectively for estimation of cefixime and linezolid in tablet dosage form. The correlation coefficient of cefixime and linezolid were found to be 0.9992 and 0.9995 respectively. The method was validated for linearity, accuracy and precision as per ICH guidelines and hence can be used for the quantitative analysis of commercially available dosage form.

Keywords: First Order Derivative Spectroscopic Method, Cefixime, Linezolid, ZCP (zero crossing point), Q2 (R1) guideline.

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INTRODUCTION

Cefixime (CEF) is an oral third generation cephalosporin antibiotic. Chemically, it is (6*R*,7*R*)-7-{[2-(2-amino-1,3-thiazol-4-yl)-2-(carboxymethoxyimino)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 gonorrhoea, otitis media, pharyngitis, lower respiratory-tract infections such as bronchitis, and urinary-tract infections[1-4].

Linezolid (LIN) is synthetic antibiotic, first drug of the oxazolidinone class. Chemically it is N-[[(5S)-3-[3-fluoro-4-(4-morpholinyl) phenyl]-2oxo-5-oxazolidinyl] methyl] acetamide, mainly used for the treatment of infections caused by multi-resistant bacteria including *streptococcus* and methicillin-resistant *Staphylococcus aureus* (MSRA).

The review of literature revealed that various analytical methods involving spectrophotometry, HPLC, have been reported for CEF in single form and in combination with other drugs[5-8]. According to literature survey LIN can be estimated by analytical methods like UV, HPLC, HPTLC methods [9, 10]. The present work describes another simple, precise, accurate and reproducible spectrophotometric method for the simultaneous estimation of CEF and LIN.

MATERIAL AND METHODS

Reagents and chemicals

Standard gift sample of cefixime was provided by Vapi Healthcare Ltd. And linezolid was provided by Alembic Pharmaceuticals Ltd. Combined dosage form of Cefixime and Linezolid tablets were purchased from local market. Other chemicals were purchased from Merck Pvt. Ltd., India.

Instrument and apparatus

Shimadzu-1800 UV-Visible Spectrophotometer was used for spectral measurements with spectral band width 1 nm; wavelength accuracy is 0.5 nm and 1 cm matched quartz cells. Software used was UV Probe (version 2.34). An Electronic analytical balance (Shimadzu) was used for weighing. Glassware used in each method were soaked overnight in a mixture of

chromic acid and sulphuric acid rinsed thoroughly with double distilled water and dried in hot air oven.

Preparation of Stock Solution: Standard stock solution of CEF and LIN were prepared by dissolving accurately 100 mg CEF and 100 mg LIN separately in 100 ml of 0.1 N NaOH in two separate 100 ml volumetric flask.(1000 µg/ml)

Preparation of working standard solution: 10 ml of stock solution is diluted upto 100 ml with distilled water (100 µg/ml). From that further dilutions were prepared with water for both drugs.

