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Research Article

ANALYTICAL PROFILE OF RAW MATERIAL AND FINISHED PRODUCT OF CEFUROXIME AXETIL

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ABSTRACT

Cefuroxime Axetil is the 1-acetoxyethyl ester of Cefuroxime. Chemically cefuroxime axetil is (*RS*)-1-hydroxyethyl (6*R*, 7*R*)-7-[2-(2-furyl) glyoxyl-amido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo-Oct-2-ene-2-carboxylate, 72-(Z)-(O-me-thyl-oxime), 1-acetate-3-carbamate. Its molecular formula is $C_{20}H_{22}N_4O_{10}S$, and it has a molecular weight of 510.48. The cefuroxime raw material was identified by HPLC and IR Spectroscopy. The sample is tested for the solubility, diastereoisomer ratio, crystallinity and bulk density. The amount of cefuroxime axetil was estimated by HPLC assay method. The Cefuroxime axetil finished product was identified by HPLC and IR Spectroscopy. The average weight of tablets was calculated by taking the weights of 20 tablets. The content uniformity of the dosage units was calculated by weight variation method. The dissolution rate was calculated by HPLC method by using Paddle apparatus. The amount of Cefuroxime present in the sample was estimated by HPLC assay method. The known and unknown related substances present in the compound were estimated by HPLC method. Results obtained during the study were satisfactory and can be used for commercial purpose.

Keywords: Cefuroxime axetil, HPLC method, IR Spectroscopy.

INTRODUCTION

Cefuroxime[1] have a broader spectrum of activity, with enhanced activity against H.*influenzae* and the Enterobacteriaceae resulting from an increased stability to β-lactamases. Oral agent in this group is the Axetil ester of Cefuroxime. After oral administration, cefuroxime axetil is absorbed from the gastrointestinal tract and rapidly hydrolyzed by nonspecific esterases in the intestinal mucosa and blood to cefuroxime. During absorption, this acid-stable, lipophilic, oral prodrug derivative of Cefuroxime Axetil is hydrolysed to Cefuroxime by intestinal and/or plasma enzymes. Cefuroxime is subsequently distributed throughout the extracellular fluids. The axetil moiety is metabolized to acetaldehyde and acetic acid. The Axetil ester provides an oral bioavailability of 35 to 50% of Cefuroxime, depending on conditions. Approximately 50% of serum cefuroxime is bound to protein. Cefuroxime is excreted unchanged in the urine. In adults, approximately 50% of the administered dose is recovered in the urine within 12 hours. In common with other antibiotics, cefuroxime axetil may affect the gut flora, leading to lower estrogen reabsorption and reduced efficacy of combined oral estrogen/progesterone contraceptives. Adverse reactions to cefuroxime have

generally been mild and transient in nature.

MATERIALS AND METHODS

1) Cefuroxime axetil raw material

Cefuroxime Axetil Ph. Eur was procured and its molecular formula $C_{20}H_{22}N_4O_{10}S$ and its category Anti-bacterial and storage conditions preserve in air tight containers protect from light.

2) HPLC

Instrumentation, Reagents, mobile phase preparation, chromatographic conditions, preparation of solutions, evaluation of system suitability and procedure proceed as directed in the 'Assay' The retention time of the principal peaks for cefuroxime axetil diasteroisomer A and diasteroisomer B in the chromatogram of the sample solution should compare to that of sample peaks in the chromatogram of sample solution.

3) IR

Perkin-Elmer FT-IR, Model- Spectrum One or Equivalent, Hydraulic pellet press, Agate mortar & pestle, 13mm die and KBr pellet holder.

3.1) Reagents - Potassium Bromide (KBr) – IR Spectroscopy grade

3.2) Procedure - Triturate about 2-3mg of sample in 200-300 mg of previously dried KBr (at 250°C for 1 hour). Make a pellet and record the IR spectrum between 650 and 4000 cm^{-1}. Do the background correction for KBr using a KBr pellet. Compare the IR spectrum with similarly recorded spectrum of Cefuroxime axetil - amorphous working standard.

