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Research Article

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Validated zero order and first order derivative spectrophotometric methods for the assay of cefpodoxime and cefprozil in tablet dosage form

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ABSTRACT

Simple, sensitive, accurate and precise zero order (methods A & B) and first order derivative (methods C & D) spectrophotometric methods have been developed and validated for the individual assay of cefpodoxime (methods A & C) and cefprozil (methods B & D). The zero order (methods A) and first derivative (methods C) spectrophotometric methods were used for the determination of cefpodoxime in the range of 10-50 µg/ml by measuring the absorbance at 234 nm and 222 nm respectively. The measurement of absorbance at 230 nm and 223 nm was used for the assay of cefrozil by the zero order (methods B) and first derivative (methods D) spectrophotometric methods in the range of 10-50 µg/ml. The developed methods were validated according to the guidelines given by International Conference on Harmonization and proved to be sensitive, robust, precise and accurate for the quality control of the selected drugs in their tablet dosage forms.

Keywords: cefpodoxime, cefrozil, zero order, first order derivative, spectrophotometry, tablet dosage form.

INTRODUCTION

Cefpodoxime [1-3] is an orally administered, semi-synthetic, third generation cephalosporin class of antibiotic. The chemical name is (RS)1(isopropoxycarbonyloxy) ethyl (+)-(6R,7R)-7-[2-(2-amino-4- thiazolyl)-2-{(Z)methoxy imino}acetamido]-3methoxymethyl-8-oxo-5-thia-1-azabicyclo [4.2.0]oct-2-ene- 2-carboxylate. Cefpodoxime is an active metabolite of prodrug, cefpodoxime proxetil. It is used to treat certain mild to moderate infections caused by susceptible strains of the bacteria such as pneumonia, bronchitis, gonorrhea, ear, skin, throat and urinary tract infections. Literature survey reveals that spectrophotometric [4-9] and chromatographic [10-20] methods, and a voltametric method [21], have been reported for determination of cefpodoxime in bulk, pharmaceutical preparations and biological samples.

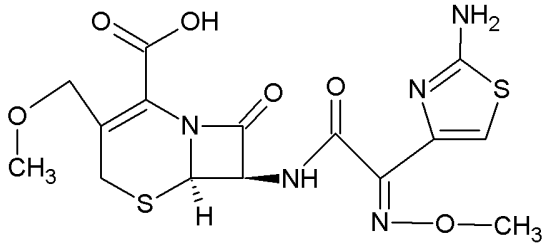

Figure 1: Chemical structure of cefpodoxime

Cefprozil [22-24], chemically known as (6R,7R)-7-[(R)-2-Amino-2-(p-ydroxyphenyl) acetamido] -8-oxo-3-propenyl-5-thia-1-azabicyclo [4.2.0]oct-2-ene-2-carboxylic acid monohydrate, is a semi synthetic, broad-spectrum, second generation cephalosporin class of antibiotic. It is used in the treatment of otitis media, skin, soft-tissue infections and respiratory tract infections caused by susceptible strains of bacteria. Several chromatographic [25-31], spectrophotometric [32-35] methods and a flow-injection chemiluminescent [36] method have been reported for cefprozil assay in bulk, pharmaceutical formulations and biological samples.

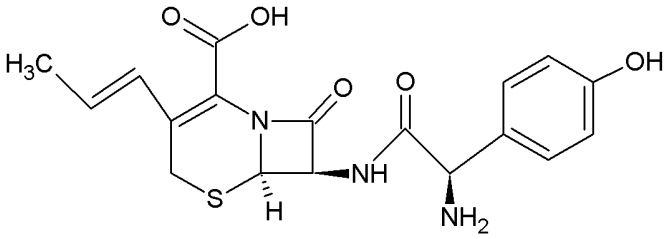

Figure 2: Chemical structure of cefrozil

EXPERIMENTAL SECTION

Apparatus:
Systronics (model SL-2201) UV-VIS Spectrophotometer with spectral bandwidth of 2.0 nm and a pair of 10 mm optical path length quartz cells were used for spectral measurements. The instrumental parameters employed are: Wavelength range: 200–400 nm; scan speed: Medium; sampling interval: 1.0 nm.

