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SIMULTANEOUS SPECTROPHOTOMETRIC METHOD FOR ESTIMATION OF CEFPODOXIME PROXETIL AND OFLOXACIN IN TABLET FORMULATION

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Abstract A new simple, precise, accurate and cost effective UV spectrophotometric method has been developed for the estimation of Cefpodoxime and Ofloxacin in combined dosage form by simultaneous equation method. This method utilized methanol: 0.1 N HCl (50:50) as common solvent. The wavelength selected for simultaneous equation method for Cefpodoxime shows maximum absorption at 276 nm and Ofloxacin shows maximum absorption at 306.4 nm. The drugs follow the Beer-Lamberts law in the concentration range of 10-30 mcg/ml. The method was validated by following analytical parameters as suggested by the ICH guideline which included accuracy, precision assay, LOD and LOQ. All validation parameters were within acceptable range. The correlation coefficient of Cefpodoxime and Ofloxacin was found to be 0.999. A % recovery was found to be 99.66 % for Cefpodoxime and 99.6 % for Ofloxacin. The proposed method is recommended for routine analysis of cefpodoxime and ofloxacin in its combined dosage forms.

Keywords Cefpodoxime proxetil, Ofloxacin, Simultaneous equation method, Methanol, HCl.

Introduction

Cefpodoxime proxetil (CEF) is chemically, 1-(isopropoxy carbonyloxy) ethyl (6R, 7R)-7-[2-(2-amino-4-thiazolyl)-(z)-2- (methoxyimino) acetamido]-3-methoxymethyl 3 cephem 4-carboxylate is a third generation cephalosporin antibiotic [1]. Ofloxacin (OFL) is chemically, 9-fluro-2-3 dihydro-3-methyl-10- (4-methyl 1-piperazinyl) - 7-oxo-7H- pyrido [1, 2, 3-de] 1, 4 benzoxazine-6-carboxylic acid is a fluoroquinolone antibacterial agent [2]. CEF is used in treatment of urinary tract and soft tissues infections and OFL is used as in the treatment of Chlamydia infections including nongonococcal urethritis and in mycobacterial infections. CEF and OFL are official in IP and USP. IP (Indian Pharmacopoeia, 2010) and USP (United States Pharmacopoeia, 2005) describe liquid chromatography methods for its estimation.

Literature survey reveals the solid-phase spectrofluorimetry [3], HPLC with fluorescence detector for estimation of ofloxacin in human plasma [4], 1st derivative fluorescence spectroscopy [5], HPLC with fluorescence detection for determination of ofloxacin in human aqueous humor [6], and chemiluminescence [7] methods for determination of OFL in pharmaceutical dosage forms as well as in biological fluids. RP-HPLC [8] and Spectrophotometric [9], methods for determination of CEF with other drugs. The combined dosage forms of these two drugs are not official in any pharmacopoeia. Literature survey reveals the absorption ratio method [10], dual wavelength spectroscopy [11], and First Order derivative Spectrophotometric [12], method for estimation of these combined dosage form. Literature survey does not reveal any simple simultaneous equation method for simultaneous estimation of CEF and OFL in combined dosage forms. The present invention describes simple, sensitive, rapid, accurate, precise and economical Spectrophotometric method based on simultaneous equation method for simultaneous estimation of both drugs in their combined tablet dosage forms.

Material and Methods

Chemicals and reagents

Analytical pure Cefpodoxime proxetil and Ofloxacin were obtained as a gift sample from Macleods Pharmaceuticals, Baddi, Himachal Pradesh, India. The formulations Zedocef-O and Cedon-Plus tablets were procured from the local market with labeled amount of 200 mg of Cefpodoxime proxetil and 200 mg of Ofloxacin. Hydrochloric acid, methanol and water were used of HPLC grade, purchased from RANKEM Ltd.

Instruments

A Shimadzu UV-1700, UV/Visible spectrophotometer with spectral band width of 1nm, wavelength accuracy of ± 0.3 nm and 1 cm matched quartz cells was used for analytical method development. The spectral data were processed by Shimadzu software kit Ver. 3.7 (P/N 206-60570-04).

