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DEVELOPMENT AND VALIDATION OF SPECTROPHOTOMETERIC METHODS FOR THE ESTIMATION OF CEFDITOREN PIVOXIL

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ABSTRACT

Three simple sensitive and economical spectrophotometric methods (A, B and C) for the quantitative estimation of cefditoren pivoxil in bulk drug and pharmaceutical dosage from have been developed. Method-A is based on UV absorption of drug in 0.1 N hydrocholoric acid exhibiting absorption maximum at 233 nm and it obyes Beer's law in the concentration range of 1 to 5 μg/mL. Method-B (MBTH) is based on oxidation followed by coupling reaction of cefditoren pivoxil with 3-methyl-2-benzothiazolinone hydrazone (MBTH) in presence of ferric chloride to form purple coloured chromogen with absorption maxima λ_{max} at 435 nm and obeyed Beer's Law in the concentration range of 5-25 μg/mL. Method-C is based on the reaction of drug with folin-ciocalteau (FC) reagent in alkaline condition to from a stable blue coloured chromogen with absorption maximum at 760 nm and obeyed Beer's law in the concentration range of 4 to 20 μg/mL. The results of the analysis for the three methods have been validated statically and by recovery studies. These method have been successfully extended to the pharmaceutical preparations (tablets) containing cefditoren.

Key words : Cefditoren pivoxil, Spectrophotometric, MBTH, FC Reagent.

INTRODUCTION

Cefditoren pivoxil is a third generation cephalosporin antibiotic for oral use, indicated for the treatment of mild and moderate infections in adults and adolacents, which are caused by susceptible strains of the designated microorganisms used to treat community acquired pneumonia, transilities etc. Cefditoren pivoxil is chemically (-)-(6R, 7R) - 2,2 - dimethylpropionyloxymethyl 7 - [(Z) - 2 - (2 - aminothiazol - 4 - yl) - 2 methoxy iminoacetamido] - 3 - [(Z) - 2 - (4 - methylthiazol - 5 - yl) ethenyl] - 8 - oxo - 5 - thia - 1 azabicyclo [4.2.0] oct - 2 - ene - 2 - carboxylate. It is not official in any pharmacopiea. Spectrophotometric analytical reports are not found in literature for its quantitative

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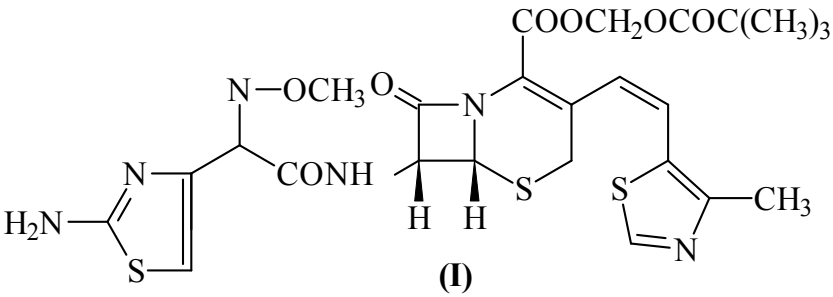
estimation in bulk drug and pharmaceutical dosage forms. Hence, it was thought worthwhile to develop spectrophotometric method for the same. This paper describes three simple, sensitive and economical UV / Visible spectrophotometric methods (A, B and C) developed for the quantitative estimation of cefditoren pivoxil.



(I)

Cefditoren pivoxil

EXPERIMENTAL

Instrument

All spectral measurements were done on Systronics UV/visible, spectrophotometer (Model 119) with 1 cm matched quartz cells.

Chemical and reagents

All chemicals used were of analytical grade from s. d. fine chem., Mumbai. Drug sample of cefditoren pivoxil was gift sample by Ranbaxy Laboratories, Solan.

(i) Folin ciocalteau reagent (2N) was diluted to 1 N with double distilled water.

(ii) 1 N soidum hydroxide in double distilled water.

(iii) 0.1 N HCl in double distilled water.

(iv) 3-Methyl-2-benzothiazolinone hydrazone (0.5% w/v in double distilled water).

(v) Ferric chloride 0.03 M in double distilled water.

(vi) Cerric ammonium sulphate 1% w/v in 0.72 N sulphuric acid.

