Simultaneous Spectrophotometric Estimation of Ciprofloxacin and Ornidazole in Tablets

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Two simple, sensitive, rapid, accurate and economical methods were developed for the estimation of ciprofloxacin and ornidazole in two-component solid dosage form. First method is based on the simultaneous equation, and second method is based on Q-analysis (absorbance ratio method). Ciprofloxacin has absorbance maxima at 271.4 nm, and ornidazole has absorbance maxima at 320 nm in distilled water. The linearity was obtained in the concentration range of 2-10 µg/ml for ciprofloxacin and 2-20 µg/ml for ornidazole. In the first method, the concentrations of the drugs were determined by using simultaneous equations; and in the second method, the concentrations of the drugs were determined by using ratio of absorbances at isoabsorptive point and at the λ_{max} of one of the drugs. The results of analysis have been validated statistically and by recovery studies.

Ciprofloxacin (CPX), 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxilic acid[1], is a broad spectrum fluoroquinolone antibacterial agent used in the treatment of various bacterial infections caused by gram-positive and gram-negative microorganisms[2]. Its antibacterial spectrum is wider than that of aminoglycosides, third generation cephalosporins and other fluoroquinolones. Ornidazole (ORN), 1-(3-chloro-2-hydroxypropyl)-2-methyl-5-nitroimidazole[3], is used as an antiinfective agent. ORN is used in combination with ciprofloxacin in the treatment of intraabdominal infection[4]. Ciprofloxacin is official in IP, USP and BP. The IP[5] and USP[6] describe HPLC methods and BP[7] describes a non-aqueous titration method for estimation of ciprofloxacin. Literature survey reveals HPLC[8,9,10] and spectrophotometric methods[11,12] for its determination. Ornidazole is not official in any pharmacopoeia. Literature survey reveals HPLC[13], chemiluminescence[14] and spectrophotometric methods[15] for its determination in dosage forms and biological fluids. The combination of two drugs is not official in any pharmacopoeia; hence no official method is available for the estimation of CPX and ORN in their combined dosage form. Literature survey

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reveals that there is no simple spectrophotometric method available for estimation of these drugs in combined dosage form. The present communication describes two simple, sensitive, accurate, rapid and economical methods for simultaneous estimation of CPX and ORN in tablet dosage form.

A Shimadzu model 1601 double beam UV/Vis spectrophotometer with spectral width of 2 nm, wavelength accuracy of 0.5 nm and a pair of 10 mm matched quartz cells was used to measure absorbance of the resulting solutions. A Sartorius CP224S analytical balance, an ultrasonic cleaner (Frontline FS 4), ciprofloxacin and ornidazole (Intas Pharmaceuticals Ltd., Ahmedabad) and double glass-distilled water were used in the study.

The standard stock solution of CPX and ORN were prepared by dissolving 10 mg of each drug in 100 ml volumetric flask separately using glass-distilled water. Final working standard solutions of 40 µg/ml of CPX and ORN were prepared by diluting 20 ml of the above solution to 50 ml with glass-distilled water.

Working standard solutions were scanned in the entire UV range of 200-400 nm to determine the λ_{max} of both drugs. The λ_{max} of CPX and ORN were found to be 271.4 nm and 320 nm respectively. Five standard solutions having concentration 2, 4, 6, 8 and 10 µg/ml for CPX and eight standard solutions having concentration 2, 4, 6, 8, 10, 12, 16 and 20 µg/ml for ORN were prepared in glass-distilled water using the working standard solution. The absorbance of resulting solutions was measured at 271.4 nm and 320 nm, and calibration curves were plotted at these wavelengths. The absorptivity coefficients of these two drugs were determined using calibration curve equation. Two simultaneous equations were formed using these absorptivity coefficient values.

A1=818×Cx + 100×Cy, A2=309×Cx + 417×Cy, where Cx and Cy are concentrations of CPX and ORN respectively in g/100 ml in the sample solution. A1 and A2 are the absorbances of the mixture at 271.4 nm and 320 nm respectively. The concentration of Cx and Cy can be obtained as Cx=[(A2×100)-(A1×417)]/ -310206 and Cy=[(A1×309)-(A2×818)]/ -310206.

Absorbance ratio method uses the ratio of absorbances at two selected wavelengths, one at isoabsorptive point and the other being the λ_{max} of one of the two components. From the overlay spectra of two drugs, it is evident that CPX and ORN show an isoabsoptive point at 290.8 nm. The second wavelength used is 271.4 nm, which is the λ_{max} of CPX.

Five standard solutions having concentration 2, 4, 6, 8 and 10 µg/ml for CPX and 2, 4, 6, 8 and 10 µg/ml for ORN were prepared in distilled water, and the absorbances at 290.8 nm (isoabsorptive point) and 271.4 nm (λ_{max} of CPX) were measured and absorptivity coefficients were calculated using calibration curve.

