WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 3, 19-27. Research Article ISSN 2277– 7105

DEVELOPMENT OF UV SPECTROPHOTOMETRIC METHODS FOR SIMULTANEOUS ESTIMATION OF CEFUROXIME AXETIL AND LINEZOLID IN PHARMACEUTICAL DOSAGE FORM

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Article Received on
28 Dec. 2019,

Revised on 18 Jan. 2020,
Accepted on 07 Feb. 2020

DOI: 10.20959/wjpr20203-16849

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ABSTRACT

In the present work two simple, accurate, sensitive, precise and economical UV spectrophotometric methods (Method-A and Method-B) have been developed for the simultaneous estimation of Cefuroxime axetil and Linezolid in pharmaceutical dosage form. Method-A is Area Under Curve Spectrophotometry, the wavelength range selected for quantitation are 271.4 – 281.4 nm and 252.4 – 262.4 nm. Whereas Method-B is Multicomponent Mode Analysis, Wavelength selected were 276.4 nm (λmax of CEF) and 257.4 nm (λmax of LIN) and 272.4 nm (isobestic point) for the analysis. Both the methods were found linear between 5-25 µg/mL for cefuroxime axetil and 6-30 µg/mL for linezolid. The methods showed good reproducibility and recovery with % RSD less than prescribed limit. Methods were successfully applied for the simultaneous determination of both the drugs in commercial tablet formulation. The results of the analysis have been validated statistically and by recovery studies. So it can be used for routine analysis of both drugs in quality control laboratories.

KEYWORDS: Cefuroxime axetil (CEF), Linezolid (LIN), Area Under Curve Method, Multicomponent Mode of Analysis.

INTRODUCTION

Cefuroxime axetil (6R, 7R)-3-{[(aminocarbonyl)-oxy]-methyl}-7{[(2Z)-2-(2-furyl)-2-(methoxy imino)-acetyl]-amino}-8-oxo-5-thia-1-azabicyclo [4.2.0]-oct-2-ene-2-carboxylic

acid. It is one of the bactericidal second generation cephalosporin antibiotic.[1] Linezolid N-[[(5S) - 3- [3- fluoro- 4 - (4 morpholinyl) phenyl] – 2 – oxo – 5 -oxazolidinyl] methyl] acetamide. It is a synthetic antibiotic of oxazolidinone class used as antibacterial and anti-infective. This combined dosage form will more usefull for the diseases.[2]

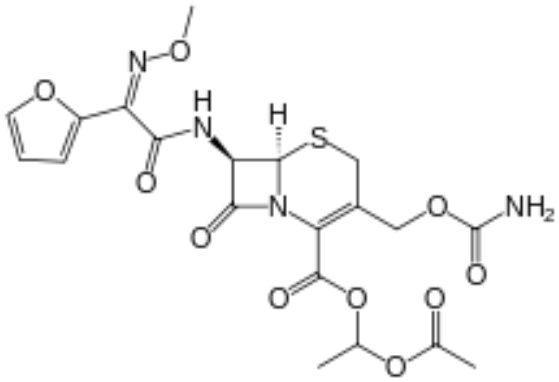

Fig. No. 1: Cefuroxime axetil

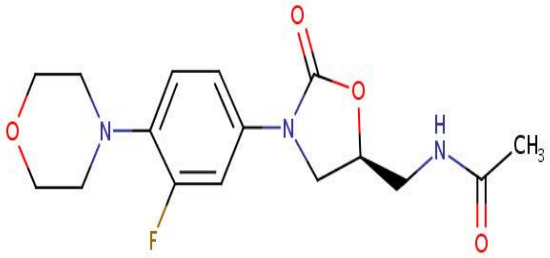

Fig. No. 2: Linezolid

As per literature survey, Cefuroxime axetil[3] and Linezolid[4] are officially in Indian Pharmacopoeia (2014), and are assayed by HPLC method. Few spectrophotometric methods are reported for determination as single drug[5-8] or in combination with another drugs.[9-12] Even very few methods are also reported for determination of both the drugs from their combined formulation.[13-18] In the present study, attempts were made to develop two hither to unreported spectrophotometric methods viz. Area under curve and Multicomponent mode for the analysis of Cefuroxime axetil and Linezolid in their combined dosage form.

MATERIALS AND METHODS

Apparatus and Instrument

UV- Visible double beam spectrophotometer (Shimadzu-1700, Japan),

Analytical balance (Shimadzu, Japan),

Ultra-sonication bath (Mumbai, India)

Materials

Cefuroxime axetil and Linezolid bulk powder were gifted by Malik Lifesciences Pvt. Ltd. Delhi (India).

