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International Journal of Current Research
Vol. 6, Issue, 12, pp.10629-10632, December, 2014

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

ESTIMATION OF CEFPODOXIME PROXETIL AND AMBROXOL HYDROCHLORIDE BY FIRST ORDER DERIVATIVE SPECTROPHOTOMETRIC METHOD IN PHARMACEUTICAL FORMULATION

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ARTICLE INFO

Article History:
Received 17th September, 2014
Received in revised form
20th October, 2014
Accepted 15th November, 2014
Published online 27th December, 2014

Key words:

First-order derivative spectroscopy,
Cefpodoxime proxetil,
Ambroxol hydrochloride

ABSTRACT

A simple, precise, sensitive and accurate first order derivative spectrophotometric method was developed and validated for the simultaneous estimation of cefpodoxime proxetil and ambroxol hydrochloride in combined tablet dosage form. For determination ofsampling wavelengths, each of cefpodoxime proxetil and ambroxol hydrochloride were scanned in the wavelength range 200–400 nm in spectrum mode and sampling wavelengths were selected at 234.3 nm (zero crossing of cefpodoxime proxetil) where ambroxol hydrochloride showed considerable absorbance and at 248.2 nm (zero crossing of ambroxol hydrochloride) where cefpodoxime proxetil showed considerable absorbance. Beer's law obeyed in the concentration range of 8-40 µg/ml for cefpodoxime proxetil and 5-25 µg/ml for ambroxol hydrochloride respectively. The correlation coefficients were found to be 0.995and 0.998 for cefpodoxime proxetil and for ambroxol hydrochloride respectively. Mean recoveries were found satisfactory.

INTRODUCTION

Cefpodoxime proxetil (CFP, Fig 1) is (6R,7R)-7-((2Z)-2-(2-amino-1,3-thiazol-4-yl)-2-(methoxyimino)acetamido)-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo(4.2.0)oct-2-ene-2-carboxylic acid (Indian Pharmacopoeia, 2010). It is an oral third generation cephalosporin antibiotic and active against most gram positive and gram negative bacteria. CPF is a prodrug which is absorbed and de-esterified by the intestinal mucosa to cefpodoxime.It is stable in the presence of beta-lactamase enzymes and commonly used to treat pharyngitis and sinusitis. Ambroxol hydrochloride (AMB) is (trans-4-(2-amino-3,5-dibromobenzylamino) cyclohexanol hydrochloride (British Pharmacopeia, 2007). It is a metabolic product of bromhexine. It is used as broncho secretolytic and expectorant. Literature survey reveals that spectrophotometric methods, HPLC and HPTLC in human plasma were reported for determination of cefpodoxime proxetil and ambroxol hydrochloride (Singh *et al.,* 2010; Nagappan *et al.,* 2008; Ambadas *et al.,* 2011). We have been developed a new simple, precise and economic first order derivative uv-spectrophotometric method for the simultaneous determination of CFD and AMB in combined tablet dosage form which is not reported.

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MATERIALS AND METHODS

Cefpodoxime proxetil and Ambroxol hydrochloride were procured from (Blue Cross Laboratories Ltd.Ambad Nashik., India). Marketed tablet formulation Fincef-AM (CFD 100 mg, AMB 160 mg, Piramal HC) and methanol as solvent were used.

Apparatus

A double beam spectrophotometer (Shimadzu-UV-2450 with 10mm path length and slit width variable) was employed for measurement of absorbance.

Standard stock solutions

A standard stock solution 100 µg/ml each of CFD and AMB was prepared separately in volumetric flask by using methanol as solvent.

Selection of analytical wavelength

From standard stock solution 10 µg/ml of CFD and 16 µg/ml of AMB were prepared separately by dissolving 0.1ml CFD and 0.16 ml AMB in 10 ml volumetric flask using methanol. The solutions were scanned in the wavelength range 200–400 nm in spectrum mode. These spectrums were converted to first order derivative spectra by using instrument mode. The wavelength 234.3 nm (zero crossing point of CFD) where

AMB showed considerable absorbance and 248.2 nm (zero crossing point of AMB) where CFD showed considerable absorbance was selected (Fig 2 and 3).

