Spectrophotometric Determination of Fluoroquinolone Dosage Forms by Charge Transfer Complexation

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A spectrophotometric method is described for the determination of several fluroquinolones as bulk drug and in dosage form by complexation of the drug with chloranilic acid. Job's method revealed a 1:1 complexation between the drug and chloranilic acid. Quantitative recoveries were obtained from bulk drug as well as from commercially available dosage forms.

Fluoroquinolones have found extensive use in therapy because of their wide antibacterial spectrum and are effective against both gram positive and gram negative bacteria[1,2].For ciprofloxacin (CFLX) USP[3] and BP[4] describe an HPLC method and for norfloxacin (NFLX) assay, a potentiometric titration procedure using 0.1 N perchloric acid is given (USP)[5]. A polarographic method for the analysis of enoxacin (ENX)[6] and complexation with ammonium reinectate[7] method for lomefloxacin (LMFX) have been reported. For CFLX in pharmaceutical formulations HPLC method[8] and spectrophotometric method using 1% $FeCl_3$[9], p-benzoquinone[10] and 3-methyl benzothiazoline-2-one[11] has been described. A colorimetric determination using 1% $FeCl_3$[12] and ion pair colorimetric method[13] for NFLX tablets and capsules respectively, has also been reported. For ENX tablets UV spectrometric method[14] has been described and for LMX tablets HPLC method[15] has been reported. The assay procedure for CFLX, NFLX, ENX and LMFX tablets and CFLX ophthalmic solution is based upon the extraction of drug and subsequent determination of its absorbance. In the present study an attempt has been made to develop a simple and sensitive spectrophotometric method for the assay of various fluoroquinolones viz. CFLX, NFLX, ENX and LMFX as bulk drug and in dosage froms based on the interaction of drug with chloranitic acid to form a 1:1 purple-violet complex.

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CFLX, CFLX HCL and LMFX were gift from Max Laboratories (New Delhi) , ENX (Parke-Davis, Germany), LMFX and LMFX. HCl pure drug powder was obtained from Systopic laboratories (Faridabad). CFLX eye drops (CIFRAN^R eye drops, Ranbaxy), CFLX(CIFRAN^R, Ranbaxy), NFLX (NORFLOX^R, Cipla), ENX (PENETREX^n, Parke Davis) and LMX (LOMEF^R, Torrent) tablets were obtained commercially. P-chloranilic acid and other chemicals used were of analyical reagent grade. Chloranilic acid 0.005 M and 0.0025 M solutions were prepared by dissolving p-chloranilic acid in 1,4 - dioxane and stored in a dry, amber colored glass bottle in a dark place and is stable up to 6 weeks. CFLX, NFLX and ENX solutions 0.005 M each were prepared 1, 4-dioxane. Solutions of CFLX. HCl and ENX. Solutions 0.005 M each were prepared in 1,4 dioxane. Solutions of CFLX. HCl and LMFX HCl. HCl 0.25% w/v were prepared by first dissolving the weighed quantity of salt in water in a separating funnel, alkalinizing it with dilute ammonia and extracting the liberated base with chloroform[16,17].

Spectrophotometric measurements were done on Bausch and Lomb Spectronic-21 or on Hitachi Model 150 double beam spectrophotometer using 1 cm^2 silica cells. For the analysis of opthalmic solutions, the contents of three botles containing 3 ml each of 0.3% w/v CFLX. HCl were pooled together. Six ml of the pooled solution was transfered into a 100 ml separating funnel containing about 5 ml water. After alkalinizing with dilute ammonia, the liberated base was extracted with three 3-ml each quantity

of chloroform and each extract was transferred to a 10 ml volumetric flask and the volume made upto mark with chloroform.

For the analysis of five tablets were weighed and crushed to a fine powder in a glass pestle and mortar. An aliquot of the powder equivalent to 250 mg of CFLX, 400 mg of NFLX, 400 mg of ENX and 400 mg of LMFX was weighed and transferred to a 25 ml volumetric flask. In case of CFLX.HCl and LMFX.HCl tablets, the tablet powder was suspended in water, alkalinized with dilute ammonia and liberated base was extracted with chloroform. For NFLX and ENX tablets, 1,4-dioxane was used as solvent. The flask was shaken and allowed to stand for 1 h. The clear supernatant solution was used for assay.

For analysis, an aliquot of the assay solution was transferred to a 10 ml volumetric flask and 2 ml of chloranilic acid solution (0.005 M or 0.0025 M) was added and the volume was made to 10 ml with 1,4-dioxane. The absorbance was measured at the corresponding λmax (530 nm for CFLX and LMFX and 540 nm for NFLX and ENX) against a blank solution prepared similarly but without any drug. The concentration was read from the calibration curve and percentage recovery was calculated.

In 1,4-dioxane/chloroform medium, the fluroquinolone drugs under study reacted instantaneously with chloranilic acid to give a purple color indicating the formation of a complex. Chloranilic acid exists in three forms[16], the neutral yellow H_2A at very low pH, the dark voilet HA^- which is most stable at pH 2,and the pale violet A^{2-},stable at high pH. It gives purple colour in water, acetonitrile, dimethylformamide and ammonia. As the reaction products in nonaqueous medium are purple it can be concluded that HA^- interacts with the fluoroquinolones drug to form complexes. Both continuous variation and molar ratio methods showed that a 1:1 complex is being formed as expected from the single donor center in the drugs. Using Benesi-Hildebrandt[18] equation the molar absorptivities and association constants for the complex were calculated (Table 1). Plots of absorbance vs concentration were linear in the concentration range shown in Table 1.

Various dosage froms of the drugs were assayed by the proposed method. The recovery values as shown in the Table 2 are based on the amount found and that calculated to be present according to the labelled strength of the product. Pharmaceutical excipients likely to be present in the dosage form e.g. starch, lactose, talc and magnesium stearate in tablets and buffers, preservatives

TABLE 1: PHYSICOCHEMICAL PARAMETERS FOR COMPLEXES

Drug chloranilic acid complex	Molar absorptivity	Association constant (K)	Concentration range for Beer's Plot (mg/ml)	Regression coefficient (r)
Ciprofloxacin	1.3×10^3	7.5×10^2	0.01-0.18	0.9976
Norloxacin	1.3×10^4	6.2×10^3	0.03-0.30	0.9992
Enoxacin	5.5×10^3	1.2×10^2	0.03-0.32	0.9974
Lomefloxacin	1.35×10^3	3.0×10^2	0.01-0.19	0.9994

TABLE 2: ANALYSIS OF BULK DRUG AND DOSAGE FORMS BY PROPOSED METHOD

Bulk drug	Recovery %*	Dosage form	Recovery %!
CFLX	98.17(±1.63)	CFLX tablets	99.16(±2.08)
CFLX.HCl	98.46(±1.64)	NFLX tablets	98.35(±2.43)
NFLX	99.10(±1.48)	ENX tablets	98.87(±1.26)
ENX	97.84(±1.47)	LMX tablets	98.54(±1.37)
LMX.HCl	97.50(±1.43)	CFLX eye drops	97.89(±1.38)

*Average of minimum 4 determinations (±SD.), ! Recovery based on label claim (±S. D.)

in eye drops exhibited no interference during the assay procedure.

The proposed procedure is useful in the routine analysis and quality control of these drugs.

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