RESEARCH ARTICLE

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SPECTROPHOTOMETRIC METHODS FOR SIMULTANEOUS ESTIMATION OF CEFPODOXIME PROXETIL AND AMBROXOL HYDROCHLORIDE IN TABLET DOSAGE FORM

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Abstract: Cefpodoxime Proxetil is 3rd generation cephalosphorin and Ambroxol hydrochloride is mucolytic expectorent. The combination formulation is used for the treatment of the chronic bronchitis,COPD,respiratory tract infection. The new, simple, accurate and precise UV spectrophotometric methods have been developed and validated for the simultaneous determination of Cefpodoxime Proxetil(CPD) and Ambroxol hydrochloride(AMB) in their combined dosage forms. Method is based on simultaneous equation method using two wavelengths, 235 nm (λmax of CPD) and 248 nm (λmax of AMB). Methanol was the solvent used in this method. Cefpodoxime showed linearity in the range of 9-27 μg/ml and Ambroxol showed linearity in the range of 8-32 μg/ml in this the method. Method was validated statistically and recovery studies were carried out. Method was found to be accurate, precise and reproducible. This method was applied to the assay of the drugs in marketed formulation, which were found in the range of 98.0% to 102.0% of the labeled value for both Cefpodoxime and Ambroxol. Hence, the methods herein described can be successfully applied in quality control of combined pharmaceutical dosage forms.

Keywords: Cefpodoxime proxetil,Ambroxol hydrochloride, Simultaneous equation method

INTRODUCTION

Cefopodoxime proxetil is 1-(isopropoxy carbonyloxy) ethyl (6R, 7R)-7-[2-(2-amino-4-thiazolyl)-(z)-2(methoxyimino)acetamido-3-methoxymethyl-3-cephem-4-carboxylate.

Cephalosporins are bactericidal and have the same mode of action as other beta-lactam antibiotics (such as penicillin) but are less susceptible to hydrolysis of β- Lactamase produced by microbes. Cephalosporins disrupt the synthesis of the peptodoglycan layer of bacterial cell walls. It is commonly used to treat acute titis media, pharyngitis, and sinusitis.It active against gram positive and gram negative bacteria.[1, 2] Ambroxol hydrochloride is *trans*-4-[(2-Amino-3,5-dibromobenzyl)amino] cyclohexanol hydrochloride. It dissolves thick mucus and to help relieve respiratory difficulties. It does so by hydrolyzing glycosaminoglycans, tending to break down/lower the viscosity of mucin-containing body secretions/components.[3, 4]

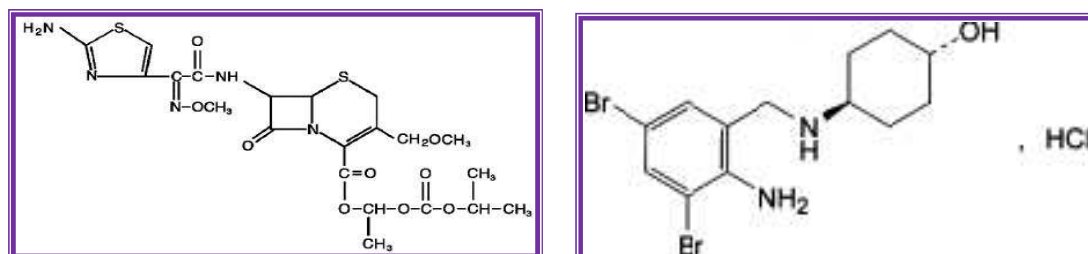The chemical structures of CPD and AMB are shown in Figure 1 (A) (B)

Figure 1 Chemical structure of (A) Cefpodoxime Proxetil (B) Ambroxol hydrochloride

CPD is official in IP and USP. In IP[5] and USP[6] describe liquid chromatography for its estimation. and AMB official in IP[7] and BP[8]. in IP and BP AMB describe potentiometry method for its estimation. A detailed survey of analytical literature for CPD revealed several methods based on varied techniques, via, HPLC[10], Spectrophotometry[11], High- Performance Thin- Layer Chromatography (HPTLC) [9] . Similarly, a survey of the analytical literature for AMB revealed methods based on varied techniques, viz, HPLC, Spectrophotometry, High-Performance Thin –Layer Chromatography individually and combination with other drugs.[12, 13, 14] .

