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DIRECT AND DERIVATIVE SPECTROPHOTOMETRIC ESTIMATION OF GEMIFLOXACIN BY CHELATION WITH PALLADIUM(II) ION

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ABSTRACT

A simple ,sensitive and accurate spectrophotometric method was described for the determination of Gemifloxacin mesylate (GFX) a broad spectrum flouroquinolone anti bacterial either in pure form or in the tablet .The method is based on chelate formation between GFX and Palladium (Pd II) in aqueous media. The complex showed an absorption maximum at 430nm,Ist derivative at 480nm and Second derivative at 500nm respectively with apparent molar absorpitivities of $1.365x10^4$ $L\text{-}M^{-1}Cm^{-1}$, $9.37x10^4$ $L\text{-}M^{-1}Cm^{-1}$ for Ist order derivative, $1.59X10LM^{-1}Cm^{-1}$ for 2nd order derivative respectively. The solution of the complex obeyed beer's law in the concentration range of 2to 14 µg/ml for zero order,1 to 10 µg/ml for Ist order and 1to 15 µg/ml for 2nd order respectively. The limit of detection and Limit of quantification were calculated and RSD were less than 0.153.The chelate composition between GFX and Pd(II) 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 GFX in tablets without interference from common excipients .The results obtained by the application of this procedure showed percentage recoveries were 99.8±0.153 for zero order , 100.02±0.177 for Ist order and 100.045±0.139 for 2nd order respectively.

Key words: Gemifloxacin mesylate, Chelate, Spectrophotometric , Pharmaceutical formulation.

INTRODUCTION

Gemifloxacin (GMF) chemically R,S-7-(3 amino methyl 4- syn methoxyimino-1pyrrolidinyl)-1cyclopropyl-6-flouro1,4,dihydro 4- oxo-1,8 napthyridine-3-carboxylic acid methane- sulphonate[1-3] is a new flouroquinolone antibacterial compound with enhanced affinity for bacterial topoisomerase-IV and is being used for the treatment of respiratory and urinary tract infections.[4-6] Literature review revealed few analytical methods for the determination of GMF include HPLC, electrophoresis, uv-spectrophotometry concerning visible spectrophotometry very few methods have been reported and no derivative spectrophotometry has been reported ,hence sensitive and accurate ,direct, derivative spectrophotometric method has been viewed[7-10]. The purpose for this present study was to develop direct and derivative spectrophotometric, stability indicating procedure for the selective determination of GFX mesylate by chelation with Pd(II)ion, to develop procedure capable of quantitation and describe and validate the structural ability of GFX to chelate with Pd(II),which is used as a catalyst in the preparation of wide range of drugs ,essentially present in biological fluids which not have been previously studied.

EXPERIMENTAL

Apparatus

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

Materials and Reagents:

Palladium chloride ($Pdcl_2$)[11-16] $1x10^{-2}$M solution in distilled water[17] was prepared.

GFX $1x10^{-3}$M solution was prepared by dissolving 38.9mg in 100ml of distilled water and GFX 0.1 mg//ml in distilled water was prepared.GFX solutions were freshly prepared and stable for 24 hours at room temperature.
Gemez (Majesta, a division of Glenmark Pharmaceuticals Ltd., Mumbai.) Labelled to contain 320 mg of Gemifloxacin mesylate. G-cin (Hetero Drugs Ltd., Hyderabad) Labelled to contain 320 mg of Gemifloxacin mesylate were used.

Chelation of GFX with Pd(II)
To a 10 ml volumetric flask, transferred 1ml of $1x10^{-3}$M GFX stock solution and 1ml of $1x10^{-2}$M Pd(II)Cl_2 and shaken vigorously for 5 minutes. The resulted yellow color chelate was scanned in between 200-800nm against a blank. The ƛ-max for the Chelate at Zero order is 430nm, first order derivative is obtained at 480 nm and second order derivative at 500 nm. The formed chelate structure was shown in 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 after 15minutes mechanical shaking was filtered into a 100ml of calibrated volumetric flask through Whatmann no: 41filter paper and was diluted to 100ml with distilled water and the same procedure was followed as described above

Optimum conditions
Effect of pH: At acidic PH there was disappearance of the Yellow color chelate and at basic PH there was formation of turbidity.
Effect of heating: There was no change in the absorbance value after heating up to 60 ^{0}C for 30 minutes.
Effect of reagent concentration: To 1ml of 1x10-^{3} M GFX stock solution, aliquots of 0.2to 4ml 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 430nm,Ist order derivative at 480nm and 2nd order derivative at 500nm were taken. Investigation of metal ion concentration revealed that 1ml of $1x10^{-2}$ M Pd(II) solution was sufficient for optimum and maximum colour intensity of the chelate of GFX using 40µg/ml concentration Fig no:4.
Effect of time:
The absorbance values of chelate of GFX and Pd(II) ion were recorded for every 10minute for 24 hours and there was no change in the absorbance values.

Determination of chelate stability and composition
The composition of the chelate[18-23] of GFX with Pd(II) ion used was studied by Job's continuous method and Molar ratio method .The chelate of 1:1 ratio was obtained between GFX and Pd(II) .The stability constants of formed chelate were calculated and the values of Log β was 6.699.The results were tabulated in Table-1.

Linearity range and quantification procedure
Beer's law was found to be obeyed in the concentration range of 2to 14µg/ml for Zero order,1 to 10µg/ml for Ist order derivative and 1to 15µg/ml for 2nd order derivative .A(1%,1Cm) was calculated .The results were tabulated in Table-2.

