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Direct and Derivative Spectrophotometric Estimation of Moxifloxacin Hydrochloride by Chelation with Ruthenium (Ru III) Ions

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A B S T R A C T

A simple ,sensitive and accurate spectrophotometric method was described for the determination of Moxifloxacin hydrochloride (MFX) a broad spectrum flouroquinolone anti bacterial either in pure form or in the tablet .The method is based on chelate formation between MFX and ruthenium(Ru III) in aqueous media at a PH 8 in presence of surfactant . The complex showed an absorption maximum at 367nm for zero order, Ist derivative at 437 nm and Second derivative at 466 nm respectively with apparent molar absorpitivity of 3.66x10 ^{4} L-M^{-1}Cm^{-1}and sandell's sensitivity of 0.055 µg/cm^{2} respectively. The solution of the complex obeyed beer's law in the concentration range of 0.5-5 µg/ml for zero order,5 to50 µg/ml for Ist order and 1to 25 µg/ml for 2nd order respectively. The limit of detection and Limit of quantification were calculated and RSD were calculated. The chelate composition between MFX and Ru(III) ion was found to be 1:1 ratio determined by Job's continuous method and by Molar ratio method. The proposed method was applied for the determination of MFX in tablets without interference from common excipients .The results obtained by the application of this procedure showed percentage recoveries were 100±0.1463 for zero order, 100.2±0.1065 for Ist order and 100.3±0.1589 for 2nd order respectively.

Keywords: Flouroquinolone, Moxifloxacin Hydrochloride, Chelate, Aqueous media, Spectrophotometric, Pharmaceutical formulation

A R T I C L E I N F O

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1. Introduction

Moxifloxacin (MFX) chemically 1-cyclopropyl-7-((s, s)-2,8- diazabicyclo(4.3.0)non-8-yl)-6-Fluoro-8-methoxy-1,4-dihydro-4-oxo-3quinoline carboxylic acid, A new flouro-quinolone antibacterial compound Moxifloxacin can be used to treat respiratory infections, including acute sinusitis, acute exacerbations of chronic bronchitis, and community-acquired pneumonia, as well as skin and skin structure infections. Moxifloxacin is used as a second-line agent in tuberculosis (TB) and may potentially have benefits in reducing treatment duration from its current six month to four months. In ophthalmology, Moxifloxacin is available in the form of eye drops, to treat conjunctival infections caused by susceptible bacteria and to prevent infection following eye surgeries [1-2]. Only few methods for the analysis of MFX are available which include derivative spectroscopy in micellar medium, simple UV spectrophotometric methods [4-5], HPLC methods, HPTLC, LC/MS/MS, Differential pulse polarography, capillary electrophoresis [17]. Complexes of drugs with Ruthenium (III) have also been studied such as with antitumour drugs. The purpose of this present study was to develop direct and derivative spectrophotometric, stability indicating procedure for the selective determination of MFX by chelation with Ru(III) ions, to develop procedure capable of quantitation, describe and validate the structural ability of MFX to chelate with Ru(III). The methods based on chelation of drug with ruthenium have been studied and prospective work will be the study using proposed chelation procedures by direct and derivative spectroscopy, which not have been previously studied [18-20]. .

2. Experimental

Apparatus: All absorption Spectra were made using Schimadzu-160 A U.V-VIS Spectrophotometer equipped with 10mm matched Quartz cells

Materials and reagents: Ruthenium Chloride ($1X10^{-2}M$): The standard ruthenium (III) solution was prepared by dissolving 0.2076 g of $RuCl_3$ (A.R LOBA) in minimum amount of dilute hydrochloric acid and diluted up to the mark using distilled water in a 100-ml standard flask. The stock solution was standardized spectrophotometrically[21]. MFX $1x10^{-3}M$ solution was prepared by dissolving 43.8mg of MFX into a 100ml volumetric flask. It was dissolved and diluted upto the mark using double distilled water and sodium dodecylsulphate (1.2 ml of 0.1M) to get $1x10^{-3}M$ concentration of MFX solution.

Chelation of Mfx with Ru(III): The following procedure was adopted for measuring the absorption spectra of complex (metal + drug) in aqueous medium. In a 10-ml standard flask, 1ml of $1x10^{-3}M$ MFX stock solution the metal complex was prepared by taking 3 ml of buffer, suitable volume of surfactant, suitably concentration of Ruthenium ion metal solution (usually 10- 15 fold molar excess to drug) solutions. The contents were diluted up to the mark with distilled water and the absorbance of the complex was measured against the reagent blank prepared identically. A plot between absorbance and the wavelength was plotted from which the analytical wavelength was selected. The ƛ-max for the Chelate at Zero order is 367 nm, first order derivative is obtained at 437 nm and second order derivative at 466 nm Fig 1- Fig 3.