Preparation of Standard solutions:
Stock standard solution (100 µg/ml solution) of cefpodoxime and cefrozil was prepared separately. The stock standard solutions were prepared separately by dissolving accurately weighed 10 mg each of pure cefpodoxime and cefrozil in methanol (analytical reagent grade, Qualigens Fine Chemicals, Mumbai, India) in a 100 ml volumetric flask and diluted up to the mark with the same solvent.

Preparation of Tablet sample solution:
Ten cefpodoxime tablets were accurately weighed and powdered. The tablet powder equivalent to 10 mg of drug was dissolved in 70 ml of methanol by sonication and transferred into a 100 ml calibrated flask and completed to the mark with the same solvent. The same procedure was followed for cefrozil tablets to get a stock solution (100 µg/ml of drug). The stock solutions of cefpodoxime and cefrozil were appropriately diluted with the methanol to get a final concentration of 30 µg/ml of drug for the analysis by the proposed methods.

General analytical procedure:
Zero order (methods A & B):
Suitable aliquots of standard stock solution (100 µg/ml) of cefpodoxime and cefrozil (1, 2, 3, 4 and 5 ml) were taken in a 10 ml volumetric flask and diluted up to the mark, to get 10, 20, 30, 40 and 50 µg/ml solution of the drugs, with methanol. The absorbance of cefpodoxime solutions were measured at 234 nm (method A) and cefrozil solutions were measured at 230 nm (method B).

First order derivative (methods C & D):
Suitable aliquots of standard stock solution (100 µg/ml) of both the drugs, namely, cefpodoxime and cefrozil (1, 2, 3, 4 and 5 ml) were taken in a 10 ml volumetric flask and diluted up to the mark with methanol, to get 10, 20, 30, 40 and 50 µg/ml solution of the drugs. The absorbances of cefpodoxime and cefrozil solutions were measured at 222 nm (method C) and 223 nm (method D), respectively.

In all the above methods (methods A-D), the calibration curve was drawn by plotting absorbance *vs* concentration of drug. Alternatively regression equation was derived. The concentrations of unknown samples were determined from the corresponding calibration curve or from the regression equation derived.

RESULTS AND DISCUSSION

Determination of analytical wavelength:

The selection of analytical wavelength in the proposed methods (methods A-D) is based on the reproducibility of the results. The zero order spectra of cefpodoxime (method A) and cefrozil (method B) working standard solution at a concentration of 30 µg/ml of drug were recorded between 200 and 400 nm and the maximum wavelength of cefpodoxime and cefrozil in methanol was found to be 234 nm (method A) and 230 nm (method B), respectively. In methods C and D, zero-order spectra were derivatized into first-order. The working standard solutions (30 µg/ml) of cefpodoxime (method C) and cefrozil (method D) were scanned in the first order derivative spectra. The cefpodoxime first order derivative spectra showed a maxima and minima at 222 and 255 nm, respectively. The first order derivative spectra showed a maxima and minima at 223 and 240 nm respectively for cefrozil. The wavelengths 222 nm and 223 nm were selected for analysis of cefpodoxime and cefrozil by methods C and D, respectively. The zero order and first order derivative spectra of cefpodoxime and cefrozil are shown in Figures 3-6.