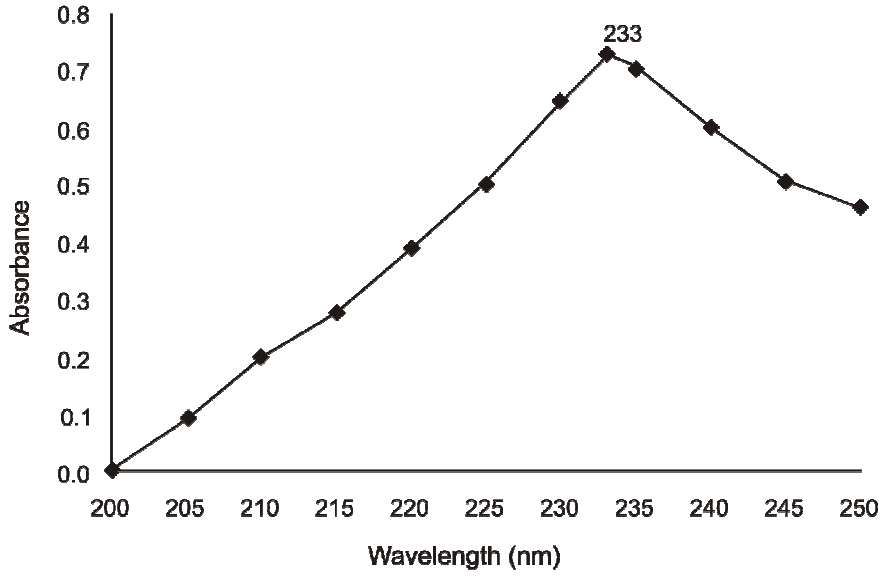


Fig. 1: Absorption maxima of cefditorein pivoxil with UV

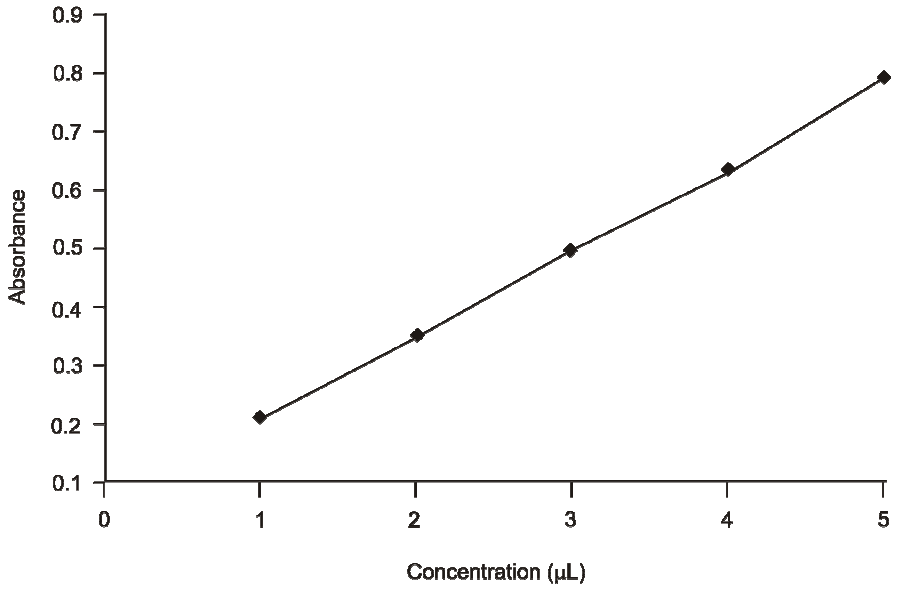


Fig. 2: Calibration curve of cefditorein with UV

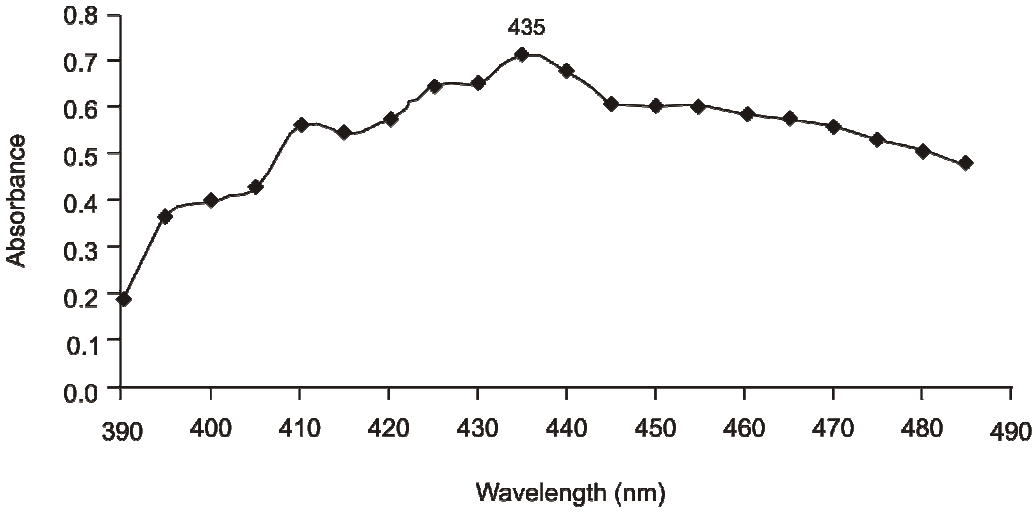


Fig. 3: Absorption maxima of cefditroein pivoxil with MBTH

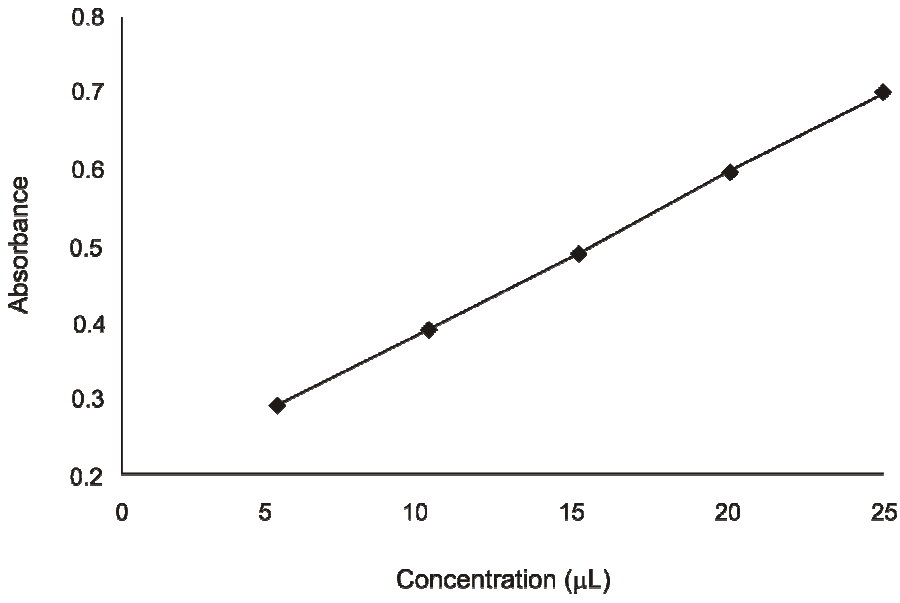


Fig. 4: Calibration curve of cefditorein with UV

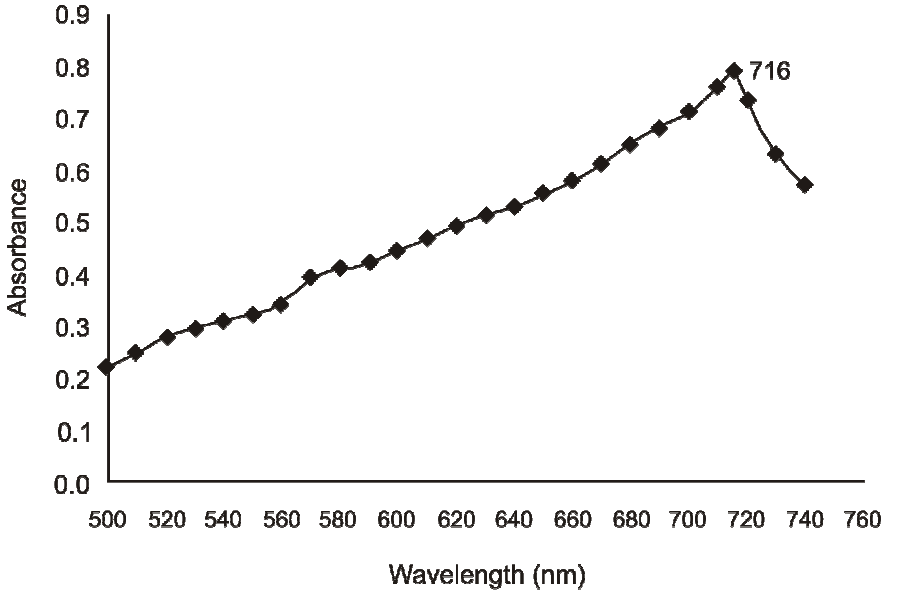


Fig. 5: Absorption maxima of cefditroein pivoxil with FC

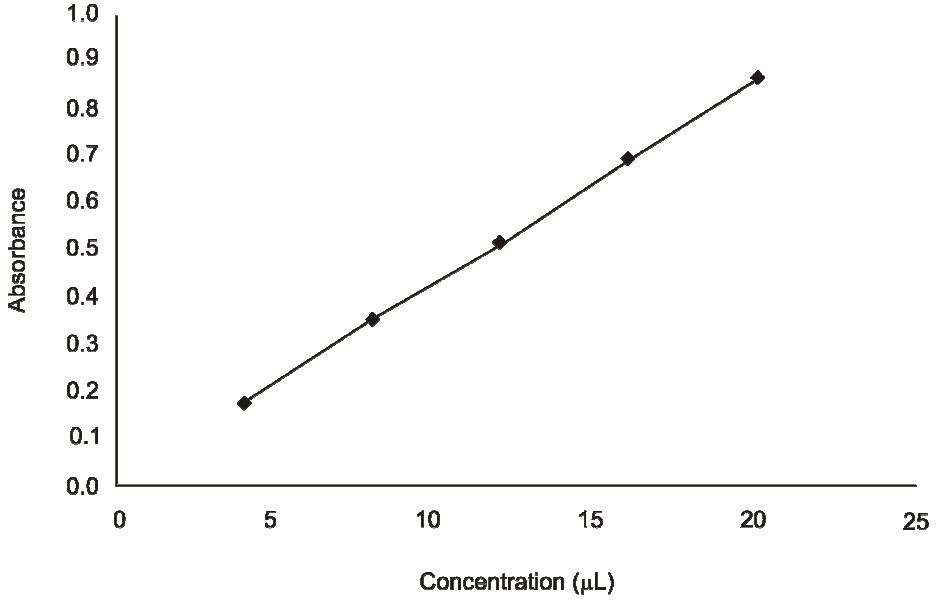


Fig. 6: Calibration curve of cefditorein with FC

Standard and sample solutions

Cefditoren pivoxil (pure or formulation)- 100 mg was accurately weighed and dissolved in 0.1 N HCl (20 mL) and transferred to standard 100 mL volumetric flask. The final volume was made upto the mark with 0.1 N HCl (1mg/mL). Final concentration was brought upto 100 μg/mL with 0.1N HCl, In case of formulation, 20 tablets of cefditorein pivoxil each containing 200 mg were accurately weighed and powedered. 100 mg of drug equivalent was taken for the study.

ASSAY

Method-A : Aliquots of cefditoren pivoxil ranging from 0.1 to 0.5 mL (1 mL = 100 μg/mL) were transferred into a series of 10 mL volumetric flasks, the volumes were made upto the mark with 0.1 N HCl. The absorbance of the solutions was measured at 233 nm against reagent blank. The amount of drug was computed from calibration curve.

Method-B : Aliquots of drug ranging from 0.5-2.5 mL (1 mL = 100 μg/mL) were transferred into a series of 10 mL volumetric flasks. To each flask, 1 mL of ferric ammonium sulphate (1% w/v in 0.72 N H_2SO_4) and 1 mL of MBTH (0.5% w/v) were added and allowed to stand for 15 min to develop colour (Purple). The volume was made upto to the mark with 0.1 N HCl. The absorbance of the purple colour chromogen was measured at 435 nm against reagent blank. The colour was stable for more than 3 hrs. The amount of cefditoren pivoxil present in the sample was computed from calibration curve.

Method-C : Aliquots of cefditoren pivoxil ranging from 0.4 to 2 mL (1 mL = 100 μg/mL) were taken in to a series of 10 mL volumetric flasks. To each flask, 1 mL of Aq 1 N sodium hydroxide and 0.5 mL of FC reagent (1N) were added. After 10 min, the volume is made upto mark with 0.1 N HCl. The absorbance of the blue coloured chromogen was measured at 716 nm against reagent blank. The colour was stable for more than five hrs. Amount of drug present in the sample was computed from calibration curve.