According to detailed survey of analytical literature none of the reported analytical procedures describes a simple and satisfactory UV spectrophotometric method for simultaneous determination of CPD and AMB in their combined dosage forms. So the objective of this work was to develop simple, precise and rapid spectrophotometric methods for combination drug products containing CPD and AMB.

MATERIALS AND METHODS

Instrumentation

A Shimadzu model 1700(Japan) double beam UV/Visible spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Probe system software (UV Probe version 2.31). An Electronic analytical balance (Acculab) and an ultrasonic bath were used in the study.

Materials and reagents

CPD and AMB bulk powder was gifted by Alps Pharmaceutical,india and Zydus lifecare Pvt. Ltd., Ahmadabad, india respectively. The commercial fixed dose combination product was procured from the local market. Methanol AR Grade was procured from S.D.Fine Chemicals Ltd., Mumbai, India.

Standard and Test Solutions

Preparation of standard solution

An accurately weighed quantity of CPD (10 mg) and AMB (10 mg) were transferred to a separate 100 ml volumetric flask and dissolved and diluted to the mark with Methanolic HCL to obtain standard solution having concentration of CPD(100 µg/ml) and AMB (100 µg/ml).

Preparation of test solution

From the tablet formulation FENECEF-AM(CPD 100mg and AMB 60mg)Twenty tablets were powdered.Powder equivalent to 100 mg of CPD and 60 mg of AMB was weighed and transferred into a 100 ml of volumetric flask, dissolved and diluted up to mark with methanol.The solution was filtered using Whatman filter paper no.42 and first few drops of filtrate were discarded. (1000 µg/ml of CPD and 600µg/ml of AMB).Transfer 1 ml of this solution into a 10 ml volumetric flask and diluted to mark with methanol (100 µg/ml of CPD and 60 µg/ml of AMB).This solution was used as working sample solution.

Methods

Simultaneous Equation Method

In this method, seven working standard solutions having concentration 9-27 μg/ml for CPD and8-32 μg/ml for AMB were prepared in Methanol and the absorbance at 235 nm (λ-max of CPD) and 248nm (λ-max of AMB) were measured and absorptivity coefficients were calculated using calibration curve.

The concentration of two drugs in the mixture can be calculated using following equations

$$Cx = \frac{A_2 a y_1 - A_1 a y_2}{a x_2 a y_1 - a x_1 a y_2} \qquad \ldots\ldots (1)$$

$$Cy = \frac{A_1 a x_2 - A_2 \, a x_1}{a x_2 a y_1 - a x_1 a y_2} \qquad \ldots\ldots.. (2)$$

Where, A_1, A_2 are absorbance of mixture at 235 nm (λ1) and 248 nm (λ2) respectively, ax1 and ax2 are absorptivities of CPD at λ1 and λ2 respectively, ay1 and ay2 are absorptivities of AMB at λ1 and λ2 respectively, Cx and Cy are concentrations of CPD and AMB respectively.

Method validation

All the methods were validated as per ICH guidelines for parameters like linearity,

accuracy, precision, limit of detection, limit of quantitation.

> **RESULTS AND DISCUSSION**

In the present work, this method, namely, Simultaneous equation method was developed for the simultaneous spectroscopic estimation of CPD and AMB in commercially available tablet dosage forms. Methanol was used as the solvent since both the drugs exhibit good solubility in it and no interference due to excipients of the opthalmic formulation were observed.