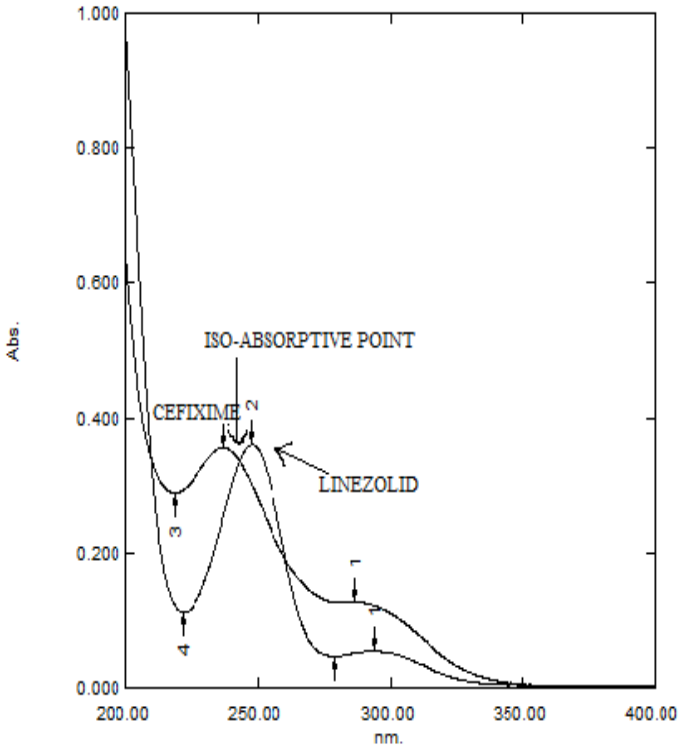
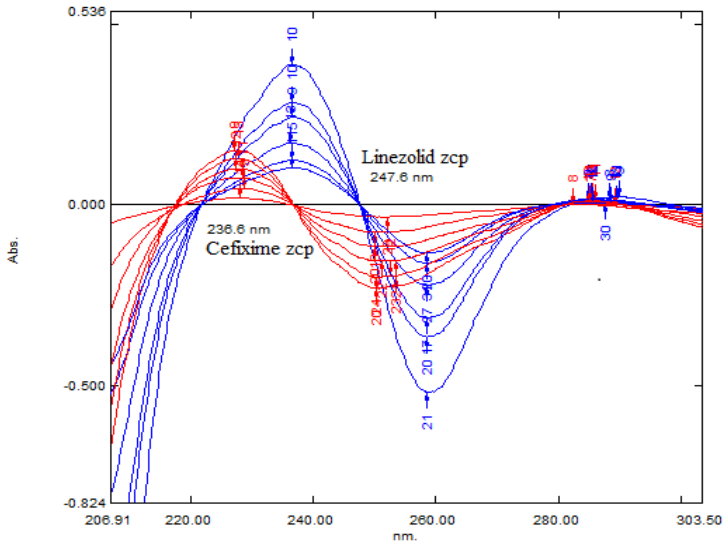


Fig. 1 Overlay spectra

Selection of wavelength: By appropriate dilution of two working standard drug solutions, solutions containing 10 µg/ml of CEF and 10 µg/ml of LIN were scanned separately in the range of 200-400 nm to determine the wavelength of maximum absorption for both the drugs. CEF and LIN showed absorbance maxima at 236.8nm and 247.6 nm respectively.

First order Derivative Spectroscopic method[11-14]: Standard solutions of both drugs (2-30 µg/ml) were scanned separately in the range of 200-400 nm. These spectrums were converted to first order derivative spectra (Figure 6) by using derivative mode. For this method, 247.6 nm and 236.6 nm were selected as wavelengths of measurements for CEF and LIN respectively. (Fig: 2)



Calibration curves and statistical analysis:

For both methods, appropriate dilutions of the standard stock solution were done separately to get 2-30 µg/ml of CEF and LIN, respectively. The absorption spectra of all solutions were recorded between 200-400 nm. These spectra were converted into first order derivative and absorbance of CEF was recorded at 247.6 nm (ZCP of LIN) and absorbance of LIN was recorded at 236.6 nm (ZCP of CEF). Beer's lamberds range for CEF and LIN were selected and calibration curves of both the drugs were plotted separately.

Method Validation[15]:

The method was validated with respect to linearity, LOD, LOQ, Accuracy and Precision, Robustness and Specificity as per ICH Q2 (R1) guidelines.

RESULT AND DISCUSSION

Derivative spectroscopy, based on a mathematical transformation of the spectra zero-order curve into the derivative spectra, allows a fast, sensitive and precise resolution of a multicomponent mixture and overcomes the problem of overlapping of a multi-component system. The method discussed in the present work provides a convenient and accurate way for simultaneous analysis of CEF and LIN.

