Estimation of cefixime and ornidazole in its pharmaceutical dosage form by spectrophotometric method

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ABSTRACT

Two accurate, precise, rapid and economical methods were developed for the estimation of Cefixime and Ornidazole in tablet dosage form. First method is first order derivative spectroscopy, wavelengths selected for quantitation were 311.5 nm for Cefixime (zero cross for Ornidazole) and 290.0 nm for Ornidazole (zero cross for Cefixime). Second method is area under curve method; area under curve in the range of 295.0-285.0 nm (for Cefixime) and 317.0-307.0 nm (for Ornidazole) were selected for the analysis. In both the methods linearity for detector response was observed in the concentration range of 10-50 µg/ml for both, Cefixime and Ornidazole. The proposed methods were successfully applied for the simultaneous determination of both drugs in commercial tablet preparation. The results of the analysis have been validated statistically and by recovery studies.

Keywords: Cefixime; Ornidazole; derivative spectroscopy; area under curve method

INTRODUCTION

Cefixime (CEF) is an oral third generation cephalosporin antibiotic. Chemically, it is (6*R*,7*R*)-7-{[2-(2-amino-1,3-thiazol-4-yl)-2-(carboxymethoxyimino)acetyl]amino}-3-ethenyl-8-oxo-5-thia-1-azabicyclo-[4.2.0]oct-2-ene-2-carboxylic acid, clinically used in the treatment of susceptible infections including gonorrhoea, otitis media, pharyngitis, lower respiratory-tract infections such as bronchitis, and urinary-tract infections[1]. Ornidazole (ORD), chemically 1-chloro-3-(2-methyl-5-nitro-imidazol-1-yl) propan-2-ol, is an antimicrobial agent used in treatment of susceptible protozoal infections and anaerobic bacterial infection[2]. Both the drugs are marketed as combined dose tablet formulation in the ratio of 200:500 mg CEF: ORD. Literature survey reveals that cefixime can be estimated by spectrophotometrically[3], HPLC4[4-8] and by HPTLC[9] individually or with other drugs in bulk drugs and in human plasma, while ornidazole can be estimated by spectrophotometrically[10-11], HPLC4[12-13] in combination with other drugs. However, there is no analytical method reported for the estimation of CEF and ORD in a combined dosage formulation. Present work describes two methods for simultaneous estimation of CEF and ORD in tablet formulation.

MATERIAL AND METHODS

Instrument: A double-beam Shimadzu UV- Visible spectrophotometer, 1700 Pharmaspec, with spectral bandwidth of 2 nm, wavelength accuracy ± 0.5 nm and a pair of 1-cm matched quartz cells was used to measure absorbance of the resulting solution.

Materials: Standard gift sample of Cefixime provided by Glenmark Pharmaceuticals Ltd, Nashik and Ornidazole by Aristo Pharmaceuticals Pvt. Ltd., Mumbai. Combined dose Cefixime and Ornidazole tab-lets were purchased from local market.

Solvent: Methanol (AR Grade) was used as solvent, procured from Universal Laboratories Private limited, Mumbai.

Stock solution: Standard stock solutions of CEF (100 µg/ml) and ORD (100 µg/ml) were prepared and used for the analysis.

Procedure

Method A- First Order Derivative Spectroscopy

In this method solutions of CEF and ORD (20 µg/ml, each), were prepared separately by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. The absorption spectra thus obtained were derivatized from first to fourth order. First order derivative spectra were selected for analysis of both drugs. From the overlain spectra of both drugs (Fig. 1), wavelength selected for quantitation were 311.5 nm for CEF (zero cross for ORD) and 290.0 nm for ORD (zero cross for CEF). The calibration curves for CEF and ORD were plotted in the concentration range of 10-50 µg/ml at wavelength 311.5 nm and 290.0 nm, respectively. The concentration of the individual drug present in the mixture was determined against the calibration curve in quantitation mode.