RESULTS AND DISCUSSION

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presented in Table 1. The regression analysis using the method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentrations and the results are summarized in Table 1. The % relative standard deviation and % range of error, (0.05 and 0.01 level of confidence limits) calculated from the eight measurements, ¾ of the upper Beer's Law limits of

cefditoren pivoxil are given in Table 1.

Table 1 : Optical characteristics and precision

	Method-A	**Method-B**	**Method-C**
λ_{max} (nm)	233	435	716
Beer's Law (μg/mL)	1-5	5-25	4-20
Molar absorptivity L/mol^{-1} cm^{-1}	1.307 x 10^3	2.056 x 10^3	2.742 x 10^3
Sandells sensitivity μg/m/cm^2/0.001 a. unit	0.030	0.062	0.045
Regression equation (y*)			
Slope (b)	0.2108	0.0185	0.0428
Intercept (a)	0.733 x 10^3	0.211 x 10^3	3.511 x 10^3
Correlation coefficient (r)	0.2108	0.9640	0.9998
% RSD	0.4111	0.2135	0.6230
Range of error**			
Confidence limits with 0.01 level.	0.2500	1.3030	1.1978
Confidence limits with 0.05 level.	0.1690	0.8806	0.8096

* y = bc + a, y is the absorbance unit and c is the concentration in μg/mL

** eight measurements

The results showed that these methods have reasonable precision. Comparison of the results was also made with the proposed and UV methods for dosage forms (Table 2), which confirms the suitability of these methods for pharmaceutical dosage forms. In order to justify the reliability and suitability of the proposed methods, known quantities of pure cefdiforen pivoxil was added to its various pre-analysed formulations and the mixture were analysed by the proposed methods. The results of recovery experiments are also summarized in Table 2. The other active ingradients and excipients usually present in pharmaceutical dosage forms did not interfere.

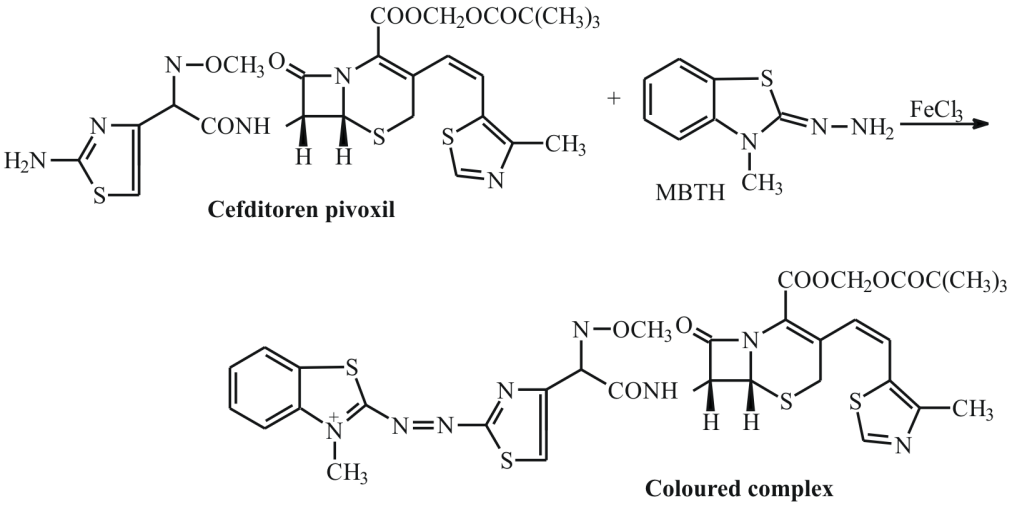
Table 2 : Evaluation of cefditoren in tablets

Sample tablets	Labelled amount (mg)	Amount obtained* (mg)			% Recovery**		
		Proposed method			Proposed method		
		A	B	C	A	B	C
T_1	200 mg	199.85	199.02	199.30	99.93	99.72	99.70

* mean ± sd of eight measurement.

The proposed methods are found to be simple, sensitive, selective, accurate, precise and economical, when compared to quantitative methods like HPLC and LCMS. It can be used in the determination of cefditforen pivoxil in bulk drug and its pharmaceutical formulation in a routine manner.

Reaction scheme of cefditoren pivoxil with MBTH



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