Reagents

All reagents were of analytical reagent grade, stock solutions of 100 mcg of CEF and 100 mcg of OFL were prepared of each drug by dissolving 10 mg and diluted to 100 ml in methanol: 0.1 N HCl (50:50). Other ranges of concentrations were prepared by appropriate dilution using the same solvent. Ranges of concentration were prepared by appropriate dilution using the respective solvent.

Method

Pure drug sample of CEF and OFL were dissolved in a mixture of methanol and 0.1 N HCl (50:50), so as to give five dilutions of standard in concentration range of 10-30 µg/ml for both the drugs. All the solutions were scanned in the wavelength range of 276 nm and 306.4 nm. Figure 1 represents the overlain spectra of CEF and OFL. Two wavelengths selected for formation and solving the simultaneous equations were 276 nm for CEF and 306.4 nm for OFL. Linearity was observed in concentration range of 10-30 µg/ml for both the drugs. Absorptivity coefficients for CEF at 276 and 306.4 nm were 40.33 $cm^{-1}g^{-1}l$ and 22.83 $cm^{-1}g^{-1}l$ respectively, while the respective values for OFL were 10.04 $cm^{-1}g^{-1}l$ and 31.41 $cm^{-1}g^{-1}l$.

$$A1 = 40.33 \times Cx + 10.04 \times Cy \quad \text{---------- (1)}$$
$$A2 = 22.83 \times Cx + 31.41 \times Cy \quad \text{---------- (2)}$$

Cx and Cy are concentrations of CEF and OFL in g/l in the sample solution. A1 and A2 are the absorbance's of the mixture at 276 nm and 306.4 nm respectively.

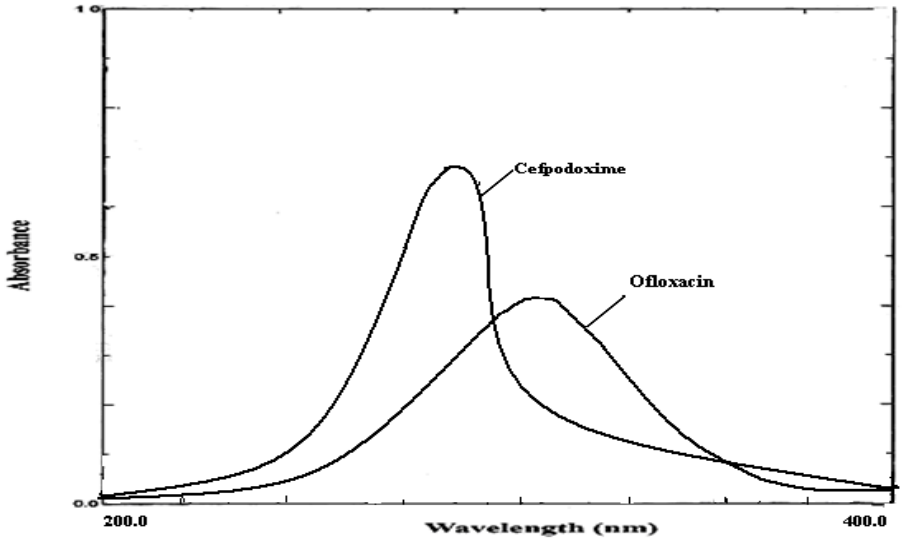

Figure 1: Overlain spectra of Cefpodoxime and ofloxacin in methanol: 0.1N HCl (50:50)

The validity of above framed equations were checked by preparing five mixed standards using pure samples of two drugs, results of which are reported in table 1.

