INTERNATIONAL JOURNAL OF PHARMACEUTICS & DRUG ANALYSIS
VOL.5 ISSUE 12, 2017; 456 – 466; http://ijpda.com; ISSN: 2348-8948

Research Article

Stability Indicating Method For The Simultaneous Estimation Of Cefuroxime Axetil And Linezolid In Pharmaceutical Dosage Forms.

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Date Received: 27th November 2017; Date accepted: 9th December 2017; Date Published: 11th December 2017

Abstract

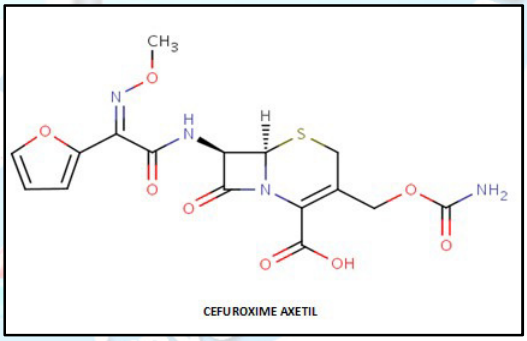
A simple, rapid, accurate and economical stability indicating RP-HPLC method has been developed for simultaneous estimation of Cefuroxime Axetil & Linezolid pharmaceutical dosage under different stress conditions For the analysis, HPLC LC- 20 AT SPD 20A UV detector at 240 nm and C_{18} (250mm x 4.6 mm) column was used. The selected mobile phase was Potassium phosphate (pH 5.0) and Acetonitrile (60:40v/v) in isocratic mode at a flow rate of 1 mL/min. Retention time of Linezolid and Cefuroxime Axetil were found to be 3.713 min and 6.107 min respectively. The methods are found to be specific as there was no interference of any co-eluting impurities after stress degradation study. The degraded products are well resolved, indicating the method can also be useful for determination of degraded products.

Key words: Cefuroxime Axetil, Linezolid, Stability indicating RP-HPLC Method.

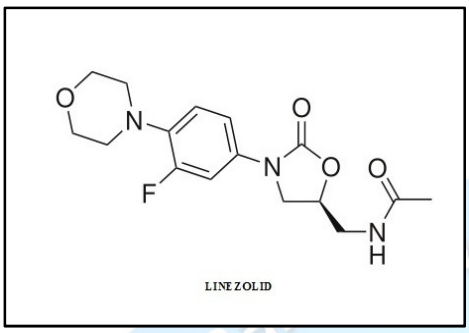
INTRODUCTION

Cefuroxime axetil (CFA) is a second-generation cephalosporin that contains the classic β-lactam ring structure. Cefuroxime axetil is an ester prodrug of cefuroxime, which is rendered more lipophilic by esterification of carboxyl group of the molecule by the racemic 1- acetoxyethyl bromide, thus enhancing absorption. The absorbed ester is hydrolysed in the intestinal mucosa and in portal circulation. Products of hydrolysis are active cefuroxime, acetaldehyde and acetic acid. Cefuroxime is chemically (1RS)-1-[(acetyl) oxy] ethyl- (6R, 7R)-3-(carbamoyloxy) methyl]-7-[(Z-2-furan- 2yl)-2-(methoxyimino) acetyl) amino]-8-oxo-5-thia-1-azabicyclo- (4.2.0)-oct-2-ene-2-carboxylate. It is used as an antibiotic for the treatment of many type of bacterial infections such as bronchitis, sinusitis, tonsillitis, ear infections, skin-infections, urinary tract infections.

Linezolid(LNZ) is chemically (*S*)-*N*-({3-[3-fluoro-4-(morpholin-4-yl) phenyl] - 2-oxo-1,3-oxazolidin-5-yl}methyl)acetamide. It is member of oxazolidinone class. It is used for the treatment of serious infection caused by Gram positive bacteria that resistance to other antibiotics. The main uses are infections of the skin and pneumonia although it may be use for a variety of other infections. Oxazolidinone bind to the 50S subunit of the prokaryotic ribosome, preventing it from complexing with the 30S subunit, mRNA, initiation factors and formylmethionyl-tRNA. The net result is to block assembly of a functional initiation complex for protein synthesis, thereby preventing translation of the mRNA.



CEFUROXIME AXETIL



LINEZOLID

Literature review reveals that numbers of individual analytical methods available for estimation of Cefuroxime Axetil and Linezolid intheir individual dosage forms.But no Stability indicating HPLC has been reported for simultaneous estimation of Cefuroxime Axetil and Linezolid in solid dosage forms. So it is develop Stability indicating HPLC method for simultaneous estimation of Cefuroxime Axetil and Linezolid in Pharmaceutical Dosage Form.[8-35]

MATERIALS AND METHODS

Apparatus and Software

HPLC was performed on isocratic Shimadzu (Shimadzu Corporation, Kyoto, Japan) chromatographic system equipped with Shimadzu LC-20AT pump and Shimadzu SPD-20AV absorbance detector Data acquisition and integration was performed using spinchrome software.