4) Diastereoisomer ratio by HPLC

Instrumentation, Reagents, Mobile phase preparation, Chromatographic conditions, Preparation of solutions, Evaluation of system suitability and procedure – proceed as directed in the "Assay". Calculate the diastereoisomer ratio from the chromatogram of sample solution as follows:

Diastereoisomer ratio = AT2 /TA

AT2 - Average of peak area counts of the Cefuroxime axetil diastereoisomer A in the chromatograms of sample solution. TA - Average to the sum of peak area counts of Cefuroxime axetil diastereoisomers A and B in the chromatograms of sample solution.

5) Assay by HPLC

5.1 Reagents

Ammonium dihydrogen orthophosphate, Orthophosphoric acid, Acetanilide used were analytical grade. Methanol used was HPLC Grade and water from - Milli-Q.

5.2 Preparation of 0.2M ammonium dihydrogen phosphate

Dissolve 23.0 gm of ammonium dihydrogen phosphate in 1000mL water. Filter through 0.45 membrane filter.

5.3 Preparation of mobile phase

Prepare a degassed mixture of 0.2M ammonium dihydrogen phosphate and methanol in the ratio of 62:38 V/V.

5.4 Preparation of ammonium dihydrogen orthophosphate buffer

Dissolve 23.0gm of ammonium dihydrogen orthophosphate in 1000mL of water. Adjust the pH to 2.4 ±0.05 with orthophosphoric acid.

5.5 Chromatographic condition

Column - Zorbax TMS, 5 (250x4.6 mm), Pump mode – Isocratic, Flow rate - 1.5 mL/min, Detection - UV, 278 nm, Injection volume - 10 L, Data acquisition time - 25 min.

6) RESULTS AND DISCUSSION

6.1) HPLC Identification

The Retention times of the principal peaks for Cefuroxime axetil diastereoisomer A and Cefuroxime axetil diastereoisomer B in the chromatogram of the sample solution corresponds to that of the sample peaks in the chromatogram of standard solution.

6.2) IR

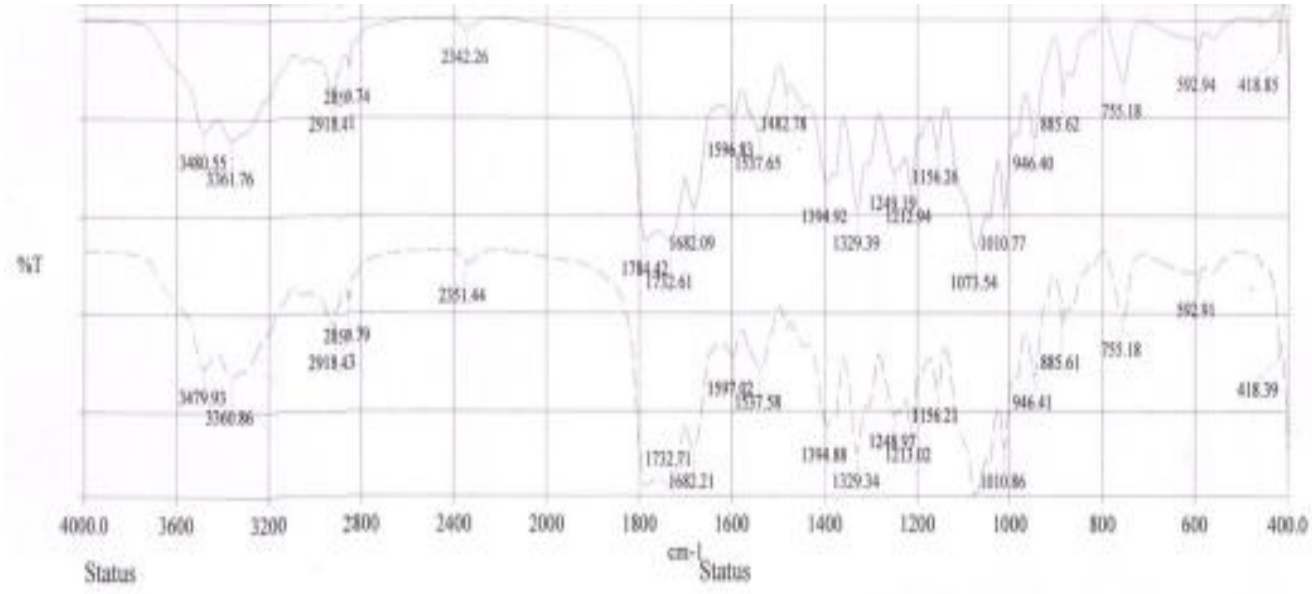
The transmission minima or absorption maxima in the spectrum obtained with the substance recorded as KBr pellet correspond in position and relative size to those in the spectrum obtained with the Cefuroxime Axetil Amorphous Working standard. The amide C=O stretch was found between 1690-1630 cm-1 in both standard and sample Cefuroxime axetil. Hence the sample is identified as Cefuroxime Axetil Raw material. The results were shown in the IR graph Fig. 1.