Cefuroxime axetil and Linezolid tablets (Brand Name- **Linox – XT, Unichem Lab**) procured from local market having labeled content 500 mg Cefuroxime axetil and 600 mg Linezolid.

Methanol (AR grade).

Selection of Common Solvent

After assessing the solubility of drugs in different solvents, Methanol was used as common solvent for developing spectral characteristics.

Preparation of Standard Stock Solution

Accurately weighed 10 mg Cefuroxime Axetil and 12 mg Linezolid standard were transferred to separate 100 ml volumetric flask and dissolved in methanol. The flasks were shaken and volume was made up to the mark with Methanol to give solution containing 100 µg/mL of Cefuroxime Axetil and 120 µg/mL of Linezolid.

Preparation of Working Standard Solution

From above standard stock solution, working standard solution of Cefuroxime Axetil having concentrations range 5-25 µg/mL and Linezolid 6-30 µg/mL were prepared by appropriate dilution.

Preparation of Standard Mixture

From the standard stock solution of CEF and LIN, 1 ml of solution was diluted upto the mark in 10 ml volumetric flask with Methanol as solvent to give standard solution containing CEF 10 µg/mL and LIN 12 µg/mL.

Test Sample Preparation

Twenty tablets were weighed and powder; the powder equivalent to 10 mg Cefuroxime Axetil (12 mg of Linezolid) was accurately weighed and transferred into clean, dry 100 mL volumetric flask.

The powder was first dissolved in 20 mL of methanol by sonication, the volume was made up to the mark and then filtered through a Whatmann filter to obtain the concentrations of 100 µg/mL and 120 µg/mL for Cefuroxime Axetil and Linezolid respectively. From the above stock, 1.0 mL was transferred into a 10 mL volumetric flask and volume made up to 10 mL with the methanol to get the concentrations of 10 µg/mL for Cefuroxime Axetil and 12 µg/mL for Linezolid respectively.

Method A: Area under curve method

From the overlain spectra of both drugs, area under the curve in the range of 271.4 – 281.4 nm and 252.4 – 262.4 nm for both drugs were selected for the analysis (Fig. No. 3). The calibration curves between concentration and AUC for CEF and LIN were plotted in the

concentration range of 5-25 µg/mL and 6-30 µg/mL respectively. The 'X' values for both the drugs were determined at the selected AUC range. The 'X' value is the ratio of area under the curve at selected wavelength ranges with the concentration of component in g/lit. These 'X' values were the mean of six readings.

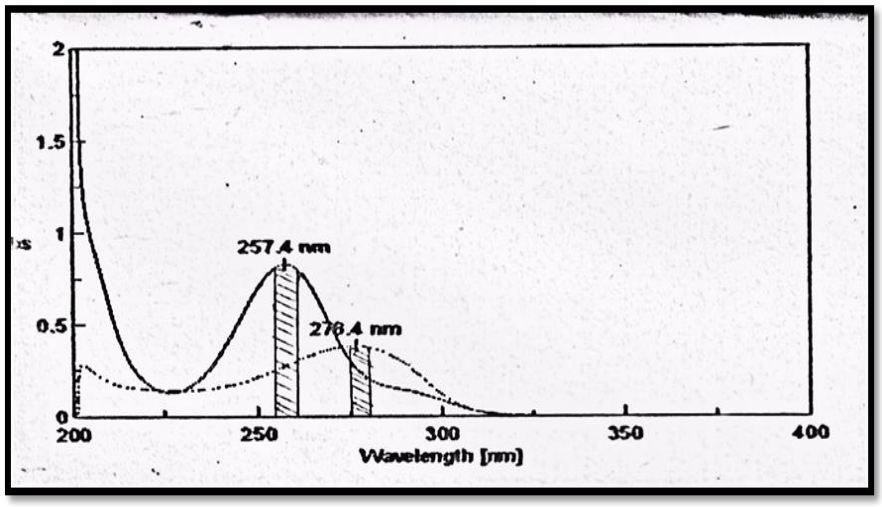

Fig. No. 3: Overlay spectrum for AUC of CEF and LIN.