In First order derivative method, ZCP of CEF and LIN were found to be 236.6 nm and 247.6 nm respectively as shown in figure-2 and linearity was obtained. Percent label claim for CEF and LIN in tablet analysis by this method was found 99.43% for CEF and 99.12% for LIN.

Lower values of LOD and LOQ indicated good sensitivity of proposed methods. Accuracy of proposed methods as shown in Table-1 was ascertained by recovery studies and the results are expressed as 98.59 and 99.19 % recovery. The method was also found to be specific, as there was no interference observed when the drugs

were estimated in presence of excipients and robust, as there was no significant change in absorbance up to 24 hours of preparation of stock solution in 0.1 N NaOH.

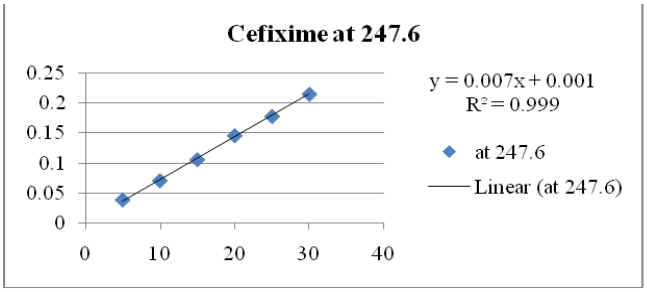


Fig. 3: calibration curve of cefixime at 247.6 nm

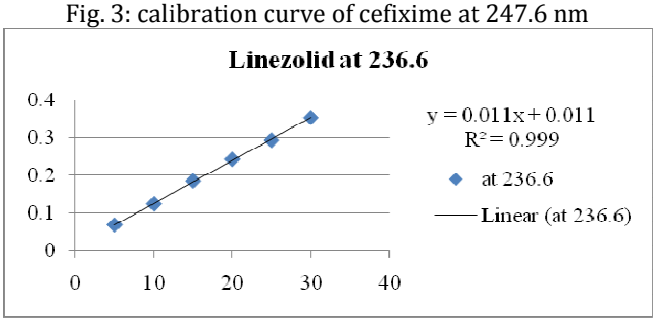


Fig. 2 Calibration curve of linezolid at 236.6 nm

Table 1- Recovery study

Mixture (µg/ml)	Wavelength	Conc. before spiking	Conc. after spiking	Actual Conc. added	% Recovery	SD	%RSD
8 (2 CEF + 6 LIN)	236.6 nm	2.014085	3	0.985915	98.591	1.00486	1.01921
	242.6 nm	5.921053	8.9035	2.982456	99.415		
	236.6 nm	2.15493	4.1267	1.971831	98.591		
	242.6 nm	6.008772	12.0614	6.052632	100.87	0.84407	0.844902
	236.6 nm	2.014085	4.97183	2.957746	98.591		
	242.6 nm	6.096491	15.0438	8.947368	99.415		

Table 2- Result Summary

First order derivative method

S. No.	Parameters	CEF	LIN
1	ZCP (zero crossing point)	236.6 nm	247.6 nm
2	Range (µg/ml)	2-30	2-30
3	Linearity	$R^2 = 0.9992$	$R^2 = 0.9995$
4	Precision (%RSD) Intraday Interday	 1.623 1.870	 1.200 1.514
5	Assay	99.43	99.12
6	LOD	0.327 µg/ml	0.443 µg/ml
7	LOQ	0.993 µg/ml	1.343 µg/ml
8	Accuracy(%recovery)	98.59	99.90
9	Robustness	Robust	Robust

CONCLUSION

The proposed Absorption ratio method provides simple, specific, precise, accurate and reproducible quantitative analysis for simultaneous determination of CEF and LIN in combined dosage form. The method was validated as per ICH guidelines in terms of specificity, linearity, accuracy, precision, limits of detection (LOD) and quantification (LOQ), robustness and reproducibility and can be used for routine analysis and quality control assay of CEF and LIN in combined dosage form.

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