Method B- Area Under Curve Method

For the selection of analytical wavelength, solutions of CEF and ORD (20 µg/ml, each), were prepared separately by appropriate dilution of standard stock solution and scanned in the spectrum mode from 400 nm to 200 nm. From the overlain spectra of both drugs (Fig. 2), area under the curve in the range of 295.0-285.0 nm (for CEF) and 317.0-307.0 nm (for ORD) were selected for the analysis. The calibration curves for CEF and ORD were prepared in the concentration range of 10-50 µg/ml at their respective AUC range. The 'X' values of the drugs were determined for both the drugs at the selected AUC range. The 'X' is the ratio of area under the curve at selected wavelength ranges with the concentration of component in gm/lit. These 'X' values were the mean of six independent determinations.

A set of two simultaneous equations obtained by using mean 'X'

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Table 1: Tablet Analysis and Recovery Studies of Cefixime and Ornidazole

Method	Label Claim (mg/tab)		Amount Found* (%)		Standard Deviation		% Recovery*	
	CEF	ORD	CEF	ORD	CEF	ORD	CEF	ORD
A	200	500	99.86	99.92	±0.8193	±0.8612	99.51±0.7978	99.38±0.7253
B	200	500	99.75	100.02	±0..4113	±0..1907	99.51±0.5365	100.07±0.2760

denotes n = 6, average of six estimations.
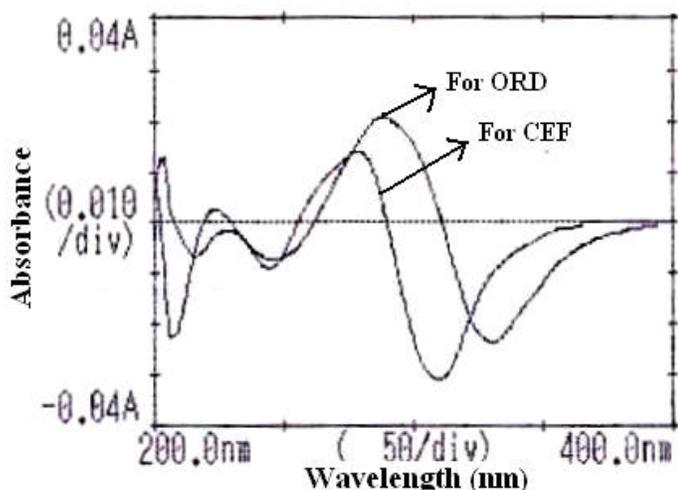
Fig.1: Overlain Spectra of Cefixime (CEF) and Ornidazole (ORD) in Method- A
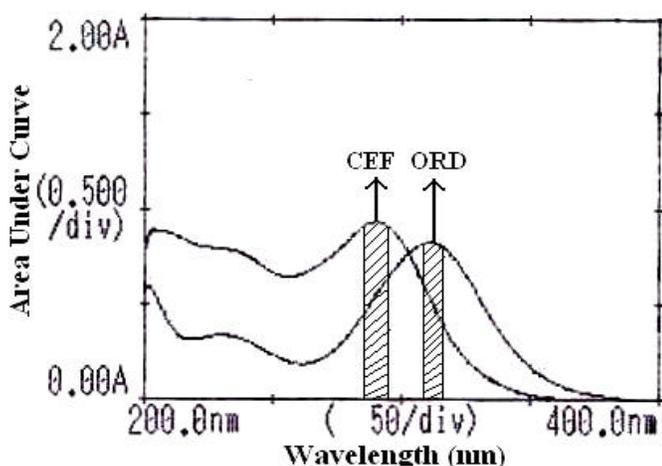
Fig.2: Overlain Spectra of Cefixime (CEF) and Ornidazole (ORD) in Method- B

values are given below.

$$A_1 = 461.08\,C_{CEF} + 276.44\,C_{ORD} \text{ — (at } ?_{295.0\text{-}285.0}\text{ nm) ————— (1)}$$
$$A_2 = 370.09\,C_{CEF} + 390.82\,C_{ORD} \text{ —(at } ?_{317.0\text{-}307.0}\text{ nm) ————— (2)}$$

Where A_1 and A_2 were area under curve of sample at the wavelength range 295.0-285.0 nm and 317.0-307.0 nm, respectively, 461.08 and 370.09 were 'X' values of CEF at wavelength range 295.0-285.0 nm and 317.0-307.0 nm, respectively. Similarly 276.44 and 390.82 were 'X' values of ORD at the wavelength range 295.0-285.0 nm and 317.0-307.0 nm, respectively. C_{CEF} and C_{ORD} were concentration of CEF and ORD, respectively. The concentration of CEF and ORD in sample was determined by using the equation (1) and (2).

