ESTIMATION OF CEFDITOREN PIVOXIL IN PHARMACEUTICAL ORAL SOLID DOSAGE FORM BY SPECTROPHOTOMETRY

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ABSTRACT

Four new, simple, sensitive and reproducible spectrophotometric methods have been developed for the estimation of cefditoren pivoxil in tablet dosage form. Method A involves the determination of cefditoren pivoxil by Standard absorbance method at 230nm and the Beer's concentration range was found to be 5-50 µg/mL. Method B and Method C involve the determination of cefditoren pivoxil by first derivative spectrophotometry and second derivative spectrophotometry respectively. The normal spectrum was derivatized to first and second order derivative spectrum and the linearity was found to lie within the Beer's range for cefditoren pivoxil. Method D involves the determination of cefditoren pivoxil by area under curve method and the linearity was established.

INTRODUCTION

Cefditoren Pivoxil[1] is   (6R,7R)-7-[[(2Z)-(2-Amino-4-thiazolyl)(methoxy imino) acetyl]amino]-3-[(1Z)-2-(4-methyl-5-thiazolyl) ethenyl]-8-oxo-5-thia-1-azabicyclo [4.2.0]oct-2-ene-2-carboxylic acid. It is a third generation cephalosporin exhibiting bactericidal action by inhibiting cell wall synthesis. Cefditoren exerts its inhibitory effect via affinity for penicillin binding proteins of the pathogens. Literature survey revealed that few sophisticated analytical methods[2-3] have been reported for the estimation of CP and newer colorimetric methods and some UV spectrophotometric methods have been reported[4-6].

EXPERIMENTAL
Instrumentation

All spectral and absorbance measurements were made on Shimadzu UV-VIS Spectrophotometer - 1650.

Preparation of Standard stock solution

It was prepared by dissolving 25mg of drug in ethanol in a 100ml volumetric flask and the volume was made up with water to produce 250µg/mL.

Preparation of Sample solution

Twenty tablets were weighed and powdered. A quantity equivalent to 25mg of CP was weighed, transferred to a 100 ml volumetric flask and shaken with ethanol to dissolve the active ingredient and made up to volume with water to produce 250µg/mL. The solution was then filtered, first few ml of the filtrate was discarded and the filtrate was used for further analysis.

ASSAY PROCEDURE
Method A – Standard absorbance method

Aliquots of standard solution of CP were suitably diluted to give varying concentrations ranging from 5-50 µg/mL and the solutions were scanned in the range of 200-400nm using distilled water as blank. It was found that CP exhibited an intense maximum absorbance at about 230nm and obeys Beer's law in the range of 5-50µg/mL. The overlain fundamental spectra is shown in Fig.1.
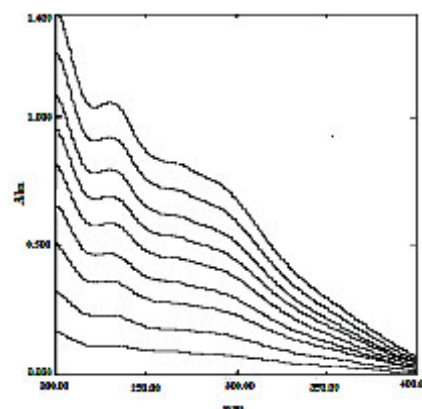

Fig 1 : The overlain fundamental spectra of cefditoren pivoxil

Method B – First derivative spectroscopy

The standard stock solution of CP was suitably diluted to give varying concentrations ranging from 5-50 µg/mL. The solutions were scanned in the range of 200- 400nm and the primary absorption spectrum was recorded .The primary spectrum was then derivatized to the first order using derivative mode. The amplitude of the negative peak maximum at the zero