Table 1: Result of validation studies of simultaneous equation method using mixed standards

S. No.	Concentration(mcg/ml)		Absorbance		% Concentration	
	CEF	OFL	276 nm	306.4 nm	CEF	OFL
1	10	20	0.6014	0.8504	99.80	99.10
2	12.5	17.5	0.6779	0.8332	99.68	99.79
3	15	15	0.7529	0.8126	99.53	100.13
4	17.5	12.5	0.8288	0.7897	99.71	99.68
5	20	10	0.8993	0.7653	99.10	99.60

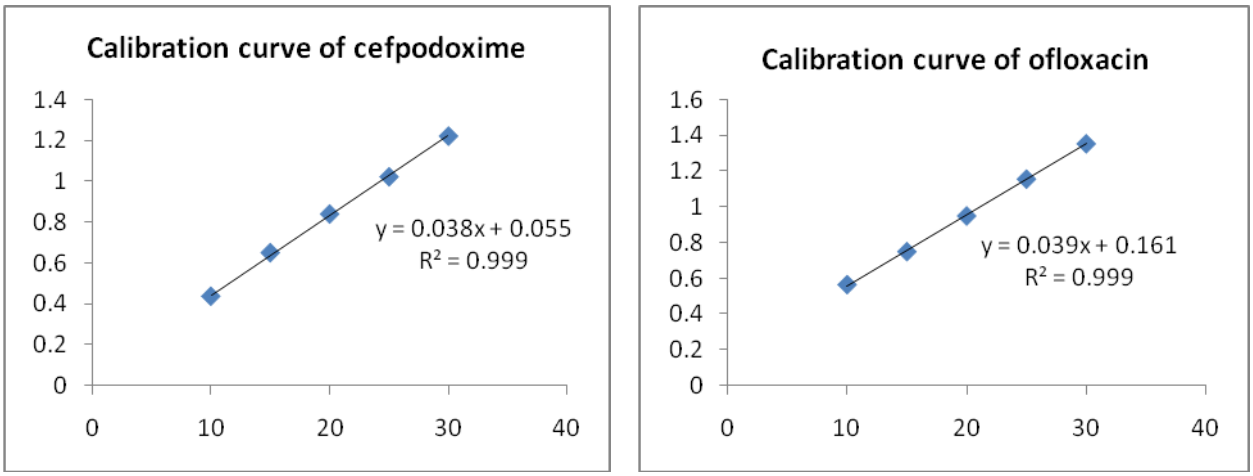

Figure 2: Calibration curve of Cefpodoxime (a) and ofloxacin (b)

Procedure for analysis of tablet formulations

Twenty tablets [Cefpodoxime (CEF) - 200 mg and ofloxacin (OFL) – 200 mg] were weighed accurately and average weight per tablet was determined. The tablet was finely powdered and powder equivalent to 10 mg of Cefpodoxime (CEF) was weighed and extracted with 50 ml of methanol: 0.1N HCl (50:50), sonicated for 10 min. The resultant was filtered through Whatman filter paper no. 41 into 100 ml volumetric flask. The filter paper was washed several times with methanol: 0.1N HCl (50:50). The washings were added to the filtrate and final volume was made up to the mark with the same. Filtrate (1.5 ml) of the sample solution was diluted to 10 ml with methanol: 0.1N HCl (50:50). The absorbance of this final dilution was measured at 276 nm and 306.4 nm. Finally, the concentration of two drugs in sample was calculated. Results of which are reported in table 2.

Table 2: Results of analysis of commercial formulations

Brand Name	Label Claim (mg/tablet.)		% Label Claim Estimated		Standard Deviation		Coefficient of Variance	
	CEF	OFL	CEF	OFL	CEF	OFL	CEF	OFL
ZEDOCEF-O	200	200	99.85	99.81	0.281	0.316	0.0028	0.0032
CEDON-PLUS	200	200	99.73	99.84	0.249	0.207	0.0025	0.0021

* Each value is an average of five determinations

Validation of the proposed method

Linearity (Calibration curve)
The calibration curves were plotted over a concentration range of 10-30 µg/ml for each CEF and OFL. Accurately measured standard stock solutions of each CEF and OFL (1.0, 1.5, 2.0, 2.5 and 3.0 ml) were transferred to a series of 10 ml volumetric flask separately and diluted up to the mark with methanol: 0.1 N HCl (50:50). The absorbances of solution were then measured at 276.0 nm and 306.4 nm. The calibration curves were constructed by plotting absorbances versus concentration and the regression equations were calculated.

