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Research Article

Simultaneous Estimation of Linezolid and Cefixime in their Combined Dosage Form

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ABSTRACT

Simple, accurate, precise, reproducible, requiring no prior separation and economical procedures for simultaneous estimation of Linezolid (LIN) and Cefixime (CEF) in tablet dosage form have been developed. The method is simultaneous equation method; in this method 257.0 nm and 288.0 nm were selected respectively for LIN and CEF to measure the absorbance of both the drugs at mentioned wavelengths. Both the drugs show linearity at 10-50 µg/mL, the range was selected by studying their ratio present in combined formulation. Recovery studies range from >99.35% for CEF and >99.23% for LIN in mentioned analytical method i.e. simultaneous equation method. The proposed methods are recommended for routine analysis since it is rapid, simple, accurate and also sensitive and specific (no heating and no organic solvent extraction is required).

Keywords: Linezolid, Cefixime, spectrophotometer, analysis

INTRODUCTION

Cefuroxime is chemically (6R,7R)-3-carbamoyloxymethyl-7-[(Z)-2-(2-furyl)-2 (methoxyimino)acetamido]-ceph-3-em-4-carboxylic acid. Cefuroxime is official in Indian pharmacopoeia. It is the first of the series of alpha methoxyiminoacyl substituted cephalosporins that constitute most of the third generation agents available for clinical use. It is active against some beta lactamase strains that are resistant to cefamandole.

Linezolid (LIN) is a synthetic antibacterial agent of the oxazolidinone class of antibiotics. Linezolid is chemically N-{[(5S)-3-[3-fluoro-4-(morpholin-4-yl) phenyl]-2-oxo-1, 3- oxazolidin-5-yl] methyl} acetamide. Clinically used for the treatment of infections caused by multi-resistant bacteria including streptococcus and methicillin resistant Staphylococcus aureus (MRSA). The drug works by inhibiting the initiation of bacterial protein synthesis.

Both the drugs are marketed as combined dose tablet formulation in the ratio of 200:600 mg CEF: LNZ. Literature survey reveals that Cefixime can be estimated by Spectrophotometrically [1-4], and by HPLC [2,3] individually or with other drugs in bulk drugs and in human plasma, while Linezolid can be estimated by Spectrophotometrically [5,7], HPLC [8,9]and determination of Linizolid in plasma[9,10] in combination with other drugs. However, there is no analytical method reported for the estimation of CEF and LIN in a combined dosage formulation

MATERIALS AND REAGENTS

A Shimadzu UV/Visible spectrophotometer (Model: UV1700) was employed with spectral bandwidth of 2nm and wavelength accuracy of ± 0.5 nm with automatic wavelength correction with a pair of 10mm quartz cells. Cefixime (Sun

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Pharmaceuticals Ltd.) Linezolid (Torrent Pharmaceuticals) and Methanol – AR grade (Qualigens Fine Chemicals, Mumbai) were used in the study.

EXPERIMENTAL PROCEDURE

Two wavelengths selected for the method are 257.0 nm and 288.0 nm that are Absorption maxima respective for LIN and CEF methanol. The stock solutions of both the drugs were further diluted separately with methanol to get a series of standard solutions of 10-50 µg /mL for both the drugs concentrations. The absorbances were measured at the selected wavelengths and absorptivities (A 1%, 1 cm) for both the drugs were determined as mean of six independent determinations. Concentrations in the sample were obtained by using following equations.

$Cx = (A_2ay_1-A_1ay_2)/(ax_2ay_1-ax_1ay_2)$

$Cy = (A_1ax_2-A_2ax_1)/(ax_2ay_1-ax_1ay_2)$

Where A_1 and A_2 are absorbances of mixture at 257.0 nm and 288.0 nm respectively, ax_1 and ax_2 are absorptivities of CEF at λ_1 and λ_2 respectively and ay_1 and ay_2 are absorptivities of LIN at at λ_1 and λ_2 respectively. Cx and Cy are concentration of CEF and LIN respectively.

Analysis of marketed tablet formulation:

Tablet sample solution was made as per the method described in Method – I and solution was diluted to get a final concentration equivalent to 10 µg/ml of CEF and 30 µg/ml of LIN (n=6) and from the overlain spectra the absorbances were measured at 257.0 nm for LIN and 288.0 nm for CEF in spectrophotometric mode of an instrument. Amount of drug present in the sample solution was obtained from the simultaneous equation.