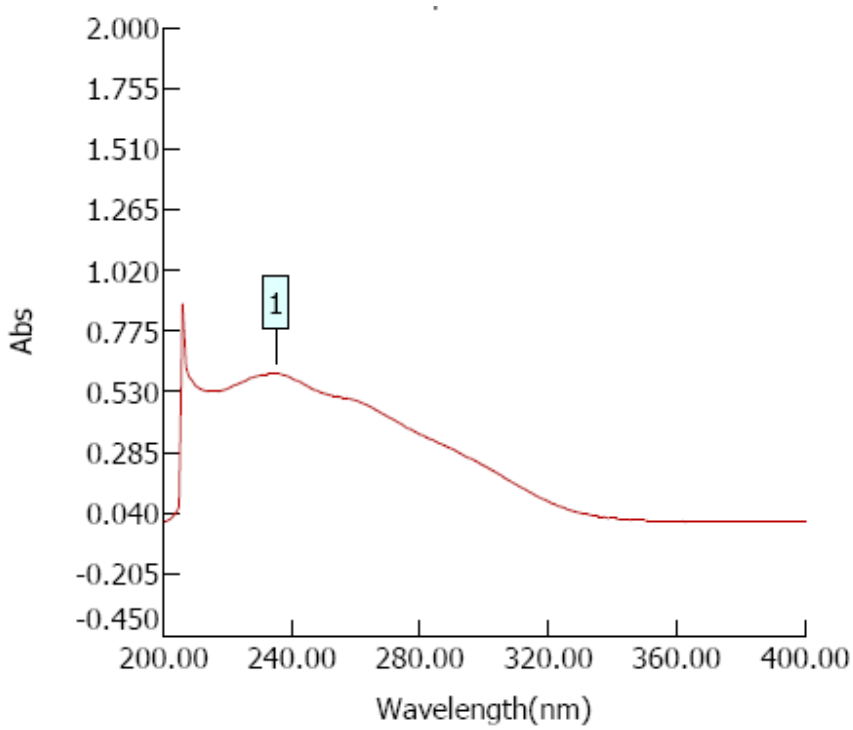

Figure 3: Zero order spectra of cefpodoxime (method A)

Method validation:

The proposed methods A-D were validated as per the guidelines of International Conference on Harmonization [37].

Linearity:

The calibration curves of the proposed methods (A-D) were constructed by plotting an increase in absorbencies *vs* concentrations. In all the proposed methods, a linear correlation was found between absorbance and concentration of selected drugs in the range 10-50 µg/ml. The regression equations for the proposed methods are presented in Table 1. The high values of the regression coefficient (R^2) and low values y-intercepts of the regression equations, proved the linearity of the proposed methods A-D.

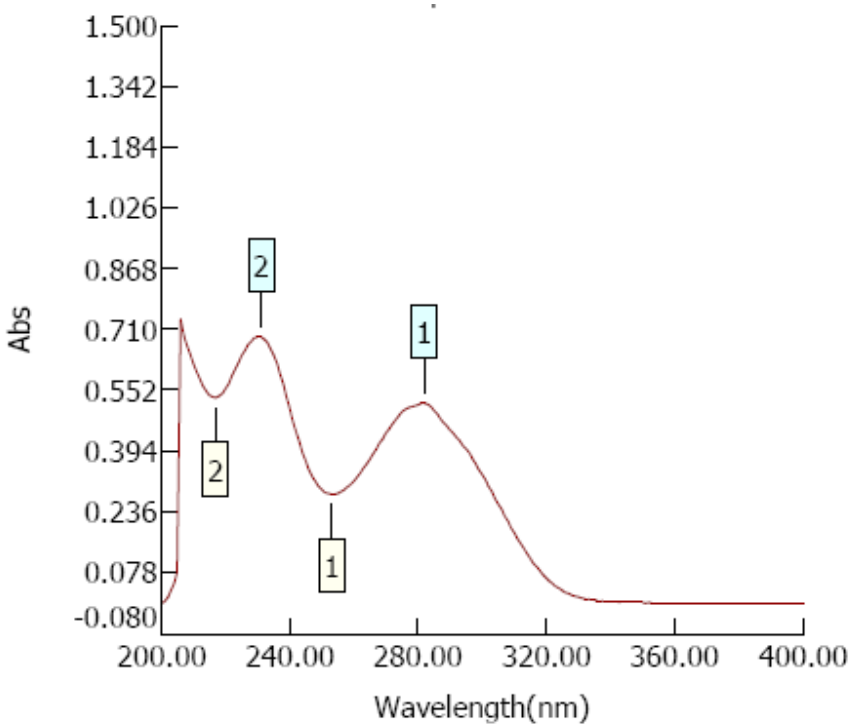

Figure 4: Zero order spectra of cefrozil (method B)