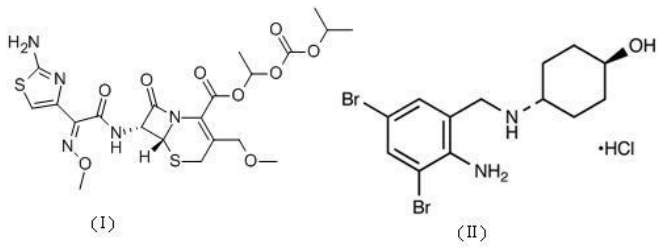

Figure 1. Structure of Cefpodoxime proxetil (I) and Ambroxol hydrochloride (II)

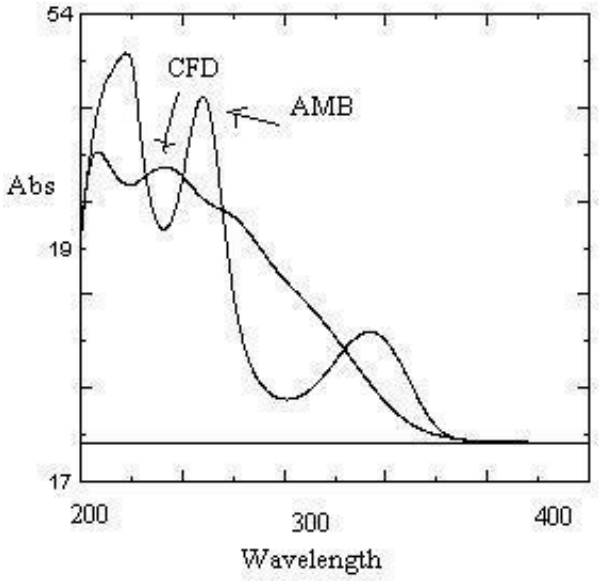

Figure 2. Zero order spectra of CFD and AMB

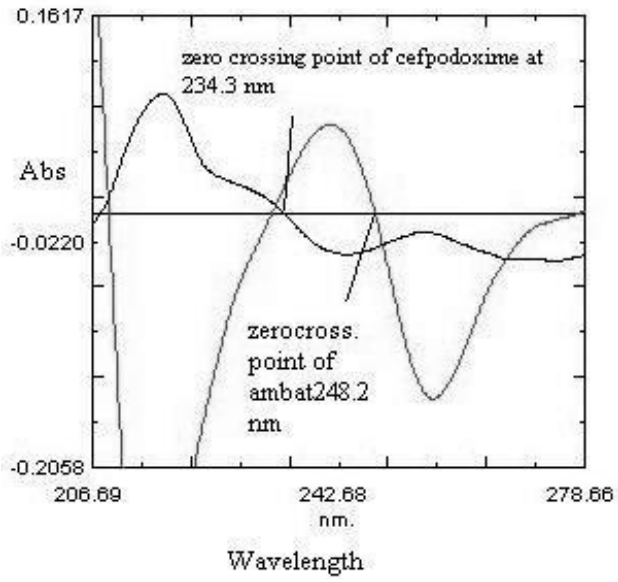

Figure 3. Overlain first order derivative spectra of CFD and AMB

Linearity (International Conference on Harmonisation (ICH) guidelines for Industry, 1996)

The linearity of the proposed method was found to be in the range of 8-40 µg/ml for CFD and 5-25 µg/ml for AMB. The calibration graph was prepared by diluting an aliquot of standard stock solution 0.8,1.6,2.4,3.2,4.0 ml of CFD and 0.5,1.0,1.5,2.0,2.5 ml of AMB to 10 ml volumetric flask using methanol to get concentration of 8 to 40 µg/ ml of CFD and 5 to 25 µg/ ml of AMB.Absorbance was measured at selected wavelength. The calibration graph of concentration against absorbance was plotted (Table 1, Fig 4 and 5).

Table 1. Optical parameters of CFD and AMB for proposed method

Parameters	CFD	AMB
Wavelength nm	248.20	234.3
Beer's law range (µg/ml)	8-40	5-25
Regression Equation (y = mx + c)		
Slope (m)	0.020	0.017
Intercept (c)	0.01	0.01
Correlation coefficient (r^2)	0.995	0.998
Limit of detection (LOD)µg/ml	1.60	1.85
Limit of quantitation (LOQ)µg/ml	4.87	5.61