Both the drugs i.e linezolid and Cefuroxime axetil were estimated by following formulae.

$$C_A = \frac{A_2\,Xa_1 - A_1\,Xa_2}{Xb_2\,Xa_1 - Xb_1\,Xa_2} \qquad C_B = \frac{A_1\,Xb_2 - A_2\,Xb_1}{Xa_1\,Xb_2 - Xa_2\,Xb_1}$$

Where,

C_A = Concentration of linezolid

C_B = Concentration of cefuroxime axetil

A_1 = Area of laboratory mixture at 262.4nm – 252.4nm

A_2 = Area of laboratory mixture at 281.4nm – 271.4nm

Xb_1 = Area absorptivity of linezolid at 262.4nm – 252.4nm

Xb_2 = Area absorptivity of linezolid at 281.4nm – 271.4nm

Xa_1 = Area absorptivity of cefuroxime axetil at 262.4nm – 252.4nm

Xa_2 = Area absorptivity of cefuroxime axetil at 281.4nm – 271.4nm

Method B: Multi-component mode analysis

In this method, the five mixed standard solutions with concentration of CEF and LIN in the ratio of 5:6, 10:12, 15:18, 20:24 and 25:30 (µg/mL) were prepared in methanol. All the mixed standard solutions were scanned over the range of 400-210 nm. In the multi-component the

wavelength Selected were 276.4 nm (λmax of CEF), 257.4 nm (λmax of LIN) and 272.4 nm (isobestic point). Sampling wavelengths were selected on trial and error basis. The concentration of individual drug was feed to the multi- component mode of the instrument. The instrument collects and compiles the spectral data from mixed standards. Overlain spectra of mixed standards solution are given in (Fig. 4). Mixed standard solution of both the drug was scanned on all the selected wavelengths to study the range of Beer's Lambert, s range. The sample solutions were scanned over the range of 400- 210 nm in the multi-component mode of the instrument and concentration of each component was obtained by analysis of spectral data of sample solution with reference to that of five mixed standards, in the terms of µg/mL.

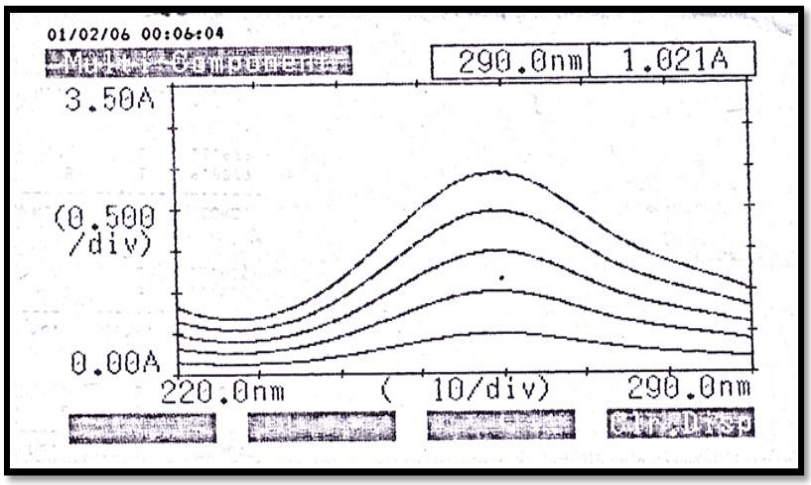

Fig. No. 4: Spectrum by Multicomponent method.

Validation

The methods were validated with respect to study of accuracy, precision and linearity.

Accuracy (Recovery studies)

To ascertain the accuracy of the proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% and120%). Observation for recovery studies are shown in table 2 and Percent recoveries for CEF and LIN by both methods were found in the range of 99.77% to 100.56%.

Precision

The reproducibility of proposed method was determined by performing tablet assay for Intra-day precision and Inter-day precision studies. Results of precision are expressed in %RSD and shown in table 3.

Linearity

The linearity of measurement was evaluated by analyzing different concentration of standard solution of CEF and LIN. For both the methods, the Beer- Lamberts concentration range was found to be 5-25 µg/mL for CEF and 6-30 µg/mL for LIN. Result are tabulated in table 4.

Table No. 1: Analysis of Commercial Formulations (precision).

Sr. No.	Wt. of tablet powder (mg)	% label claim method A		% label claim method B	
		CEF	LIN	CEF	LIN
1.	28.7	100.01	100.02	98.70	98.26
2.		99.90	99.98	99.40	99.05
3.		100.07	100.04	98.98	98.57
4.		100.28	100.14	99.61	99.21
5.		99.93	99.89	99.75	99.31
Mean		**100.03**	**100.01**	**99.07**	**98.88**
±SD		**0.1508**	**0.0909**	**0.656**	**0.448**
%RSD		**0.15**	**0.09**	**0.66**	**0.45**

Table No. 2: Results of Recovery Study.