The results of analysis and statistical validation for the marketed tablet formulation are reported in Table-1 and Table-2 respectively. The results of recovery studies conducted by the addition of different amounts of pure drugs at 80%, 100% and 120% levels to a tablet solution were found to be satisfactory and are given in the Table-3.

RESULT AND DISCCUSION

The simultaneous equation method, also called as verdict's method, employs the absorption at two selected wavelengths and can be employed for the routine analysis of the two drugs in the combined dosage forms using simple instrument which requires more accuracy. The method is used to eliminate the spectral interference from one of the two drugs as the wavelength for estimation of the other drug. This method requires spectral data processing and hence can be performed only on recording spectrophotometers with such facilities.

The amount found from the proposed methods was in good agreement with the label claim of the formulation. Also the value of standard deviation and coefficient of variation calculated were satisfactorily low, indicating the suitability of the proposed methods for the routine estimation of tablet dosage forms.

CONCLUSION

From above it is concluded that the simple, economical, precise and accurate spectrophotometric simultaneous equation method (Verdicts Method) had been developed for simultaneous determination of Cefixime and Linezolid in bulk and tablet formulation was developed and validated as per ICH guidelines. Thus it can be used as IPQC test and for routine simultaneous determination of Cefixime and Linezolid in tablet dosage form. The method had been validated by different parameters like accuracy, precision; Linearity, LOD and LOQ which was found to be with in mentioned limit as per ICH guidelines.

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TABLE 1: ANALYSIS OF TABLET FORMULATION

Label claim (mg/tab)				Amount Found* (mg/tab)				Label claim (%)			
T1		T2		T1		T2		T1		T2	
CEF	LIN	CEF	LIN	CEF	LIN	CEF	LIN	CEF	LIN	CEF	LIN
200	600	200	600	197	592	203	911	98.51	98.66	101.49	101.83

T1 = **LCZ-2** (IIFA pharmaceuticals India Ltd)
T2 = **LINCEF (**Alkem Pharmaceuticals)

TABLE 2: STATISTICAL VALIDATION OF TABLET FORMULATION

Standard Deviation				% coefficient of variation				Standard error			
T1		T2		T1		T2		T1		T2	
CEF	LIN	CEF	LIN	CEF	LIN	CEF	LIN	CEF	LIN	CEF	LIN
0.115	0.1236	0.1241	0.0562	0.414	0.36	0.145	0.86	0.021	0.023	0.036	0.014

TABLE 3: STATISTICAL VALIDATION OF RECOVERY STUDIES

Type of Reco-very in %	Mean ± S D*				Coefficient of variation*				Standard Error*			
	T1		T2		T1		T2		T1		T2	
	CEF	LIN	CEF	LIN	CEF	LIN	CEF	BEN	CEF	LIN	CEF	LIN
80	98.23 ±0.09	99.54 ±0.13	100.38 ±0.83	98.50 ±0.43	99.26± 0.21	99.54 ±0.25	101.83 ±0.52	99.50 ±0.43	99.13± 0.62	99.86 ±0.43	99.36 ±0.14	101.25 ±0.41
100	99.87 ±0.21	99.80 ±0.15	98.46 ±0.77	101.03 ±0.37	99.82± 0.19	100.52 ±0.25	99.76 ±0.31	100.97 ±0.37	99.26 ±0.21	98.65 ±0.37	99.86 ±0.17	98.17 ±0.17
120	99.10 ±0.21	100.07 ±0.21	99.61 ±1.15	100.09 ±0.43	100.21 ±0.21	101.06 ±0.19	99.16 ±0.27	100.10 ±0.12	99.36 ±0.27	100.10 ±0.2179	100.08 ±0.21	101.09 ±0.11

CEF is cefuxime and LIN is Linezolid
* Denotes average of six estimation.