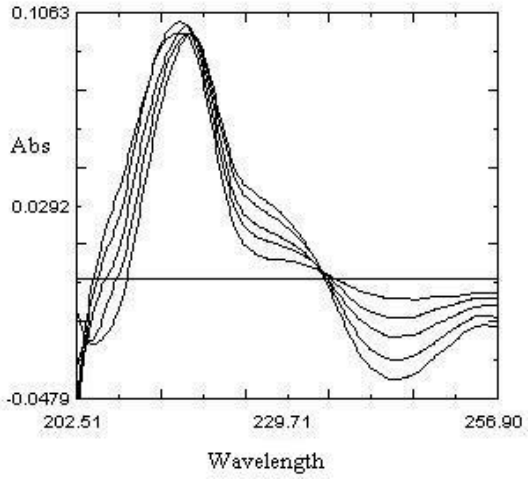

Figure 4. Derivative spectra of CFD 8-40µg/ml in methanol

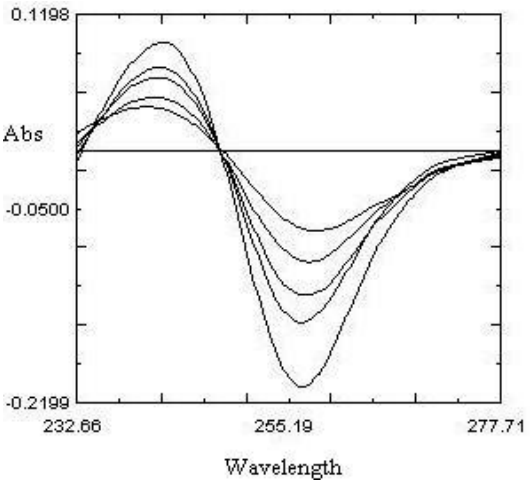

Figure 5. Derivative spectra AMB 5-25µg/ml in methanol

Analysis of tablet formulation

Twenty tablets were weighed accurately and powdered. Powder equivalent to 100 mg of CFD (containing 160 mg of AMB) was weighed and transferred to 100 ml volumetric flask. Then it was dissolved in 10 ml methanol by shaking the flask for 15 minutes and volume was made up to the mark with methanol. The solution was filtered through Whatman filter paper no. 41. An aliquot of above solution was diluted with methanol to get concentration of 10 µg/ ml of CFD and 16 µg/ ml of AMB. The absorbance was measured at selected wavelength. The amount of CFD and AMB in tablets was calculated by using calibration graph (Table 2).

RESULTS AND DISCUSSION

A simple, sensitive and accurate first order derivative uv spectrophotometric method has been developed for the simultaneous estimation of cefpodoxime proxetil and ambroxol hydrochloride in combined tablet dosage form. The linearity was found to be in the range of 8-40 µg/ml for CFD and 5-25 µg/ml for AMB using methanol. The percentage purity of CFD and AMB in tablet formulation was found to be 99.53 and 99.93 with percent RSD 0.41 and 0.065 respectively. Correlation coefficient for calibration curve of CFD and AMD was found to be 0.995 and 0.998 respectively.

Table 2. Results of commercial formulation analysis for first order derivative spectroscopy

S.No.	Labeled Claim(mg)		Amount Found (µg/ml)		% of Labeled Claim	
	CFD	AMB	CFD	AMB	CFD	AMB
1.	100	160	99.4	159.8	99.4	99.87
2.	100	160	99.2	159.9	99.2	99.93
3.	100	160	100.0	160.0	100	100
		Mean			99.53	99.93
		±SD			0.4163	0.0651
		%RSD			0.41	0.065

RSD –relative standard deviation, SD-standard deviation

Table 3. Results of accuracy for first order derivative spectroscopic method

Level of % Recovery	% Recovery*		% RSD		Standard error	
	CFD	AMB	CFD	AMB	CFD	AMB
80	99.90	100.32	0.0326	0.035	0.0091	0.012
100	101.05	101.48	0.028	0.033	0.001	0.015
120	102.09	102.12	0.013	0.0126	0.005	0.007

RSD –relative standard deviation

Table 4. Results of method precision for first order derivative spectroscopic method

S.No	Parameters	Intra day		Inter day	
		CFD	AMB	CFD	AMB
1	% RSD	0.045	0.68	1.08	1.113
2	Standard error	0.0071	0.001	0.007	0.002

RSD –relative standard deviation

Accuracy

Recovery study was carried out by addition of standard drug solution to pre-analyzed sample solution at three different levels 80 %, 100 % and 120 %. Recovery study for CFD was found to be 99.9 to 102.09 % and for AMB 100.32 to 102.12 (Table 3).

Precision

The Intraday precision and Inter day precision of the proposed method was assessed by using formulation solutions. In triplicate measurements of one set of three solutions CFD and AMB were used for Intra-day variation. For Inter day variations study analysis was carried out for three consecutive days with same concentration. LOQ and LOD were determined using the following equation LOQ-10s/m, LOD-3.3s/m ,where s is the standard deviation of the response and m is the slope of the related calibration curve. The values of LOQ and LOD were found to be 0.732 and 0.241µg/ml respectively (Table 4).

For cefpodoxime proxetil and ambroxol hydrochloride the detection limit 1.60 and 1.85 µg/ml and quantitation limit 4.87 and 5.61 µg/ml was found respectively The % RSD was found to be less than 2 shows method is accurate and precise.

Conclusion

The proposed first order derivative spectroscophotometric method for the estimation of cefpodoxime proxetil and ambroxol hydrochloride is selective and sensitive. It can be used in industry for routine analysis.

Acknowledgement

The authors are thankful to the Management and Principal, M. G. V.'s Pharmacy College, Nashik for providing necessary facilities for the research work. The authors are also thankful to Blue Cross Laboratories Ltd. Ambad Nashik., India for providing cefpodoxime proxetil and ambroxol hydrochloride as a gift sample for the research work.

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