Procedure for dosage form:

An accurately weighed amount of finely powdered tablet equivalent to 100mg of drug was dissolved in about 10ml of distilled water and transferred in to 100ml of calibrated volumetric flask and 1.2 ml of 0.1 M sodium dodecyl sulphate was added , after 15minutes mechanical shaking was filtered into a 100ml of calibrated volumetric flask through Whatmann no:41filter paper ,diluted to 100ml with distilled water and the same procedure was followed as described above

Optimum conditions

Effect of pH: To arrive the optimum pH required for achieving the maximum and constant absorbance, the effect of pH on the absorbance of the Ruthenium(III)–MFX complex was studied by employing in a set of 10-ml standard flasks, 3 ml of buffer (different pH values 1.0 to 11.0) solution, constant amount of drug and metal ion(usually 10- 15 fold molar excess to drug) solution were taken, made up to the mark with distilled water. The absorbance of each solution (metal complex) was measured at a selected wavelength (λ_{max}) against corresponding reagent blank prepared accordingly. A plot was made between absorbance and pH from which the working pH was selected. The complex shows maximum and constant absorbance in the pH range 8.0. Therefore, buffer solution having pH 8.0 was chosen for further studies. Fig 4.

Effect of reagent concentration:

To 1ml of $1x10^{-3}$ M MFX stock solution, aliquots of 0.5to 3ml of $1x10^{-2}$M reagent solution was added into 10 ml Volumetric flask and make upto the volume to 10ml with distilled water and the absorbance values at 367nm Investigation of metal ion concentration revealed that only ten-fold molar excess of reagent was sufficient for optimum and maximum colour intensity of the chelate of MFX using 43.8µg/ml concentration Fig no:5.

Effect of time:

The absorbance of MFX-Ru(III) complex was measured at different time intervals to ascertain the time stability of the complex. The full colour development of the complex remains constant for twenty four hours.Then the absorbance of MFX-Ru(III) complex was measured at 367 nm.

Determination of chelate stability and composition

The composition of the chelate [21-26] of MFX with Ru(III) ion used was studied by Job's continuous method and Molar ratio method .The chelate of 1:1 ratio was obtained between MFX and Ru(III).The stability constants of formed chelate were calculated and the values of Log β was 7.26.The results were tabulated in Table no:1.

Linearity range and quantification procedure

Beer's law was found to be obeyed in the concentration range of 0.5to 5µg/ml for Zero order,5 to 50µg/ml for Ist

order derivative and 1to 25µg/ml for 2nd order derivative .A(1%,1Cm) was calculated .The results were tabulated in Table no:2.

Assay of dosage form [27-35]

An accurately weighed amount of finely powdered tablet equivalent to 100mg of drug was dissolved in about 10ml of distilled water and transferred in to 100ml of calibrated volumetric flask, 1.2 ml of 0.1 M sodium dodecyl sulfate was added and after 15minutes of mechanical shaking was filtered into a 100ml of calibrated volumetric flask through Whatmann no:41 filter paper and was diluted to 100ml with distilled water and the same procedure was followed as described above. The results were tabulated in Table no:3.

Interference study

Potential interference by the excipients in the dosage form was also studied, samples were prepared by mixing fixed amounts of common excipients such as lactose, Micro crystalline cellulose, Talc, Magnesium sterate and Starch. The good percentage recoveries were obtained indicating no interference was observed .The results were tabulated in Table no:4.

3. Results and Discussion

The linearity range of MFX-Ru(III) chelate covered over a range of 0.5-5 μg /ml of drug with A(1%,1cm)equals to $3.66x10^4$ L $Mole^{-1}cm^{-1}$.The drug chelate absorbance were plotted against the corresponding concentrations . Data were fitted to the equation Y=a+bx, where Y is the absorbance at relevant maximum is the Drug concentration in mcg/ml; b is the slope and a is the intercept of the calibration curve. The correlation coefficient is 0.999 indicating exact linearities. The Accuracy of the proposed procedure was 100%. Repeatability and reproducibility were evaluated. The limit of detection does not exceed 0.33 μg /ml where as limit of quantification was between 1.0 μg /ml. Proposed procedure for MFX is a stability indicating one which can be used for the determination without interference with the excipients. The drug being soluble in presence of surfactant in aqueous medium and considered more selective drug to chelate with Ru(III) ion, in addition, the derivative spectra normally contain more apparent spectral details than the normal spectra, more selective and sensitive in eliminating the background interference of complex matrix in resolving individual drug ,drug additives and drug decomposition both interfered.