Application of the proposed method for the determination of CEF and ORD in tablets Twenty tablets were weighed and average weight was calculated. The tablets were crushed to obtain fine powder. Tablet powder equivalent to 40 mg of CEF was transferred to 100.0 ml volumetric flask, methanol added, ultrasonicated for 10 minutes and volume was made-up to the mark with methanol and. The solution was then filtered through a Whatmann filter paper (No. 41). The filtrate was further diluted with methanol to obtain 8 µg/ml of CEF and 20 µg/ml of ORD. In Method-A, the concentration of both CEF and ORD were determined by measuring the absorbance of the sample at 311.5 nm and 290.0 nm in first order spectrum mode. The results of the tablet analysis were calculated against the calibration curve in quantitation mode. For Method-B, the concentration of both CEF and ORD were determined by measuring area under curve in the range of 295.0-285.0 nm (for CEF) and 317.0-307.0 nm (for ORD) and values were substituted in the respective formula to obtain concentrations.

Validation

The methods were validated with respect to linearity, accuracy, precision and selectivity.

Accuracy: To ascertain the accuracy of proposed methods, recovery studies were carried out by standard addition method at three different levels (80%, 100% & 120%). Percent recovery for CEF and ORD, by both the methods, was found in the range of 98.28 % to 100.76 %.

Linearity: The linearity of measurement was evaluated by analyzing different concentration of the standard solution of CEF and ORD. For both the methods, the Beer-Lambert's concentration range was found to be 10-50 µg/ml for both, CEF and ORD.

Precision: The reproducibility of the proposed method was determined by performing tablet assay at different time intervals (morning, afternoon and evening) on same day (Intra-day assay precision) and on three different days (Inter-day precision). Result of intra-day and inter-day precision is expressed in % RSD. Percent RSD for Intraday assay precision was found to be 0.8205 (for CEF) and 0.8619 (for ORD) in first order derivative spectroscopy method; 0.2707 (for CEF) and 0.2919 (for ORD) in area under curve method. Inter-day assay precision was found to be 0.4825 (for CEF) and 0.7650 (for ORD) in first order derivative spectroscopy method; 0.0590 (for CEF) and 0.0188 (for SAT) in area under the curve method.

RESULTS AND DISCUSSION

The methods discussed in the present work provide a convenient and accurate way for simultaneous analysis of CEF and ORD. In first order derivative spectroscopy, wavelengths selected for quantitation were 311.5 nm for CEF (zero cross for ORD) and 290.0 nm for ORD (zero cross for CEF). In area under curve method, the area under curve in the range of 295.0-285.0nm (for CEF) and 317.0-307.0nm (for ORD) were selected for the analysis. In both the methods linearity for detector response was observed in the concentration range of 10-50 µg/ml for both, CEF and ORD. In method A, concentration of the individual drug present in the mixture was determined against the calibration

curve in quantitation mode. In method-B, 'X' values were calculated for both the drugs at selected wavelengths and substituted in equations for determining concentration of CEF and ORD in tablet sample solution. Percent label claim for CEF and ORD in tablet analysis, by both the methods, was found in the range of 98.50 % to 101.00 %. Standard deviation and coefficient of variance for six determinations of tablet sample, by both the methods, was found to be less than ± 2.0 indicating the precision of both the methods. Accuracy of proposed methods was ascertained by recovery studies and the results are expressed as % recovery. Percent recovery for CEF and ORD, by both the methods, was found in the range of 98.28 % to 100.76 %., values of standard deviation and coefficient of variation was satisfactorily low indicating the accuracy of both the methods. Based on the results obtained, it is found that the proposed methods are accurate, precise, reproducible & economical and can be employed for routine quality control of Cefixime and Ornidazole in combined dose tablet formulation.

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