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RESEARCH ARTICLE

Spectrophotometric Method for Estimation of Linezolid in Tablet Formulation

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ABSTRACT

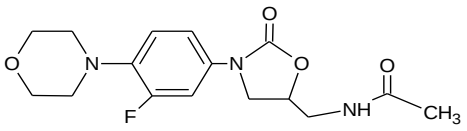
The present study describes a simple, accurate, precise and sensitive spectrophotometric method for the determination of linezolid (LZD) in pure and tablet forms. The method is based on the oxidation of LZD by Ferric citrate in the presence of 1,10-phenanthroline. The colored complex was measured at 510 nm. Beers law was observed in the concentration range of 1-10µg/ml with correlation coefficient 0.991. The method was validated for several parameters like accuracy, precision and linearity. The values of relative standard deviation and % recovery were found to be satisfactory, indicating that the proposed method is precise and accurate and can be used for the determination of Linezolid in tablet dosage forms.

Keywords: Linezolid, Spectrophotometry, ferric citrate, 1, 10-phenanthroline.

1. INTRODUCTION:

The oxazolidinones are a new class of antimicrobials with good activity against gram positive bacteria. Antimicrobial resistance is a significant nosocomial problem and is of increasing importance in community-acquired infections. Linezolid, (*S*)-*N*-[[-(3-(3-fluoro- 4 (4-morpholinyl) phenyl]-2-oxo-5-oxazolidinyl]-methyl] acetamide (Fig. 1), is a synthetic compound that acts by inhibiting the formation of initiation complex in bacterial protein synthesis, a mechanism of action which is distinct from that of any other antibiotics that are commercially available[1]. It is available for oral administration as film-coated compressed tablets containing 600 mg linezolid.

Literature survey revealed several methods reported for the estimation of Linezolid alone or in combination with other agents based on different techniques, RP-HPLC[1-6], LC-MS-MS[7], RP-LC[6], HPLC[7], UV[8], HPTLC[9] and Chiral HPLC[10] and Spectrophotometric method[11]. The proposed method is based on the reducing property of Linezolid drug. Linezolid is found to quantitatively reduce ferric (III) form of iron to ferrous (II) form, which is then made to interact with 1,10-phenanthroline to give reddish orange coloured complex, whose absorbance is measured at its λ max of 510 nm.



Linezolid

Fig. 1: Chemical Structure of Linezolid

2. METHODS AND MATERIALS

2.1. Instrument

A Labindia Analytical UV 3000 double beam UV/Visible spectrophotometer with spectral bandwidth of 1 nm and a pair of matched quartz cells were used for measuring the absorbance.

2.2. Materials

All the chemicals and reagents used in the spectrophotometric analysis were of analytical grade. Gift sample of standard Linezolid was kindly provided by Symed Laboratories Hyderabad India. 0.005M Ferric citrate, 0.02M 1,10-phenanthroline and distilled water was used in the present study. Tablets – Linid, manufactured by Zydus Cadila containing 600 mg per tablet was purchased from the market.

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2.3. Preparation of standard stock solution

Standard stock solution of Linezolid was prepared by dissolving 10 mg, in 10 ml of distilled water and final volume adjusted with same solvent. Working standard solutions (100 µg/ml) were prepared by subsequent dilution to 10 ml with same solvent.

2.4. Preparation of standard calibration curve

Into a series of 10ml volumetric flasks appropriate aliquots of the standard solution was taken to finally produce a concentration range of 1-10 µg/ml. To each volumetric flask 0.2ml of 0.005M ferric citrate was added. The contents in the flasks were mixed for 5 min and further 3 ml of 0.02M 1, 10-phenanthroline was added. The solutions were allowed to stand at room temperature for 10 min and the volume made up to the mark with distilled water. Absorbance of the resulting red coloured chromophore was measured at 510 nm against reagent blank prepared in the same manner as described above, but omitting the standard substance. Calibration curve of the drug was then plotted by taking the absorbance obtained on y-axis and the concentration of the solution on x-axis. (Fig.2). The curve showed linearity in the concentration range of 1-10 µg/ml with correlation coefficient 0.991.