Reagents and materials

Cefuroxime Axetiland Linezolid were procured from Gujarat laboratory, Ahmedabad, Gujarat.Tablet samples were purchased from local pharmacy (**Stafcure-LZ**- Labelled claim: 500mg Cefuroxime and 600 mg Linezolid). HPLC grade methanol (Merck Ltd., Mumbai, India) and acetonitrile (Finar Chemicals Ltd., Mumbai, India) were used during study. Double distilled water (Purified HPLC grade water) was obtained by filtering double distilled water through nylon filter paper 0.2 µm pore size and 47 mm diameter (Pall Life Sciences, Mumbai, India). Potassium dihydrogen orthophosphate purified was procured from S D Fine Chem. Ltd, Mumbai.

Chromatographic Condition

Chromatographic separation was performed using C18 (25cm x 0.46 cm) Hypersil BDS, at ambient temperature, eluted with mobile phase at a flow rate of 1.0 ml/min. The mobile phase consisted of Potassium phosphate (pH 5.0): Acetonitrile (60:40 v/v). Measurements were made with an injection volume of 20 µL and UV detection at 240 nm, as both components showed reasonably good response at this wavelength.

Selection of wavelength

Standard solution of CefuroximeAxetil (10 µg/mL) and Standard solution of Linezolid (12 µg/mL) were scanned between 200-400 nm using UV-visible spectrophotometer. Wavelength was selected from the overlay spectra of above solutions.Both Cefuroxime Axetil and Linezolid show reasonably good response at 231nm.

Preparation of mobile Phase

Take 6.8 gmPotassium Hydrogen Phosphate in 1000 ml water and dissolve, adjust pH 5.0 with 10 M potassium hydroxide. Filter it with 0.45 micron filter paper and mix with Acetonitrile. The mobile phase composition is Buffer:Acetonitrile 60:40(v/v). Sonicate the solution for 15 min.

Preparation of standard stock solution

Standard solution of Cefuroxime Axetil (100 µg/ml) and linezolid (120µg/ml) was prepared by transferring accurately weighed Cefuroxime Axetil (10 mg) and linezolid (12 mg) in 100 ml volumetric flask separately and dissolving in methanol. The solution was diluted to 100 ml with methanol in separate volumetric flask to inject in chromatographic system.

FORCE DEGRADATION STUDIES:

Acid degradation

Acid decomposition studies were performed by Refluxing 1 mlof stock solution was transferred in to 10 ml of volumetric flask. Two ml of 0.1 N HCl solutions was added and mixed well and put for 5 hrs at 70 ºC 250 ml Round bottom flask. After time period the content was cooled to RT. Then the volume was adjusted with diluents to get 10 µg/ml for Cefuroxime Axetil and 12 µg/ml for Linezolid.

Base degradation

Basic decomposition studies were performed by refluxing 1 ml of stock solution was transferred in to 10 ml of volumetric flask. 2 ml of 0.1 N NaOH solutions was added and mixed well and put for 5 hrs at 70 ºC 250 ml Round bottm flask. After time period the content was cooled to RT. Then the volume was adjusted with diluent to get 10 µg/ml for Cefuroxime Axetil and 12 µg/ml for Linezolid.

Oxidation degradation

Oxidative decomposition studies were performed by refluxing One ml of stock solution was transferred in to 10 ml of volumetric flask. Two ml of 3% H_2O_2 solutions was added and mixed well and put for 5 hrs at 70 ºC 250 ml Round bottom flask. After time period the content was cooled to RT. Then the volume was adjusted with diluents to get 10 µg/ml for Cefuroxime Axetil and 12 µg/ml for Linezolid.

Photo degradation

Photo decomposition studies were performed by taking 1 ml of stock solution was transferred in to 10 ml of volumetric flask, put for 24 hrs in Sunlight. After time period the content was cooled to RT. Then the volume was adjusted with diluents to get 10 µg/ml for Cefuroxime Axetil and 12 µg/ml for Linezolid.

Thermal degradation

Thermal decomposition studies were performed by taking 1 ml of stock solution was transferred in to 10 ml of volumetric flask, put for 5 hrs in 80 ºC Temperature in Oven. After time period the content was cooled to RT. Then the volume was adjusted with diluent to get 10 µg/ml for Cefuroxime Axetil and 12 µg/ml for Linezolid.