6.3) DIASTEROISOMER RATIO BY HPLC

Diastereoisomer ratio = AT2/TA

AT2 - Average of peak area counts of the Cefuroxime axetil diastereoisomer A in the chromatograms of sample solution. TA - Average to the sum of peak area counts of Cefuroxime axetil diastereoisomers A and B in the chromatograms of sample solution.

Fig. 1 IR spectra of Cefuroxime Axetil (amorphous)



AT2 = 1733107 + 1733532= 1733319.5
2

TA = (1802752 + 1733107) + (1803728 + 1733532)/2
= 3536559.5

Diastereoisomer Ratio = 1733319.5/3536559.5 = 049011. The Cefuroxime axetil contains two diastereoisomers A and B. The diastereoisomer ratio was calculated by taking the peak areas from HPLC graph as 49011.

6.4) ASSAY BY HPLC

Assay (%m/m, as C20H22N4O10S) (X1) = (At1×Ws×10×50×50×P)/(As ×50×50×WT×10)

Assay (%m/m, as C20H22N4O10S) (X2) = (At2×Ws×10×50×50×P)/(As×50×50×WT×10)

At1 - Ratio of Sample Solution-1 (Sum of the peak areas of the Cefuroxime Axetil Diastereoisomer A and B to the peak area of Internal Standard) = 4.4655

At2 - Ratio of Sample Solution-2 (Sum of the peak areas of the Cefuroxime Axetil Diastereoisomer A and B to the peak area of Internal Standard) = 4.4705

As - Average Ratio of Standard Solution (Sum of the peak areas of the Cefuroxime Axetil Diastereoisomer A and B to the peak area of Internal Standard) = 4.43098

Ws - Weight of Standard = 60.86 mg

WT - Weight of Sample = 60.86 mg

P - Potency of Cefuroxime Axetil working standard used = 98.8%

$$X1 = \frac{4.4655 \times 60.86 \times 10 \times 50 \times 50 \times 98.8}{4.43098 \times 50 \times 50 \times 60.86 \times 10} = 99.56\%$$

$$X2 = \frac{4.4705 \times 60.86 \times 10 \times 50 \times 50 \times 98.8}{4.43098 \times 50 \times 50 \times 60.86 \times 10} = 99.68\%$$

Average = X1 + X2 = 99.56 + 99.68 = 99.62%
2 2

Assay (%m/m, as $C_{20}H_{22}N_4O_{10}S$) = 99.62%

The content of Cefuroxime axetil was calculated by HPLC assay method by using Ammonium dihydrogen phoasphate:methanol (62:38 v/v). The retention time of Cefuroxime axetil-A was found at 13.18 min and for Cefuroxime axetil-B was at 11.34 min. The percentage potency was calculated by taking the peak areas from the HPLC graph. The average percentage potency of two samples was calculated as 99.62%. The results were shown in **Fig. 2, 3, 4 & 5.**

7) CEFUROXIME AXETIL FINISHED PRODUCT IDENTIFICATION

HPLC

The retention time of the principal peaks for Cefuroxime axetil diastereoisomer A and Cefuroxime axetil

diastereoisomer B in the chromatogram of the sample solution corresponds to that of the sample peaks in the chromatogram of Standard solution.