Method-A: Area under curve method									
Level of % Recovery	Wt. of tablet pow. (mg)	Amount of standard drug added (mg)		Total drug estimated (mg)		Amount of pure drug recovered (mg)		%Recovery	
		CEF	LIN	CEF	LIN	CEF	LIN	CEF	LIN
80	28.7	8.00	9.6	17.97	21.57	7.975	9.577	99.69	99.76
100		10.00	12.00	20.07	24.01	10.078	12.01	100.78	100.08
120		12.00	14.4	21.99	26.32	11.991	14.326	99.92	99.49
							Mean	**100.13**	**99.77**
							±SD	**0.574**	**0.295**
							%RSD	**0.57**	**0.30**

Method-B: Multicomponent mode analysis									
Level of % Recovery	Wt. of tablet pow. (mg)	Amount of standard drug added (mg)		Total drug estimated (mg)		Amount of pure drug recover		%Recovery	
		CEF	LIN	CEF	LIN	CEF	LIN	CEF	LIN
80	28.7	8.00	9.6	18.09	21.55	8.095	9.554	101.19	99.53
100		10.00	12.00	19.97	24.11	9.976	12.116	99.76	100.97
120		12.00	14.4	22.08	26.29	12.089	14.298	100.74	99.29
							Mean	**100.56**	**99.93**
							±SD	**0.731**	**0.908**
							%RSD	**0.73**	**0.91**

Table No. 3: Intraday and Interdays data of tablet formulation.

Methods	Drug	Intraday precision (%label claim mean ± %RSD)	Interday precision (%label claim mean ± %RSD)
Method-A	CEF	99.98 ± 0.03	99.93 ± 0.06
	LIN	99.97 ± 0.07	100.31 ± 0.61
Method-B	CEF	100.11 ± 0.24	100.16 ± 0.37
	LIN	100.04 ± 0.22	100.29 ± 0.33

Table No. 4: Optical characteristics of the proposed methods.

Parameters	Method A		Method B	
	CEF	LIN	CEF	LIN
λ max (nm)	271.4 – 281.4	252.4 – 262.4	276.4	257.4
Beer's lambert's range (µg/mL)	5-25	6-30	5-25	6-30
Regression equation, Y=mx+c	Y = 0.3485x - 0.0104	Y = 0.6163x + 0.3206	Y = 4.6432x + 0.6507	Y = 5.7551x + 0.5157
Slope(m)	0.3485	0.6163	4.6432	5.7551
Intercept (c)	0.0104	0.3206	0.6507	0.5157
Correlation coefficient (r^2)	0.999	0.9981	0.9987	0.9998

RESULT AND DISCUSSION

For, both the methods linearity was observed in the concentration range of 5-25 µg/mL and 6-30 µg/mL for cefuroxime axetil and linezolid, respectively. Commercial formulations containing cefuroxime axetil and linezolid were analyzed by the proposed methods. Five replicate analysis of formulation were carried out and the mean assay values were found in the range of 98.88 to 100.03% shown in table no.1. The proposed methods were validated as per the ICH guidelines. The accuracy of the proposed method was determined by recovery studies. Pure cefuroxime axetil and linezolid was added to the pre-analyses tablet powder at three levels viz 80, 100, 120%. Three replicate analyses were carried out at each level. The mean percent recovery was found in the range of 99.77 to 100.56% as well as the Percent relative standard deviations was less than 2, for both the methods shown in table no.2. Precision is calculated as intraday and interday variations for both the drugs. Percent relative standard deviations for estimation of cefuroxime axetil and linezolid under intraday and interday variations were found to be less than 1.

CONCLUSION

Both the methods were validated as per ICH guidelines. The standard deviation and % RSD calculated for the proposed methods are low, indicating high degree of precision of the methods. The results of the recovery studies performed show the high degree of accuracy of the proposed methods. Hence, it can be concluded that the developed spectrophotometric

methods are simple, accurate, precise and selective and can be employed successfully for the estimation of cefuroxime axetil and linezolid in pharmaceutical formulation.

ACKNOWLEDGEMENTS

The authors are thankful to the Malik Lifesciences Pvt. Lid. Delhi (INDIA) for providing the gift sample of Cefuroxime axetil and Linezolid. The authors are also thankful to the Principle, Dr. M. J. Umekar Smt. K.B. College of Pharmacy, Kamptee, India, for providing the required facilities to carry out this research work and Mr. R.T. Lohiya for continuous support.

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