Method precision (repeatability)
The precision of the instrument was checked by repeated scanning and measurement of the absorbances of solutions (n = 6) of CEF and OFL (15 µg/ml for both drugs) without changing the parameters of the proposed method.

Intermediate precision (reproducibility)
The intraday and interday precisions of the proposed method was determined by estimating the corresponding responses 3 times on the same day and on 3 different days over a period of one week for 3 different concentrations of standard solutions of cefpodoxime and ofloxacin.

Accuracy (Recovery studies)
Recovery studies were carried out for both the formulations by addition of known amount of standard drug solution to pre-analyzed tablet sample solution at three different concentration levels. The resulting solutions were analyzed by proposed method. The results of recovery studies were found to be satisfactory and are results are reported in table 3.

Table 3: Results of recovery studies

Brand Name	**Label Claim (mg/tablet.)**		**Amt. Added to Final Dilution (µg/ml)**		**Amt. Recovered (µg/ml)**		**% Recovery**	
	CEF	**OFL**	**CEF**	**OFL**	**CEF**	**OFL**	**CEF**	**OFL**
ZEDOCEF-O	200	200	2.5	2.5	2.46	2.47	98.40	98.80
			5.0	5.0	4.97	5.02	99.40	100.40
			10	10	9.96	9.95	99.60	99.50
CEDON-PLUS	200	200	2.5	2.5	2.52	2.47	100.80	98.80
			5.0	5.0	5.03	5.01	100.60	100.20
			10	10	9.92	10.02	99.20	100.20

Result and Discussion

The developed method is simple, precise, accurate and cost effective for the estimation of Cefpodoxime and Ofloxacin in combined dosage form. This method utilized methanol: 0.1 N HCl (50:50) as common solvent. The wavelength selected for simultaneous equation method for Cefpodoxime shows maximum absorption at 276 nm and Ofloxacin shows maximum absorption at 306.4 nm. The drugs follow the Beer-Lamberts law in the concentration range of 10-30 mcg/ml. The method was validated by following analytical parameters as suggested by the ICH guideline which included accuracy, precision, assay LOD and LOQ (Table 4). All validation parameters were within acceptable range (Table 4). The correlation coefficient of Cefpodoxime and Ofloxacin was found to be 0.999. A % recovery was found to be 99.66 % for Cefpodoxime and 99.6 % for Ofloxacin. The proposed method is recommended for routine analysis of cefpodoxime and ofloxacin in its combined dosage forms.

Conclusion

The validated spectrophotometric method employed here is simple, rapid, accurate, precise, sensitive and cost which can be used for routine analysis of cefpodoxime proxetil and ofloxacin in combined dosage form.

Table 4: Regression analysis data and summary of validation

Parameters Drugs	**Cefpodoxime(CEF)**	**Ofloxacin(OFL)**
Wavelength range (nm)	276	306.4
Beer's law limit (µg/ml)	10-30	10-30
Regression equation (y =a + bc)	y = 0.038x + 0.055	y = 0.039x + 0.161
Slope (b)		
Intercept (a)	0.038x	0.039x
Correlation Coefficient(r2)	0.055	0.161
Accuracy(Recovery)(n = 3) I	$R^2 = 0.999$	$R^2 = 0.999$
II		
III	99.60	98.80
Method precision (Repeatability)		
(% RSD, n=3)	100.01	100.3
Interday (n = 3) (% RSD)		
Intraday (n = 3) (% RSD)	99.40	99.85
LOD (µg/ml)	0.5510	0.8002
LOQ (µg/ml)		
	0.32 - 1.37	0.27 - 1.09
	0.30 – 1.25	0.24 – 0.99
	2.40	1.85
	4.47	4.25

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