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crossing of the first order curve was measured in mm at 230 nm. A calibration graph was obtained by plotting concentration versus amplitude. The sample solution was suitably diluted to get a concentration between 5-50 µg/mL and the same procedure was adopted. The amplitude obtained for the sample was then interpolated on the calibration graph and the concentration of CP in the sample was then determined. The overlain spectra for this method is shown in Fig 2.
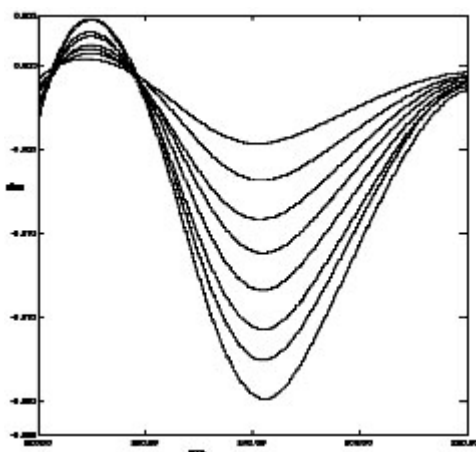

Fig 2 : The overlain first derivative spectra of cefditoren pivoxil

Method C – Second derivative spectroscopy
The primary spectrum obtained for the above was then derivatized for the second order. The amplitude of the negative peak maximum was measured in mm at 232nm.The respective overlain spectra is shown in Fig 3.
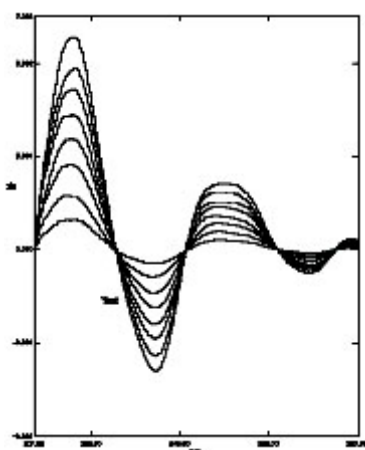

Fig 3 : The overlain second derivative spectra of cefditoren pivoxil

Method D – Area under curve
The standard stock solution of CP was suitably diluted to give varying concentrations ranging from 5-50 µg/mL. The solutions were scanned in the range of 200-400nm. The area under the curve between 220-250 nm was measured by using the inbuilt software. The inbuilt software calculates the area bound by the curve and the horizontal axis. The horizontal axis is selected

by entering the wavelength range over which the area has to be calculated .The wavelength range is selected on the basis of repeated observations so as to get the linearity between area under curve and concentration. The AUC spectrum is shown in Fig 4.
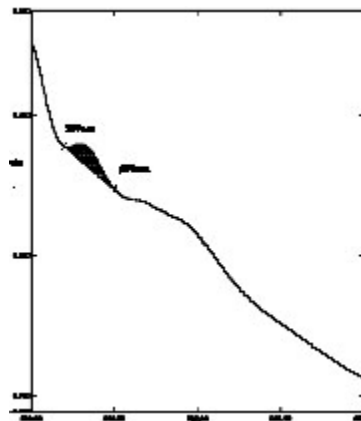

Fig 4 : The AUC spectrum of cefditoren pivoxil

RESULTS AND DISCUSSION
To study the accuracy and reproducibility of the proposed methods, recovery experiments were carried out by adding a known amount of drug to preanalysed sample and the percentage recovery was calculated. The results indicate that there is no interference of other ingredients present in the formulation. All the methods were stable and were conducted at different time schedules. Thus, the proposed methods are simple, sensitive, precise, accurate and reproducible and useful for the routine quality control.

Method A – Standard absorbance method
In this method[7], CP showed an absorption maximum at 230nm and was subjected for quantification. The drug obeyed Beer's law in the range of 5-50µg/mL. regression equation was found to be 0.023102X+0.000509. The molar absorptivity obtained was 14345.19(Lmol^{-1} cm^{-1}). The correlation coefficient was found to be 0.9996 which shows good linearity between concentration and absorbance. The percentage recovery obtained was 102.72% to 103% indicating the accuracy of the method. The amount present in the formulation was found to be 198.99-200.63 mg. The results of the analysis of formulation show that the proposed method is in good agreement with the labeled amount of the drug. The regression characteristics like slope, intercept, and correlation co-efficient (r), obtained from different concentrations were calculated.