Simultaneous Equation Method

Estimation of drugs by Simultaneous Equation equation method was carried out at 235 nm (λmaxof CPD) and 248 nm (λmax of AMB). The standard solutions of CPD and AMB were prepared to determine the absorptivity values of the subject analyte at the two selected wavelengths. The method showed good linearity in the range of 9-27 μg/mL for CPD and 8-32 μg/mL for AMB. Overlain spectra of both drugs shown in figure 2.
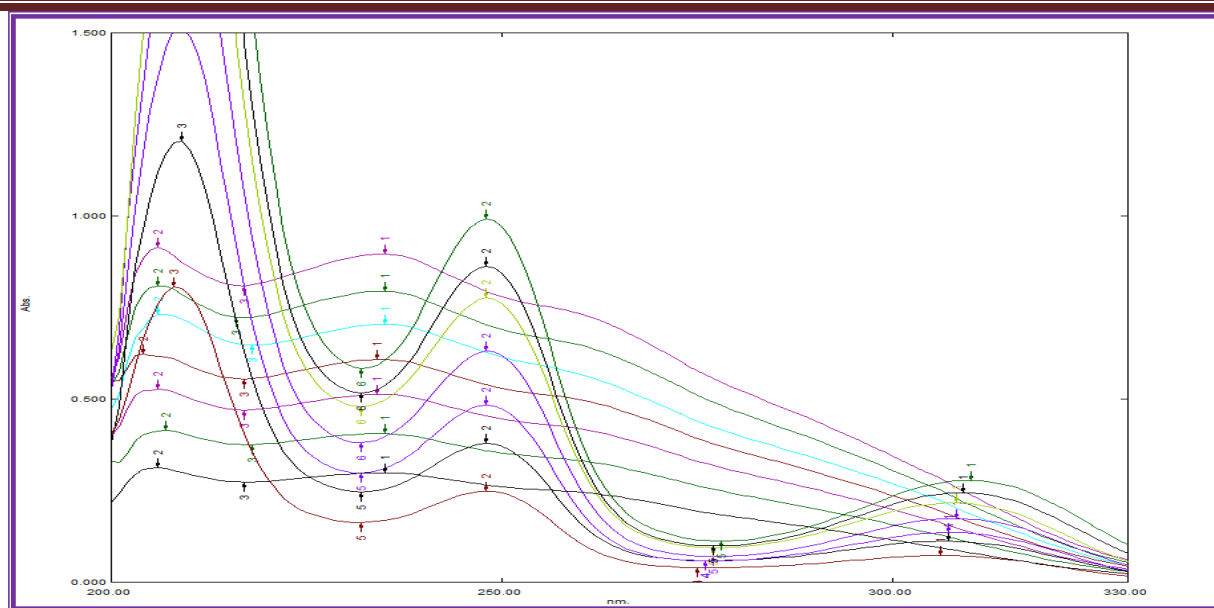
Figure 2 Overlain zero order spectra of CPD and AMB (Simultaneous Equation Method)

CONCLUSION

The developed spectroscopic methods are found to be simple, sensitive, accurate and precise and can be used for routine analysis of CPD and AMB. The developed methods were validated as par ICH guidelines. Statistical analysis proved that the method is repeatable and selective for the analysis of CPD and AMB in combination as a single drug in bulk as well as in pharmaceutical formulations.

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Table 1

Data showing linearity of the developed method

Methods	Simultaneous Equation Method	
Parameters	**CPD**	**AMB**
Linearity range	9-27 µg/ml	8-32 µg/ml
Slope	0.032	0.043
Intercept	0.011	0.141
Correlationco-efficient	0.999	0.999

Table 2

Data showing Accuracy of the developed method

DRUG	Amt. taken (µg/ml)	Amt. added (µg/ml)	Amt. added %	Simultaneous Equation method (%RSD) (n=3)
CPD	15	1.38	25 %	98.66±0.28
	15	2.75	50 %	99.73±0.34
	15	4.18	75 %	99.34±0.54
AMB	9	0.25	25 %	99.11±0.62
	9	0.50	50 %	99.55±0.58
	9	0.75	75 %	99.25±0.78

(n = number of repetition)

Table 3

Data showing Precision of the developed method

Methods		Simultaneous Equation Method (%RSD) (n=3)	
		CPD	**AMB**
System precision	**Intraday**	0.147-0.171	0.178-0.303
	Interday	0.190-0.220	0.230-0.256
Method precision	**Intraday**	0.225-0.262	0.138-0.266
	Interday	0.302-0.310	0.215-0.222

(n = number of repetition)

Table 4

Data showing LOD and LOQ of the developed method

Methods	Simultaneous Equation Method	
	CPD	**AMB**
LOD(µg/ml)	0.222	0.212
LOQ(µg/ml)	0.332	0.645

Table 5

Result of Analysis of formulation

Methods	Simultaneous Equation Method	
	CPD	**AMB**
%Assay	99.88	99.45
S.D.(n=3)	0.035	0.045

(n = number of repetition)

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