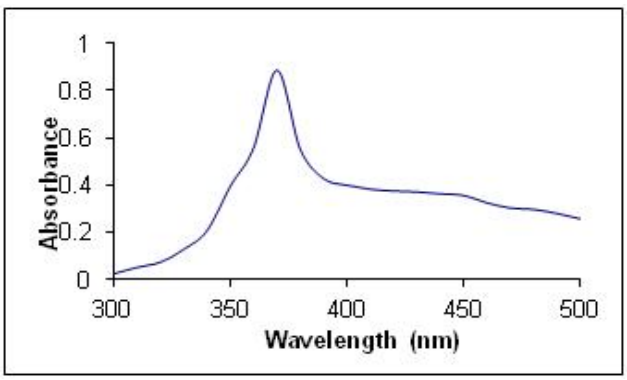

Figure1: Absorption spectra of 43.8µg/ml MFX complex with $1x10^{-2}$M Ru(III)

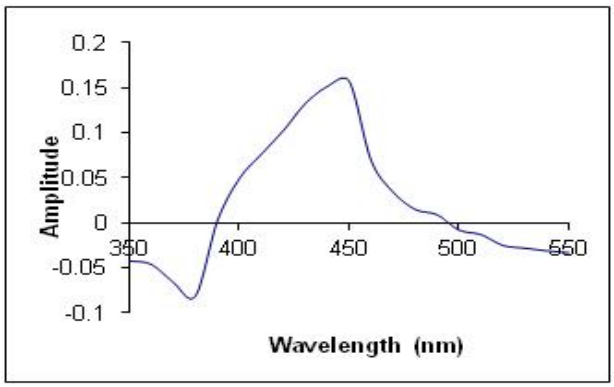

Figure 2: First order derivative spectra of43.8µg/ml MFX complex with $1x10^{-2}$M Ru (III)

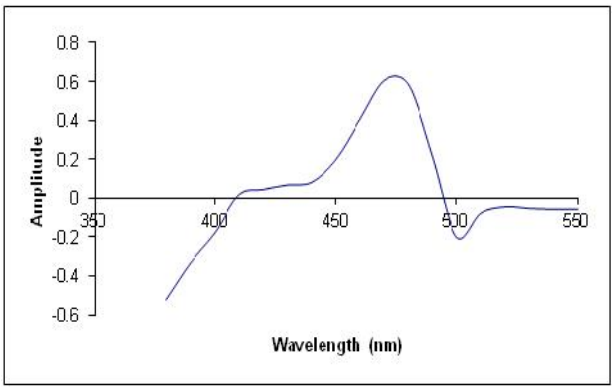

Figure 3: Second order derivative spectra of of43.8µg/ml MFX complex with $1x10^{-2}$M Ru(III)

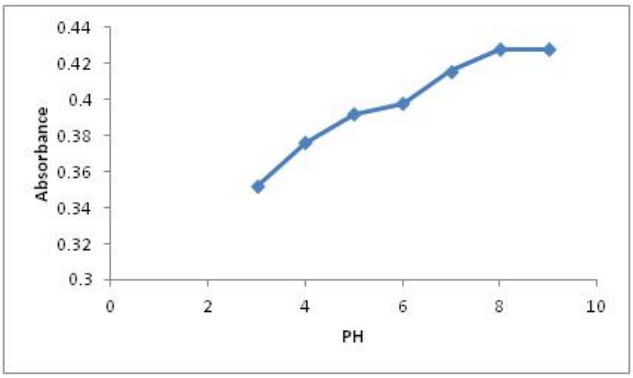

Figure 4: Effect of P_H on the formation of MFX complex with Ru (III) ion

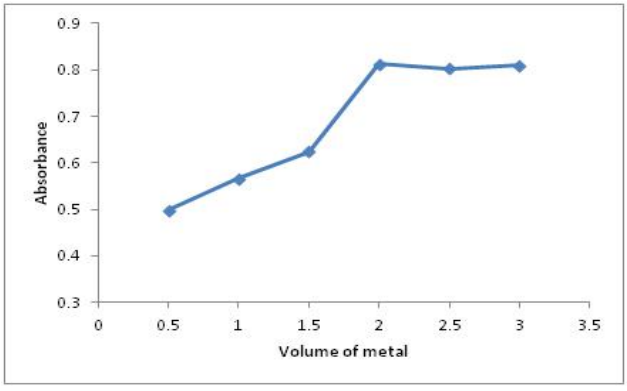

Figure 5: Effect of reagent concentration on the formation of MFX complex with Ru (III) ion