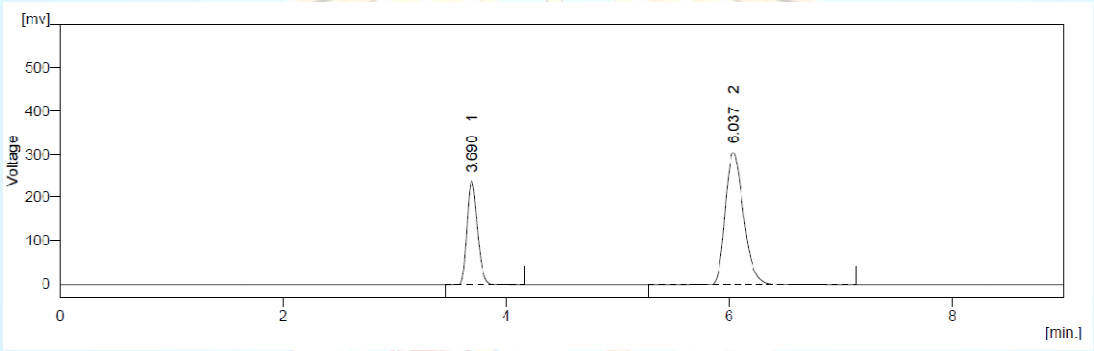


Fig. 1. Linezolid and Cefuroxime Axetil Standard for stability

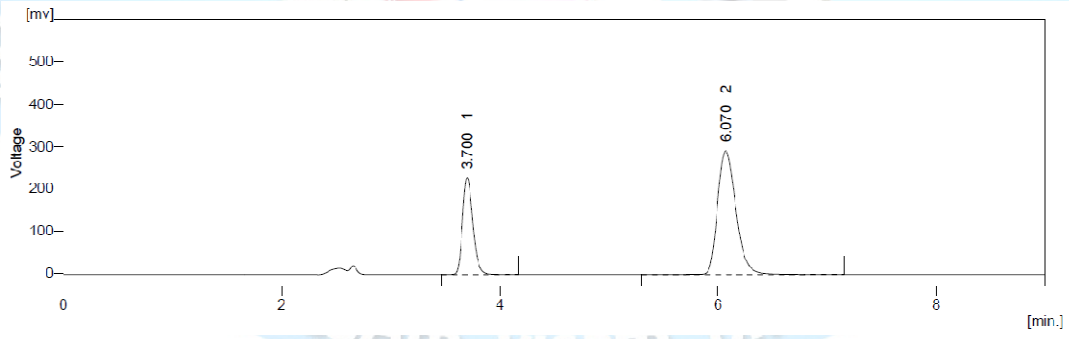


Fig. 2. Linezolid and Cefuroxime Axetil sample

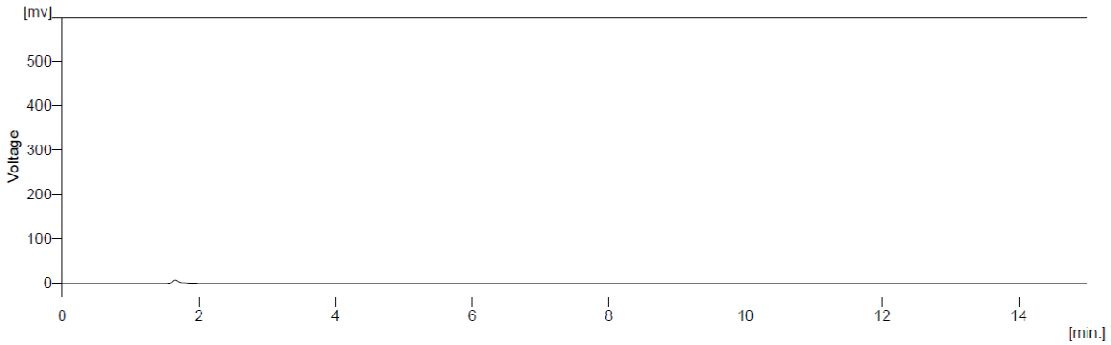


Fig. 3. Acid Degradation Blank

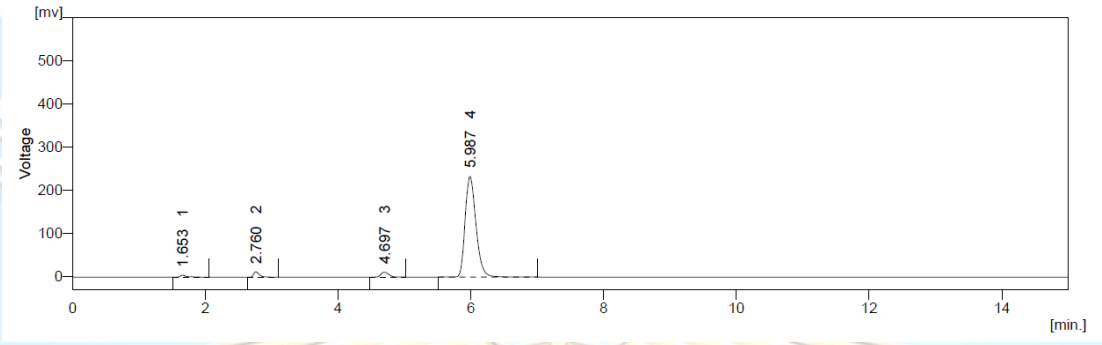


Fig. 4. Cefuroxime Axetil Acid Degradation Standard at 5 hrs

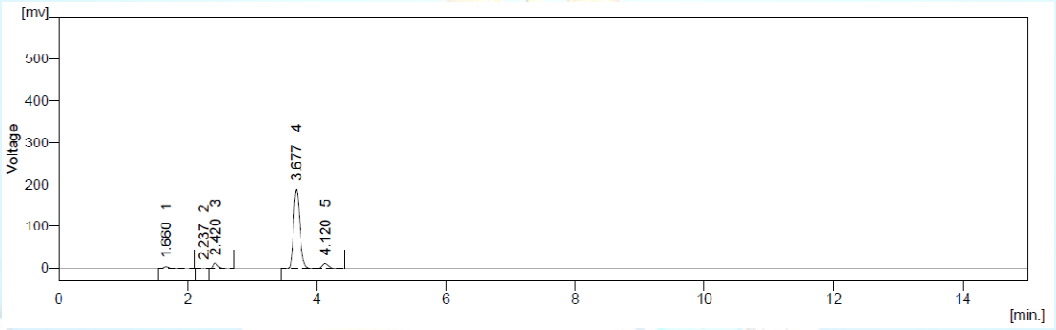


Fig. 5. Linezolid Acid Degradation Standard at 5 hrs

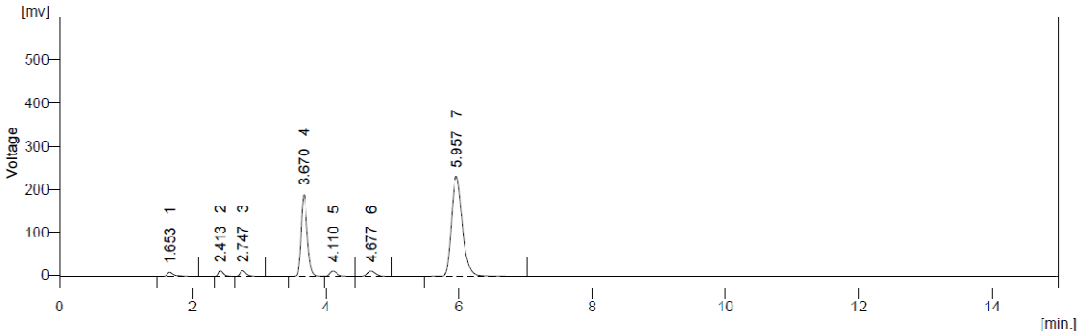


Fig. 6. Linezolid and Cefuroxime Axetil Acid Degradation Sample at 5 hrs