Method B – First derivative spectroscopy
This method[8] is simple, accurate, rapid and reproducible. When the first derivative method was applied to CP estimation, it produced good results without any interference from excipients. The amount

present in the formulation was found to be 202.13-203.7 mg. The results of the analysis of formulation show that the proposed method is in good agreement with the labeled amount of the drug. The recovery studies were done, where the value was 100.00-103.57% indicating the accuracy of the proposed method. From the Table 1, The regression equation being Y = 2.706723X-0.17647. The correlation coefficient was found to be 0.998177. The % RSD was found as 0.18507 proving the precision of the method. The regression characteristics like slope, intercept, and correlation co-efficient (r), obtained from different concentrations were calculated.

Table 1: Optical characteristics of CP

Parameters	UV spectro Photometry	First derivative	Second derivative	Area under curve
λmax (nm)	230	230	232	220-250
Beer's law limit (µg/mL)	5-50	5-50	5-50	5-50
Molar absorptivity (L mol⁻¹ cm⁻¹)	14345.19	-	-	-
Sandell's sensitivity (µg cm⁻²/0.001 abs. unit)	0.0438847	-	-	-
Slope (m)	0.023102	2.706723	1.155806	0.035608
Intercep t(c)	0.000609	-0.17647	-1.155806	-0.00829
Regression equation*	0.023102X +0.000609	2.706723X -0.17647	1.155806X -1.155806	0.035608X -0.00829
Correlation coefficient(r)	0.9996	0.998177	0.99909	0.999563
Standard deviation	0.001075	-0.37815	-2.42651	-0.0175
RSD (%)**	0.00053465	-0.18507191	-1.22235	-0.00088149B
Limit of detection (LOD)	0.153623	-0.46104	-6.928342	-1.96079
Limit of quantification (LOQ)	0.465222	-1.397082	-20.99498763	-5.911491

* (y=mx+c)   ** Each value is the mean of 3 determinations.

Method C – Second derivative spectroscopy

When the second derivative spectroscopy method[8] was applied to CP estimation, it produced good results without any interference from excipients. The amount present in the formulation was found to be 200.00 mg. The results of the analysis of formulation show that the proposed method is in good agreement with the labeled amount of the drug. The recovery studies were done, where the value was 99.05-101.59% indicating the accuracy of the proposed method. From the Table 1, The regression equation being Y = 1.155806X-1.155806. The correlation coefficient was found to be 0.9991. The % RSD was found as -1.22235 proving the precision of the method. The optical characteristics like slope, intercept, and correlation co-efficient (r), obtained from different concentrations were calculated.

Method D – Area under curve

In AUC method[9], the normal spectra were subjected to AUC mode. The AUC from wavelengths 220-250nm were selected to estimate the amount of CP present in tablet dosage form. The amount present in the formulation was found to be 201.08 mg. The results of the analysis of formulation show that the proposed method is in good agreement with the labeled amount of the drug. The area under the curves was noted and the calibration curve was plotted. The correlation coefficient was found to be 0.9996 which shows a good linearity between concentration and area. The percentage recovery 100.35% to 103.25% proves the accuracy of the proposed method and proves the non-interference from excipients used in formulation. The optical characteristics like slope, intercept, and correlation co-efficient (r), obtained from different concentrations were calculated.

CONCLUSION

The percentage recovery of all the four methods lies between 99-104%. The correlation coefficient for all the four methods is 0.999 and the recovery studies indicate that there is no interference of other ingredients present in the formulation. Thus these four methods are simple, precise, accurate, less time consuming and useful for the routine analysis.

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