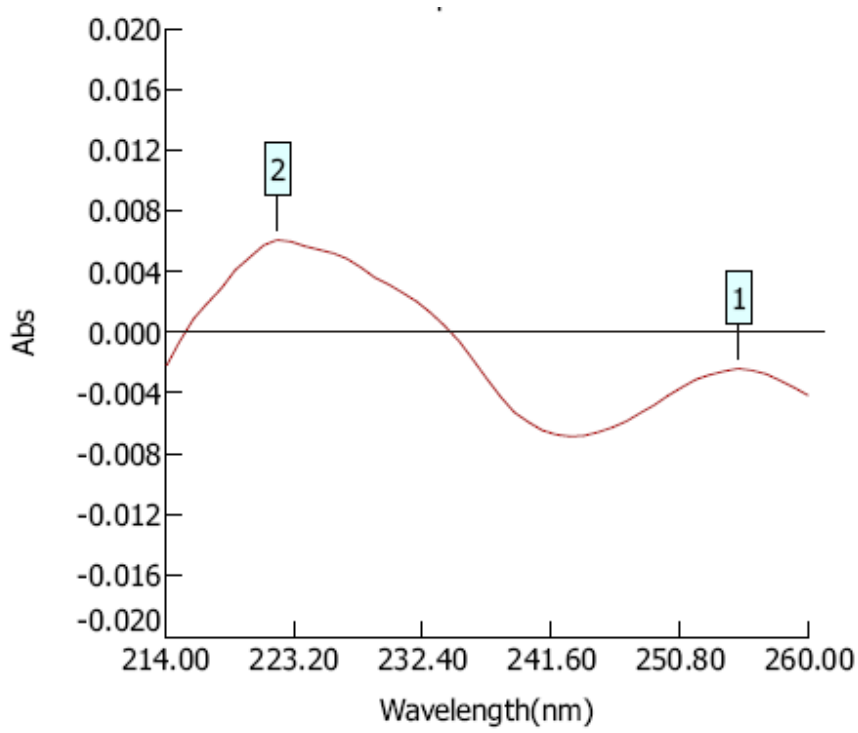

Figure 5: First order derivative of cefpodoxime (method C)

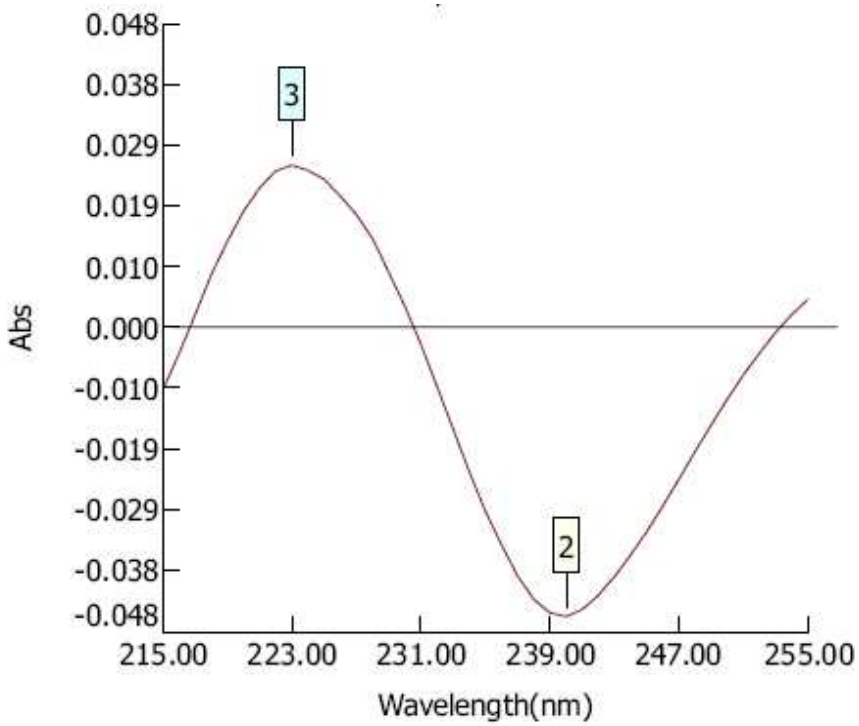

Figure 6: First order derivative spectra of cefrozil (method D)

Table 1: Linearity and Sensitivity characteristics

Parameters	Cefpodoxime		Cefrozil	
	Zero order	First order	Zero order	First order
Linearity (µg mL^{-1})	10-50	10-50	10-50	10-50
Regression equation (A= mC + I)$^{\$}$	-	-	-	-
Slope (m)	0.00993	0.0001	0.0227	0.00054
Intercept (I)	0.1097	0.001	- 0.0009	0.0018
Regression coefficient (R^2)	0.9990	0.9999	0.9996	0.9993
Molar Absorbitivity (L $mole^{-1}$ cm^{-1})	9.0193×10^4	8.549×10^3	8.450×10^4	2.724×10^3
Sandell's sensitivity (µg cm^{-2})	4.739×10^{-4}	5.00×10^{-2}	4.608×10^{-4}	1.428×10^{-2}
LOD (µg mL^{-1})	0.252	1.200	0.240	0.280
LOQ (µg mL^{-1})	0.840	4.000	0.800	0.933

$^{\$}$*A = mC + I, where A is the absorbance and C is the concentration of drug in µg* mL^{-1}.