IR

The transmission minima or absorption maxima in the spectrum obtained with the substance recorded as KBr pellet correspond in position and relative size to those in the

Fig. 2: System suitability

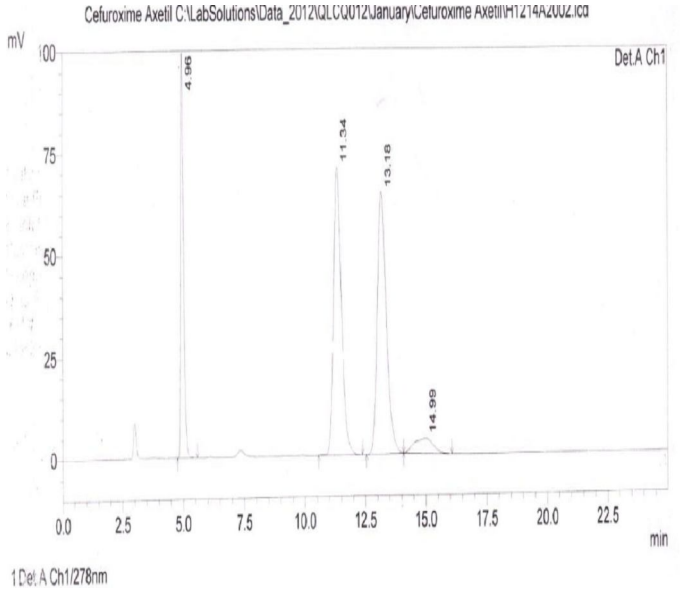