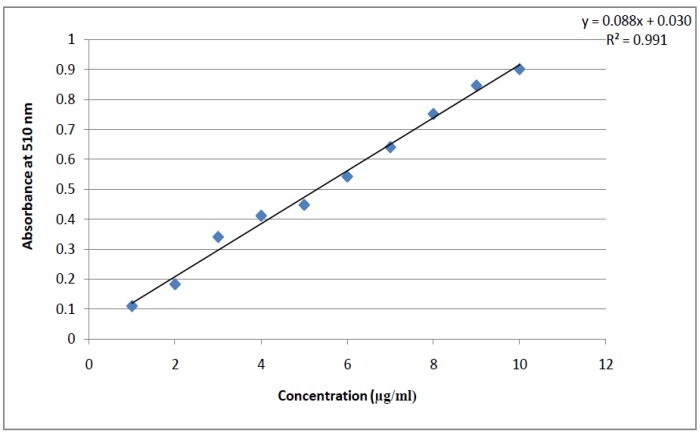

Fig:2 Standard calibration curve of linezolid

2.5. Determination of Linezolid in marketed tablet dosage formulation

Ten tablets purchased from the market were weighed and grounded. Powder equivalent to 10 mg of Linezolid was weighed accurately and dissolved in 10 ml distilled water. The resulting solution was filtered through Whatmann no.42 paper. Then the filtrate was diluted to 10 ml with water. The procedure given for standard calibration curve was then followed for development of colour.

2.6. Optimization of reagent volumes and conditions:

The volume of reagent concentrations required for obtaining maximum absorbance for the solutions has been optimized.

2.7. Validation study

With optimized conditions, the proposed method has been validated for several parameters like linearity, accuracy, precision, sensitivity (sandell's sensitivity) and stability of colour.

2.7.1. Linearity

The linearity of the analytical method was its ablity to elicit test results which are directly proportional to analyte concentration in samples within a given range. To establish the linearity of the proposed method, various aliquots of the standard solution of the drug were prepared from stock solution and analysed. The drug showed linearity in the range of 1-10µg/ml with correlation coefficient 0.991.

2.7.2. Precision

Precision studies were carried out to ascertain the reproduciblity of the proposed method. Repeatablity was determined by preparing six replicates of same concentration of the sample and the absorbance was measured. The results were reported as %RSD. The precision result showed a good reproducibility (Table 1) with percent relative standard deviation less than 2.

2.7.3. Accuracy

Accuracy of the proposed method was determined using recovery studies. The recovery studies were carried out at 3 levels by adding different amounts (80%,100%,120%) of the pure drug to the pre-analysed formulation. The solutions were prepared in triplicates and the % recovery was calculated. The results are shown in (Table 2).

Parameters	Observations
Absorption Maximum	510 nm
Linearity range	1-10 µg/ml
Correlation coefficient	0.991
Regression equation	0.088X + 0.030
Slope	0.088
Intercept	0.030
Accuracy	101.04 – 101.93%
Precision (%RSD)	0.949%
Stability of colour	>3 hours
Sandell's Sensitivity	9.09×10^{-3} µg/cm^2

Table 1: Validation parameters

Concentration of sample (µg/ml)	Concentration of standard Added (µg/ml)	Absorbance at 510nm*	Concentration from graph (µg/ml)	% Recovery
4	3.2	0.648	7.33	101.85
	4	0.714	8.08	101.04
	4.8	0.792	8.97	101.93

(*Average of three determinations)

Table 2: Recovery study of Linezolid from tablet samples

3. RESULTS AND DISCUSSION

The proposed method provides a simple, accurate, economical and convenient method for the analysis of linezolid using UV spectrophotometry. The use of ferric citrate instead of other ferric salts like chloride or sulphate is recommended as the solubility of citrate salts is

generally satisfactory in aqueous medium and resulting solutions are stable for longer duration of time. The Beers law was obeyed in the concentration range of 1-10 µg/ml, with correlation coefficient 0.991. Accuracy of the proposed method was determined by the recovery studies, and good %recovery (101.04 – 101.93%) of the drug obtained indicate that the method is accurate. The method was found to be precise as %RSD value was found to be less than 2.

4. CONCLUSION

The present work describes simple, precise, accurate and economic method for selective determination of linezolid (LZD) in formulation based on the oxidation of LZD by Ferric citrate in the presence of 1,10-phenanthroline. The colored complex was measured at 510 nm. Beers law was observed in the concentration range of 1-10µg/ml with correlation coefficient 0.991. Ferric citrate can suitably replace the commonly used ferric chloride and ferric sulphate salts used in such methods of analysis.

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Conflict of Interest: None Declared

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