The concentration of two drugs in the mixture can be calculated using equations $Cx=Q_M- Q_Y/Q_X-Q_Y\times A_1/ax_1$, $C_Y=A_1/ax_1-Cx$, where A_1 and A_2 are absorbances of mixture at 290.8 nm and 271.4 nm; and ax_1 and ay_1 are absorptivities of CPX and ORN respectively at 290.8 nm; ax_2 and ay_2 are absorptivities of CPX and ORN respectively at 271.4 nm; and $Q_M=A_2/A_1$, $Q_X=ax_2/ax_1$ and $Q_Y=ay_2/ay_1$.

Twenty tablets were weighed and crushed to a fine powder. An accurately weighed powder sample equivalent to 10 mg of CPX and ORN was transferred to a 100 ml volumetric flask and dissolved in 50 ml glass-distilled water and sonicated for 10 min, and volume was made up to the mark with glass-distilled water. The solution was then filtered through Whatman filter paper no. 41. The solution was further diluted to get a final concentration of 6 µg/ml of both CPX and ORN. For method I, the absorbances of the sample solution, i.e., A_1 and A_2, were recorded at 271.4 nm and 320 nm respectively, and concentration of two drugs in the sample were determined using the equations Cx=[(A2×100)-(A1×417)]/-310206 and Cy=[(A1×309)-(A2×818)]/-310206. For method II, the absorbances of the sample solution, i.e., A_1 and A_2, were recorded at 290.8 nm (isoabsorptive point) and 271.4 nm (λ-max of CPX) respectively, and ratios of absorbances were calculated, i.e., A_2/A_1. Relative concentration of two drugs in the sample was calculated using the equations $Cx=Q_M-Q_Y/Q_X-Q_Y\times A_1/ax_1$ and $C_Y=A_1/ax_1-Cx$. The analysis procedure was repeated five times with tablet formulation. The result of analysis of tablet formulation is shown in Table 1.

To study the accuracy and precision of the above-proposed methods, recovery studies were carried out by addition of known amount of standard drug solutions of CPX and ORN to preanalyzed tablet solution. The resulting solution was then analyzed by proposed methods. Results of recovery studies were found to be satisfactory and are reported in Table 2.

TABLE 1: ANALYSIS OF CIPROFLOXACIN AND ORNIDAZOLE IN TABLETS

Method	Label claim (mg/tab)		Amount found (mg/tab)		% of label claim* ± S.D	
	CPX	ORN	CPX	ORN	CPX	ORN
I	500	500	509.5	491.9	101.9±0.49	98.4±0.35
II	500	500	504.2	496.4	100.8±0.78	99.3±0.69

*Mean of five determinations, CPX – ciprofloxacin and ORN – ornidazole.

TABLE 2: RECOVERY STUDY DATA

Method	Amount ofdrug taken (µg/ml)		Amount ofdrug added (µg/ml)		Amount of drug found (µg/ml)		% recovery* ± S.D	
	CPX	ORN	CPX	ORN	CPX	ORN	CPX	ORN
I	6.0	6.0	2.0	2.0	7.86	7.91	98.3±0.46	98.9±0.82
II	6.0	6.0	2.0	2.0	8.13	8.10	101.6±1.19	101.3±0.78

*Mean of five determinations, CPX – ciprofloxacin and ORN – ornidazole

The proposed methods were found to be simple, accurate, economical and rapid for the routine simultaneous estimation of two drugs. The values of standard deviation and coefficient of variation were satisfactory, and recovery studies ranging from 98.3-101.6% (for CPX) and 98.9-101.3% (for ORN) were indicative of the accuracy and precision of the proposed methods.

In simultaneous equation method (method I), two wavelengths of respective absorbance maxima, i.e., 271.4 nm for CPX and 320 nm for ORN, were used for the analysis of the drugs. The criteria for obtaining maximum precision[16] by this method were calculated and found to be outside the range of 0.1-2. In absorbance ratio method (method II), the primary requirement for developing a method for analysis is that the entire spectra should follow the Beer's law at all the wavelengths[16], which was fulfilled in case of both these drugs. The two wavelengths used for the analysis of both drugs were 290.8 nm (isoabsorptive point) and 271.4 nm (λ-max of CPX).

The validation parameters were studied at all the three wavelengths for both the methods. Accuracy was determined by calculating the recovery, and the mean was determined. Precision was calculated as repeatability (standard deviation and relative standard deviation) and inter- and intra-day variation (%CV) for both the drugs. Both the methods were successfully used to determine the amounts of CPX and ORN present in the tablets. The results obtained were in good agreement with the corresponding labelled amount (Table 1). By observing the validation parameters, both the methods were found to be simple, specific, accurate and precise. Hence both the methods can be employed for the routine analysis of these two drugs in combinations.

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