Sensitivity:

The parameters, limit of detection (LOD) and limit of quantification (LOQ), were calculated to assess the sensitivity of the proposed methods. The results are summarized in Table 1. The LOD and LOQ values indicated the adequate sensitivity of the proposed methods

Table 2: Precision of the proposed methods

Type of assay	Drug	Method	Absorbance*	SD	% RSD
Intra-day precision	Cefpodoxime	A	0.411	0.000707	0.172
	Cefrozil	B	0.700	0.00070	0.100
	Cefpodoxime	C	0.0040	0.000040	1.110
	Cefrozil	D	0.01802	0.000040	0.248
Inter-day precision	Cefpodoxime	A	0.413	0.000837	0.202
	Cefrozil	B	0.703	0.00180	0.258
	Cefpodoxime	C	0.0040	0.000040	1.112
	Cefrozil	D	0.01804	0.000050	0.303

**average of five determinations; SD=standard deviation; %RSD=percent relative standard deviation*

Precision:
The precision of the proposed methods (A-D) was expressed as the percent relative standard deviation of the series of measurements. Precision was ascertained by estimation of cefpodoxime (by methods A & C) and cefrozil (by methods B & D) at 30 µg/ml concentration level. The assay involves intraday precision and intermediate precision (also known as Ruggedness). For intraday precision, the analysis was carried out five times on the same day, and for intermediate precision, the analysis was carried out on different day by using same experimental conditions. Results are reported in Table 2. The proposed methods are proven as precise and rugged since the percent relative standard deviation vales are within the acceptable limit (<2%).

Accuracy:
The accuracy of the proposed methods (A-D) was determined by performing recovery study at 50, 100, and 150% level (with respect to target assay concentration) for cefpodoxime (by methods A & C) and cefrozil (by methods B & D). The recovery study was done by adding pure drug solution to the preanalyzed sample. The concentrations of cefdinir and cefditoren were once again determined by the proposed methods. The results of the recovery study are shown in Table 3. The values of recovery studies were showing acceptable accuracy of the proposed methods.

Table 3: Accuracy of the proposed methods

Drug	Method	Spiked level (%)	Amount Added (µg/ml)	Amount Found (µg/ml)*	Recovery (%)	Mean Recovery (%)
Cefpodoxime	**A**	50	5.0	5.0	101.0	100.0
		100	10.0	9.98	99.8	
		150	15.0	14.8	99.2	
Cefrozil	**B**	50	5.0	4.95	99.0	99.5
		100	10.0	9.93	99.3	
		150	15.0	15.0	100.3	
Cefpodoxime	**C**	50	5.0	4.99	99.8	99.8
		100	10.0	9.98	99.8	
		150	15.0	14.9	99.8	
Cefrozil	**D**	50	5.0	4.99	99.8	99.8
		100	10.0	9.98	99.8	
		150	15.0	14.9	99.8	

**average of three determinations*

Robustness:
As part of the robustness, deliberate change in the wavelength is made. The wavelength was varied by ±2 nm. Standard solutions of cefpodoxime and cefrozil at a concentration level 30 µg/ml were prepared and analysed using the varied wave length along with analytical wavelength. The results are reported in Table 4. On evaluation of the results, it can be concluded that the variation in wave length did not affected the methods significantly. Hence it indicates that the methods (A-D) are robust by change in the wave length ±2 nm.

Table 4: Robustness of the proposed methods

Method	Drug	Wave length (nm)	Absorbance
A	Cefpodoxime	232	0.407
		234	0.408
		236	0.406
B	Cefrozil	228	0.685
		230	0.692
		232	0.683
C	Cefpodoxime	220	0.003
		222	0.004
		224	0.002
D	Cefrozil	221	0.011
		223	0.018
		225	0.017

CONCLUSION

Zero order (methods A & B) and first order derivative (methods C & D) spectrophotometric methods were developed for the individual quantification of cefpodoxime (methods A & C) and cefrozil (methods B & D) in tablet

dosage forms. The advantages of the proposed methods are: simple, precise, accurate and robust for the quantization of cefpodoxime and cefrozil in the presence of common excipients. The four methods were validated showing acceptable results for all the method validation parameters tested. The developed and validated methods (A-D) are capable of conveniently used by quality control laboratories for the assay of cefpodoxime and cefrozil.

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