Fig. 4: Sample solution

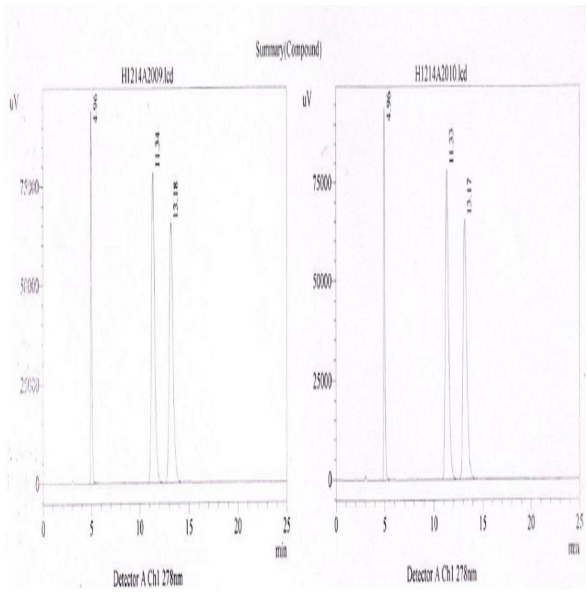


Fig. 3: Standard Cefuroximeaxetil

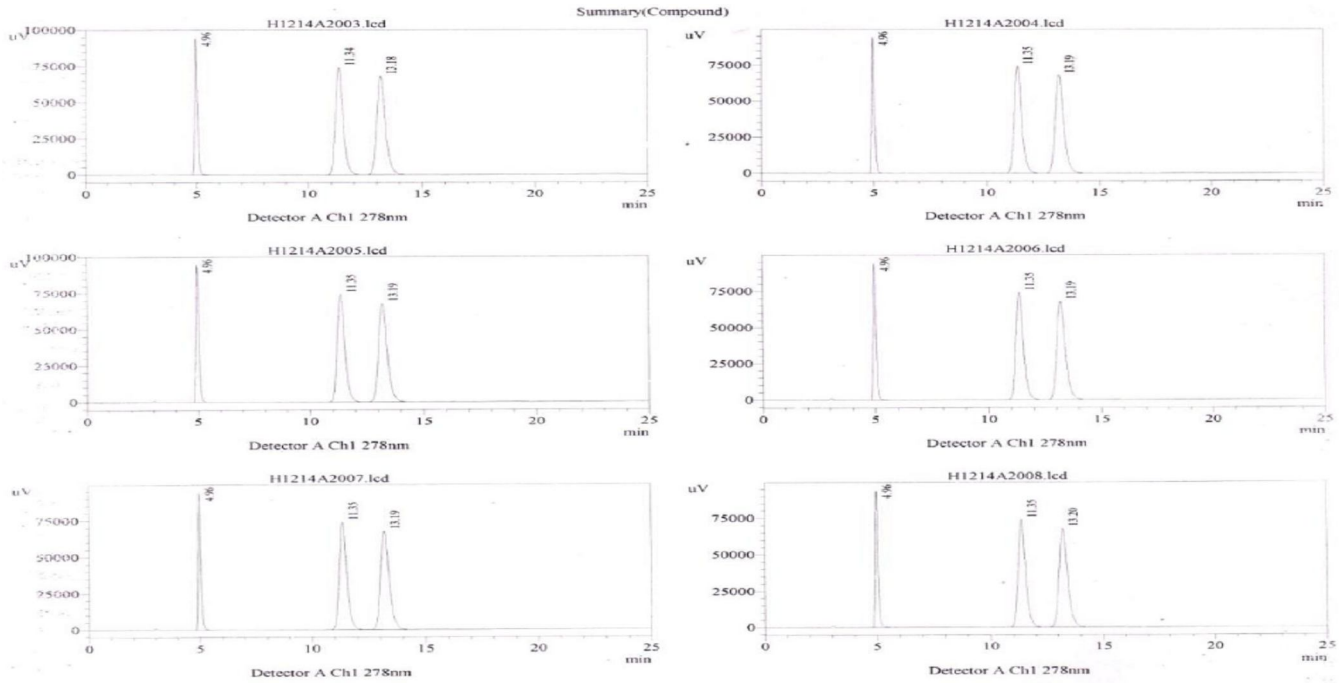


Fig. 5: Bracketing Standard

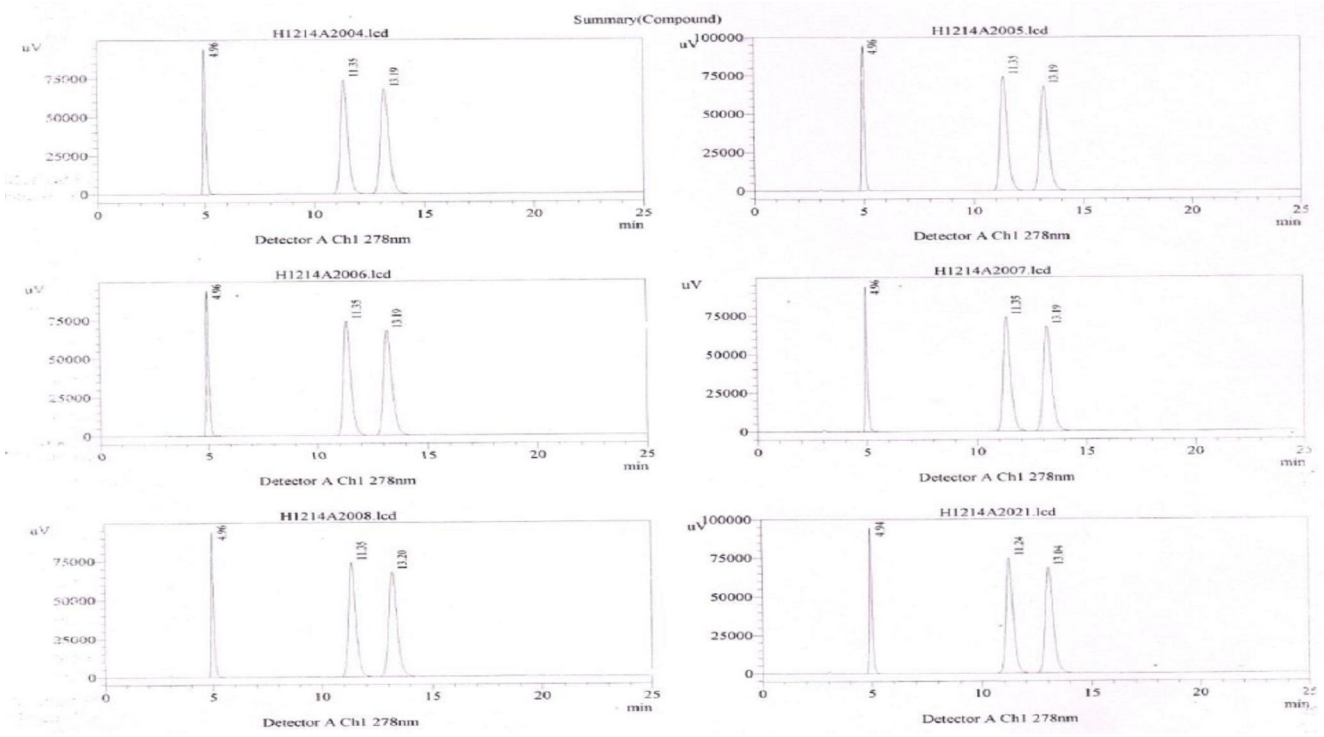
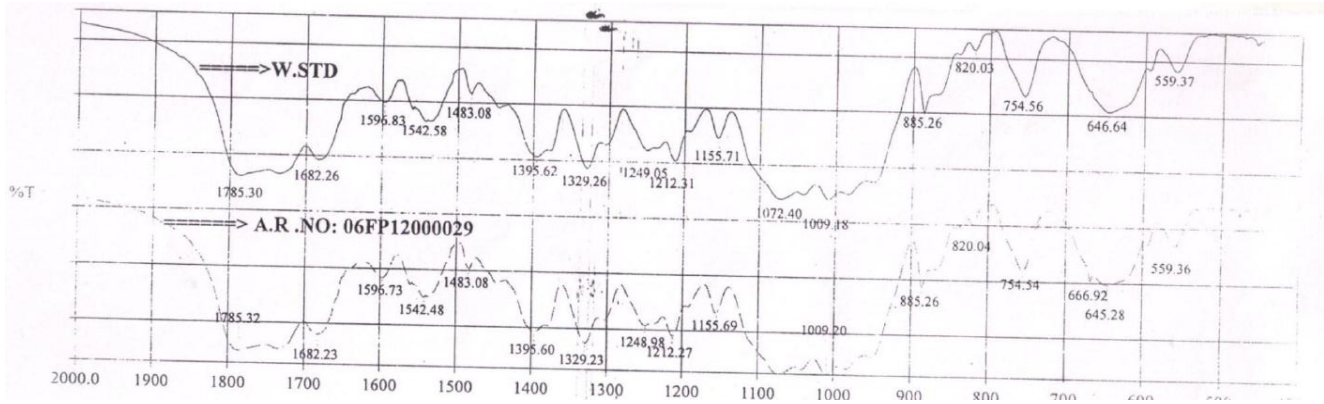