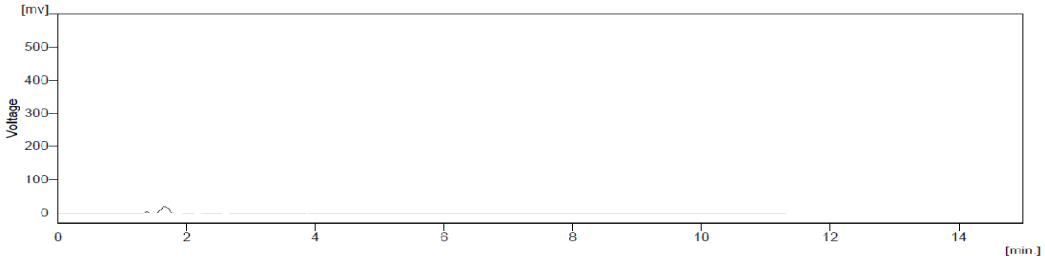


Fig. 7. Base Degradation Blank

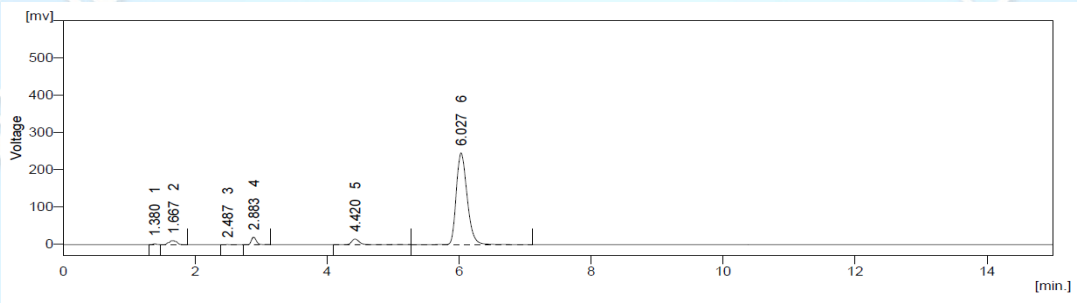


Fig. 8. Cefuroxime Axetil Base Degradation at 5 hrs

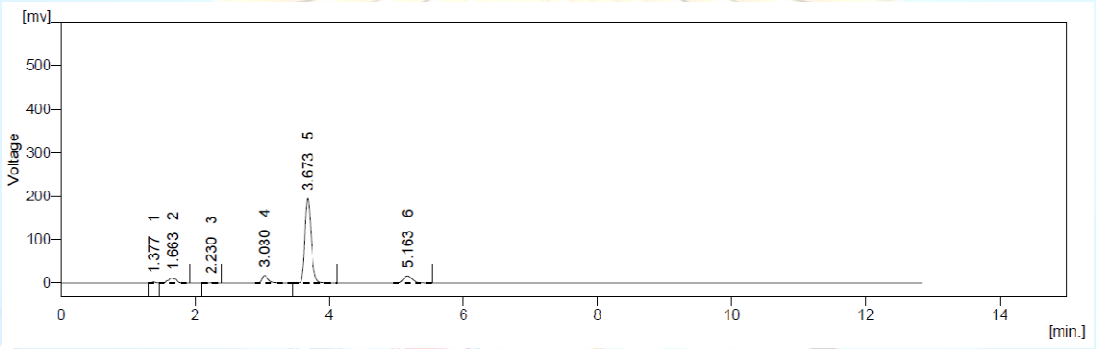


Fig. 9. Linezolid Base Degradation at 5 hrs

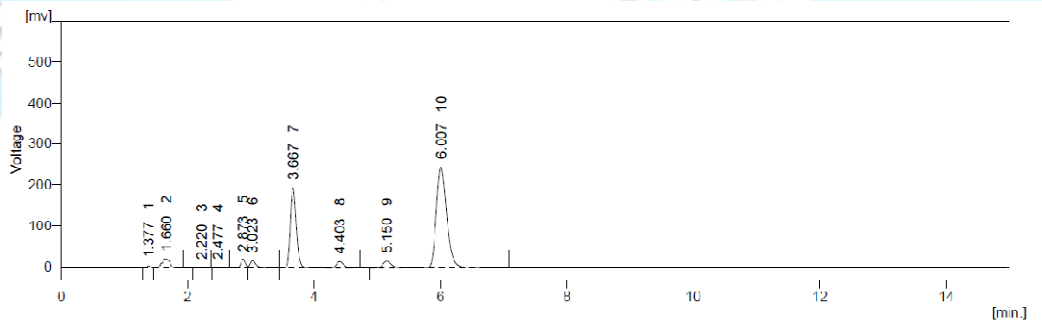


Fig. 10. Linezolid and Cefuroxime Axetil Base Degradation Sample at 5 hrs

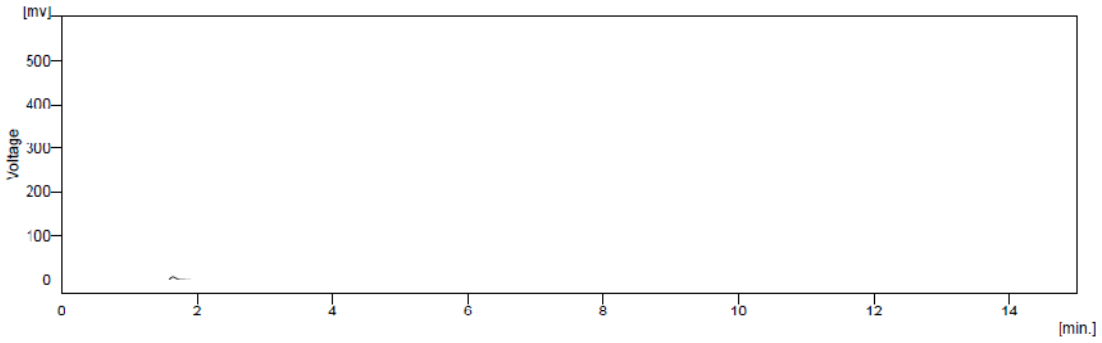


Fig. 11. Oxidation Degradation Blank

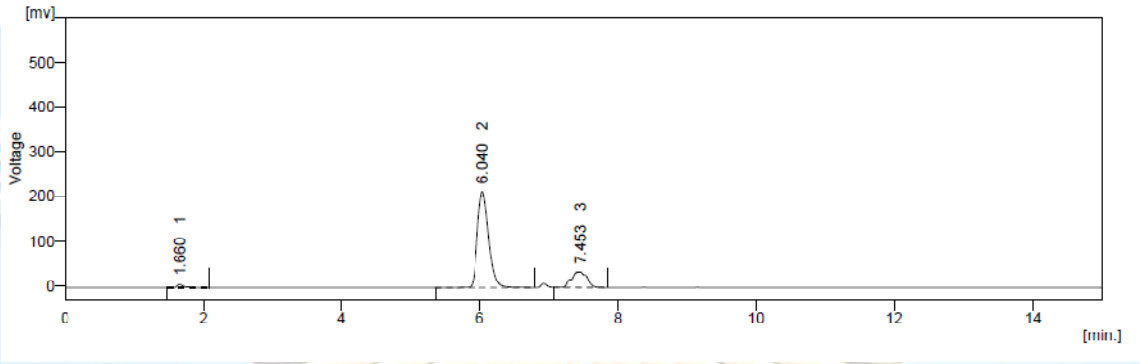


Fig. 12. Cefuroxime Axetil Oxidation Degradation at 5 hrs

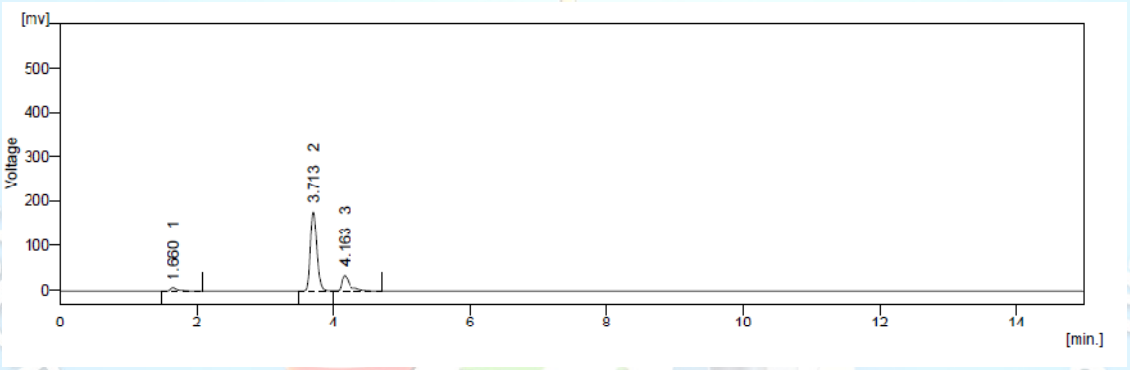