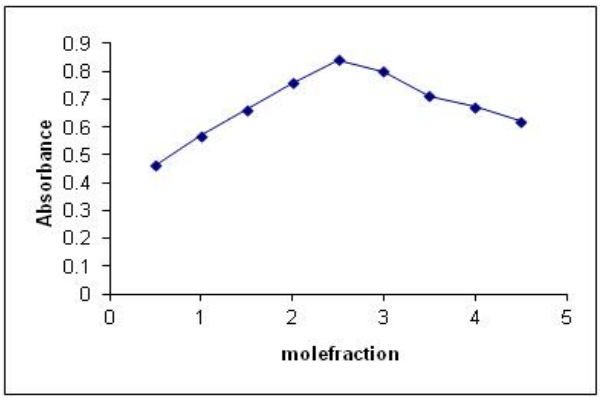

Figure 6: Job's method for MFX complex with Ru (III) ion at 367nm.

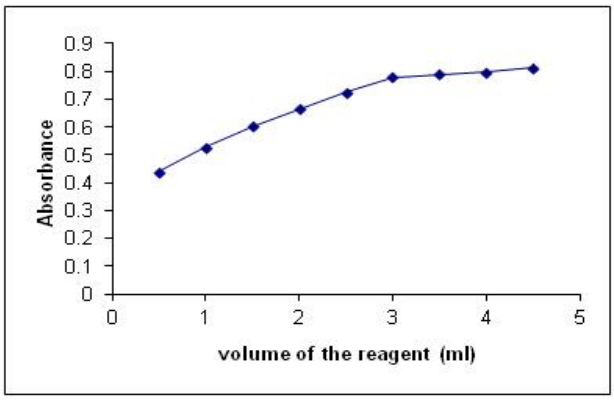

Figure 7: Mole ratio method for MFX complex with Ru (III) ion at 367nm.

Table 1: Stability constants of Moxifloxacin hydrochloride chelate with ruthenium ion by Job's method.

Parameters	MFX-Ru(III) λmax at 367nm
Total molar conc	$1x10^{-5}$M
N	2.303
β*	$18.63x10^{6}$
Logβ	7.26

Table 2: Results of validation

Parameter	MFX-Ru(III) 367nm	MFX-Ru(III) Ist derivative	MFX-Ru(III) 2nd derivative
Linearity range (µg/ml)	0.5-5	5-50	1-25
LOD(mcg/ml)	0.33	0.6	0.49
LOQ(mcg/ml)	1.0	1.84	1.5
Slope	0.011	0.012	0.027
Intercept	0.184	0.009	0.019
Correlation coefficient	0.999	0.999	0.999
Accuracy	100.0	100.2	100.3
Repeatability(n=6)	0.1463	0.1065	0.1589

Table 3: Results of the determination of MFX by the proposed method in their dosage form

Dosage Form	MFX-Ru(III) At 367nm	MFX-Ru(III) At 437	MFX-Ru(III) At 466	LIMIT
Tablet 1	100.03±0.1105 N=6	100.20±0.1065 N=6	100.30±0.1209 N=6	The Assay of Moxifloxacin Hydrochloride tablets should be within 98%-102%
Tablet 2	100.01±0.1213 N=6	100.20±0.1210 N=6	100.30±0.1339 N=6	

Table 4: Determination of Moxifloxacin in presence of common excipients by the proposed method

Excipient	Recovery ±RSD At 367nm	Recovery±RSD 1st derivative At437nm	Recovery±RSD 2nd derivative at 466nm
Lactose(10mg)	100.03±0.0815	100.13±0.1245	100.30±0.1101
Talc(10mg)	100.05±0.0956	100.20±0.1372	100.30±0.1209
Magnesium sterate(10mg)	100.10±0.0999	100.20±0.1065	100.30±0.1154
Starch(10mg)	100.00±0.0816	100.20±0.0998	100.25±0.1603
Microcrystalline cellulose	100.10±0.0815	100. 10±0.1211	100.30±0.0814

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