Fig. 6: IR graph of Cefuroxime axetil tablets BP 500 mg



spectrum obtained with the Cefuroxime Axetil Working standard. The amine C–N stretch was found between 1340-1020 cm-1 in both standard and sample Cefuroxime axetil. Hence the sample is identified as Cefuroxime axetil. The results were shown in the IR graph Fig. 6.

8) Average Weight

The weights of 20 tablets were mentioned in Table: 1. Average weight = 997.695 mg. Pass Limit - 1000.0 mg ± 2.0% (980 mg - 1020 mg). The average weight of Cefuroxime axetil tablets was calculated by taking the weights of 20 tablets as 997.695 mg. The result obtained was within the standard limits.

CONCLUSION

In the present work Cefuroxime axetil raw material was identified by HPLC and IR Spectroscopy. The sample is tested for the solubility, diastereoisomer ratio, crystallinity, and bulk density. The amount of cefuroxime axetil was estimated by HPLC assay method. The Cefuroxime axetil Finished product was identified by HPLC and IR Spectroscopy. The average weight of tablets was calculated

Table.8.1. Weights of 20 Tablets

No.	Weight of tablet	No.	Weight of tablet	No.	Weight of tablet	No.	Weight of tablet
1	992.50	6	997.54	11	995.67	16	1001.56
2	985.92	7	1001.73	12	999.83	17	997.49
3	1002.73	8	999.74	13	989.58	18	1000.78
4	1001.99	9	1002.84	14	996.99	19	994.55
5	1000.59	10	994.77	15	998.76	20	998.34

by taking the weights of 20 tablets. The content uniformity of the dosage units was calculated by weight variation method. The dissolution rate was calculated by HPLC method by using Paddle apparatus. The amount of Cefuroxime present in the sample was estimated by HPLC assay method. The known and unknown related substances present in the compound were estimated by HPLC method. In the near future the process has to be validated for quality assurance of Cefuroxime axetil tablets.

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