Fig. 13. Linezolid Oxidation Degradation at 5 hrs

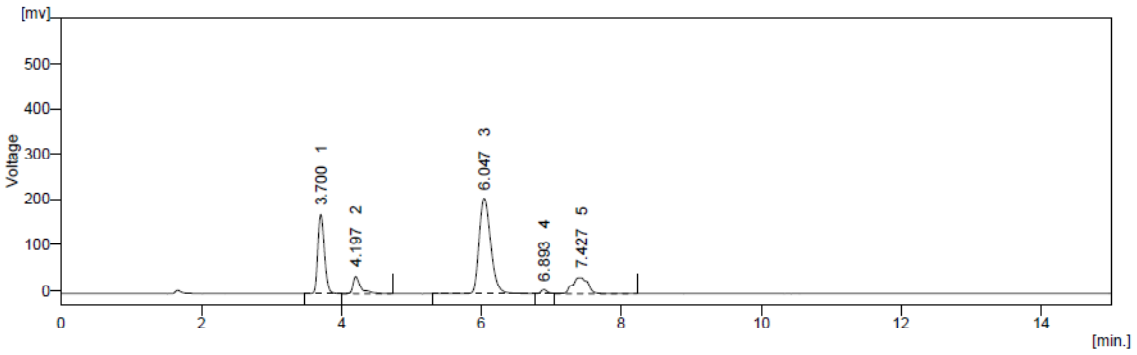


Fig. 14. Linezolid and Cefuroxime Axetil Oxidation Degradation Sample at5 hrs

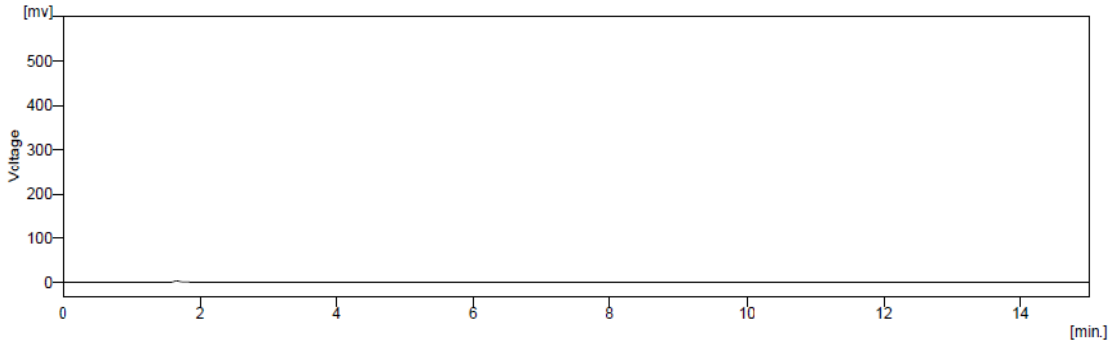


Fig. 15. Photo Degradation Blank

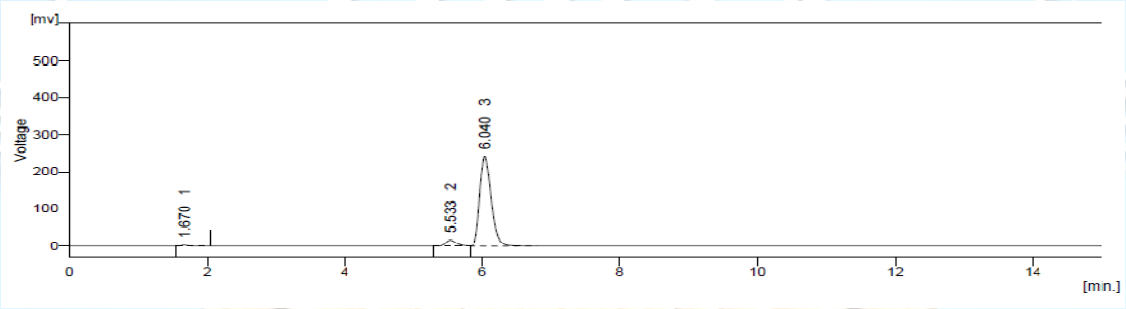


Fig. 16. Cefuroxime Axetil Photo Degradation at 24 hrs

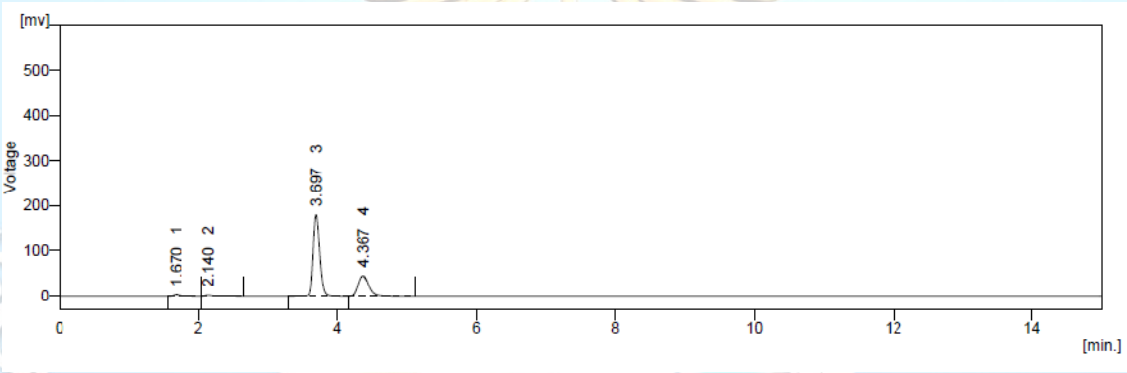


Fig. 17. Linezolid Photo Degradation at 24 hrs

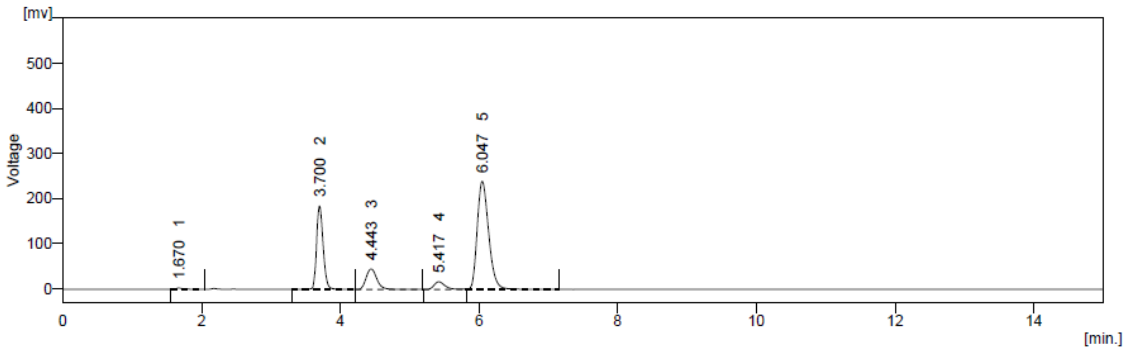


Fig. 18. Linezolid and Cefuroxime Axetil Photo Degradation Sample at 24 hrs

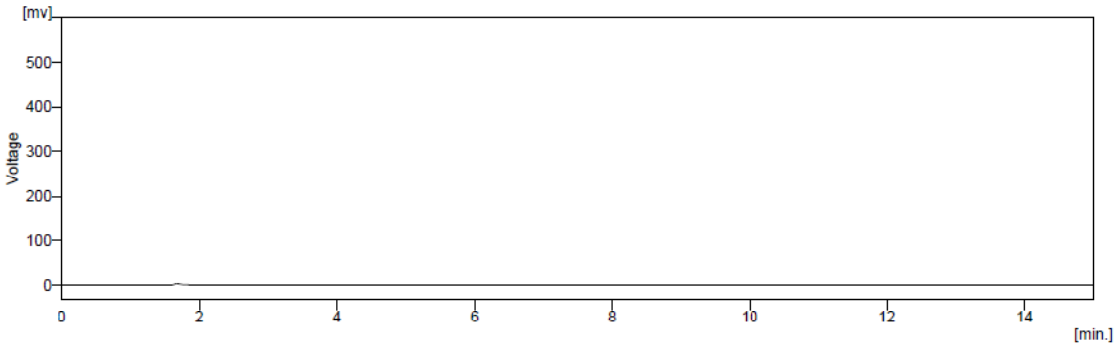