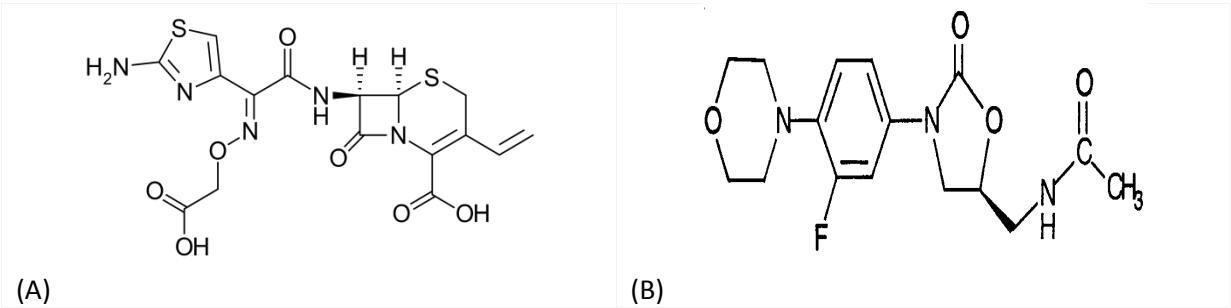

Fig1: Chemical structure of Cefixime (A) and Linezolid (B)

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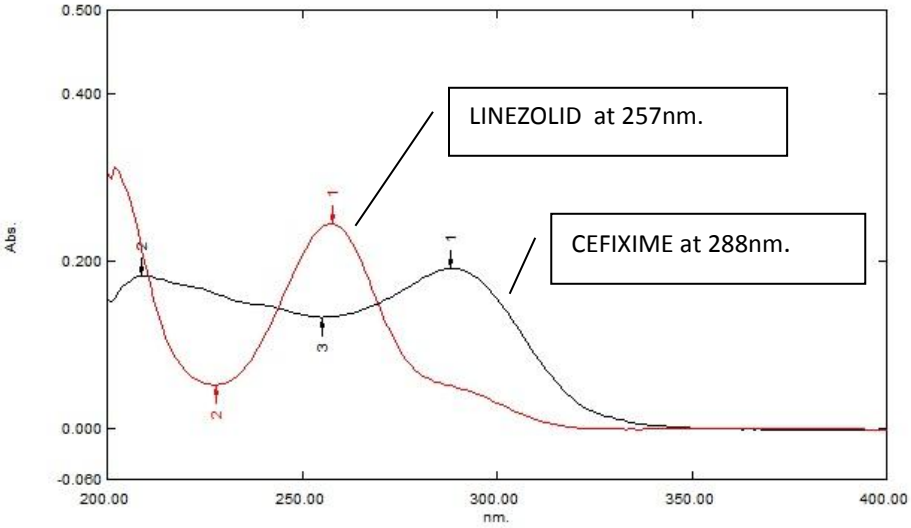
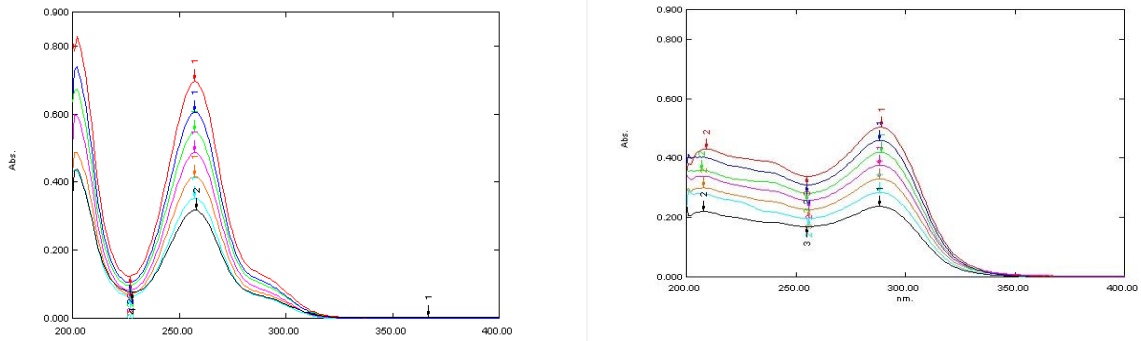


Fig:2 Overlein spectra if Cefixime(10 ppm) and Lilezolid (10 ppm)



(A) (B)

Fig:3 Overlein spectra if Cefixime(A) and Lilezolid(B)

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