Fig. 19. Thermal Degradation Blank

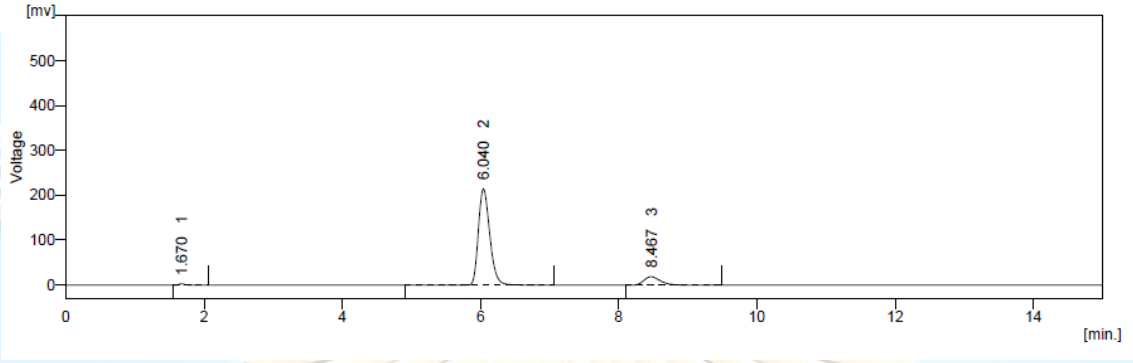


Fig. 20. Cefuroxime Axetil Thermal Degradation at 5 hrs

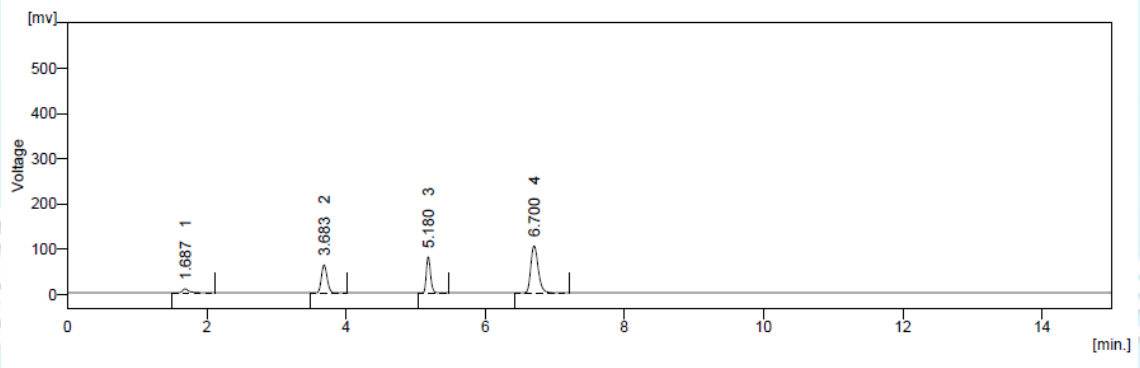


Fig. 21. Linezolid Thermal Degradation at 5 hrs

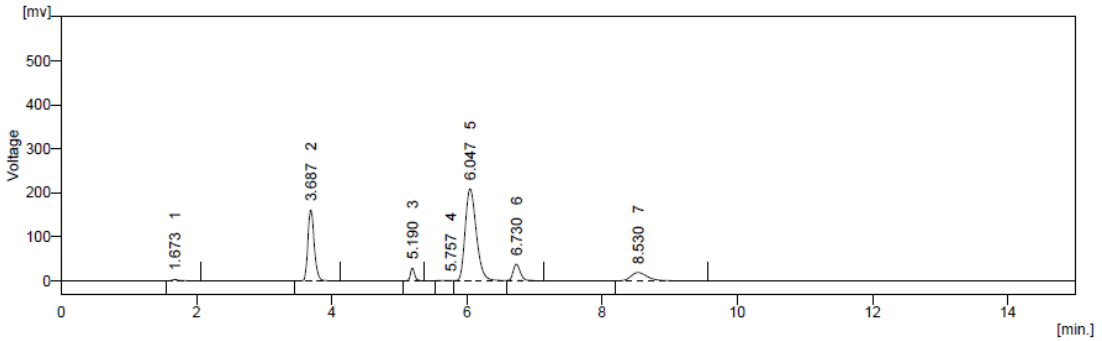


Fig. 22. Linezolid and Cefuroxime Axetil Thermal Degradation Sample at 5 hrs

Calculation for Stability:

Table 1. Linezolid and Cefuroxime Axetil std for Stability

Drugs	Area
Cefuroxime Axetil	1562.410
Linezolid	3537.78

Table 2. Cefuroxime Axetil % Degradation

Parameter	Standard		Sample	
	Area	%Degradation	Area	%Degradation
Acid	1237.01	20.83	1233.37	21.06
Base	1258.93	19.42	1254.18	19.73
Oxidation	1161.49	25.66	1124.32	28.04
Photo	1179.45	24.51	1213.25	22.35
Thermal	1012.12	35.22	1043.39	33.22

Table 3. Linezolid % Degradation

Parameter	Standard		Sample	
	Area	%Degradation	Area	%Degradation
Acid	2652.15	25.03	2633.59	25.56
Base	2824.17	20.17	2806.63	20.67
Oxidation	2467.828	30.24	2406.465	31.98
Photo	2786.432	21.24	2755.239	22.12
Thermal	2483.982	29.79	2388.286	32.49

Discussion

A new stability indicating RP-HPLC method has been developed for simultaneous estimation of Cefuroxime Axetil and Linezolid in tablet dosage form was rapid, accurate, precise, specific, sensitive & robust.

From the above study we can conclude that the Cefuroxime Axetil and Linezolid both the drug were subjected to acid, alkali, hydrolysis, oxidation, thermal and photo degradation.

From the peak purity profile studies, it was confirmed that peak of the degradation product and excipint was not interfering with the peak of drug. Hence, this method can be used for analysis of Cefuroxime Axetil and Linezolid in bulk drug and pharamaceutical dosage form in quality control department for routine analysis.

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