Assay of dosage form[24-32]
An accurately weighed amount of finely powdered tablet equivalent to 100mg of drug was dissolved in about 10ml of distilled water and transfered in to 100ml of calibrated volumetric flask 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-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-4.

RESULTS AND DISCUSSIONS

The linearity range of GFX and Pd(II) chelate covered over a range of 2to 14µg/ml to 1to20µg/ml of GFX and A(1%,1Cm) were $1.365x10^{4}$ for Zero order,$9.37x10^{4}$ for Ist order and $1.59 x10^{5}$ LM^{-1} cm^{-1} for 2^{nd} order respectively. The drug chelate absorbances were plotted against the corresponding concentrations. The data fitted to the equation Y=a+bx, where Y is absorbance at relevant maxima, X is the drug concentration in µg/ml , b is the slope and a is the Intercept of the calibration curve. The regression parameters were shown in Table no:2. The correlation Coefficient ranged from 0.998 to 0.999 indicating exact linearity. The accuracy of the proposed procedure were 99.8 to100.05%.Repeatability and reproducibility were evaluated and RSD % ranged from 0.011to 0.1507.The limit of detection does not exceed 0.6 and whereas limit of Quantification was between1.79 to 2.39 . Proposed procedure for GFX is a stability indicating one which can be used for the determination without interference with the dosage form. The drug being water soluble and considered more selective in determining the structure ability of the drug to chelate with Pd(II) 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.

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Table-1: Stability constants of Gemifloxacin mesylate chelate with metal ion in distilled water by Job's method

Parameters	GFX-Pd(II) λmax at 430nm
Total molar conc	$1x10^{-5}$M
N	2.303
A/Aex	0.91
β*	$4.993x10^{6}$
Logβ	6.699

Table-2: Results of validation Gemifloxacin mesylate chelate with metal ion in distilled water by the proposed method

Parameter	GFX-Pd(II) 430nm	GFX-Pd(II) Ist derivative 480nm	GFX-Pd(II) 2nd derivative 500nm
Linearity range(µg/ml)	2-20	1-10	1-15
LOD(mcg/ml)	0.8	0.75	0.6
LOQ(mcg/ml)	2.39	2.26	1.79
Slope	0.014	0.011	0.015
Intercept	0.001	0.001	0.003
Correlation coefficient	0.998	0.999	0.998
Accuracy	99.8	100.02	100.045
%RSD	0.1530	0.017713	0.01383

Table-3: Results of the determination of GF X by the proposed method in their dosage form compared with reference methods

	Recovery±%S.D				
	GFX-Pd(II) At430nm	GFX-Pd(II) At 480nm 1st derivative	GFX-Pd(II) At 500nm 2nd derivative	Reference methods [a,b]	
GEMEZ	99.8±0.1530 N=6	100.02±0.178 N=6	100.045±0.1384 N=6	99.89±0.48 N=6	99.99±0.39 N=6
G-CIN	99.8±0.1507 N=6	100.016±0.1106 N=6	100.04±0.1526 N=6		

a, b indicates utility of σ and π acceptors for the spectrophotometric determination of Gemifloxacin Mesylate in pharmaceutical formulation

Table-4: Determination of Gemifloxacin Mesylate in presence of common excipients

	Recovery[a] (%±S.D)		
Excipient	At 430nm	1st derivative at480nm	2nd derivative at 500nm
Lactose(10mg)	100.013±0.0149	100.0133±0.01795	100.023±0.02426
Talc(10mg)	100.013±0.0221	100.011±0.0146	100.026±0.02748
Magnesium sterate(10mg)	100.02±0.02034	100.02±0.0129	100.04±0.0175
Starch(10mg)	100±0.0911	100.02±0.01244	100.02±0.0273
Microcrystalline cellulose	100.02±0.013	100.026±0.0149	100.03±0.0173

a; Values are mean of six determinations.

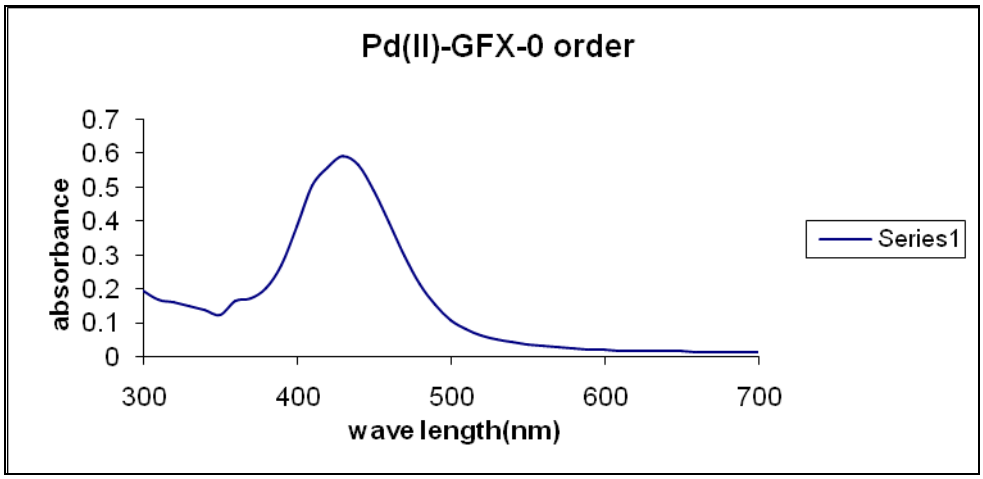

Fig.-1: Absorption spectra of 40µg/ml GFX complex with $1x10^{-2}$M Pd(II) ion solution

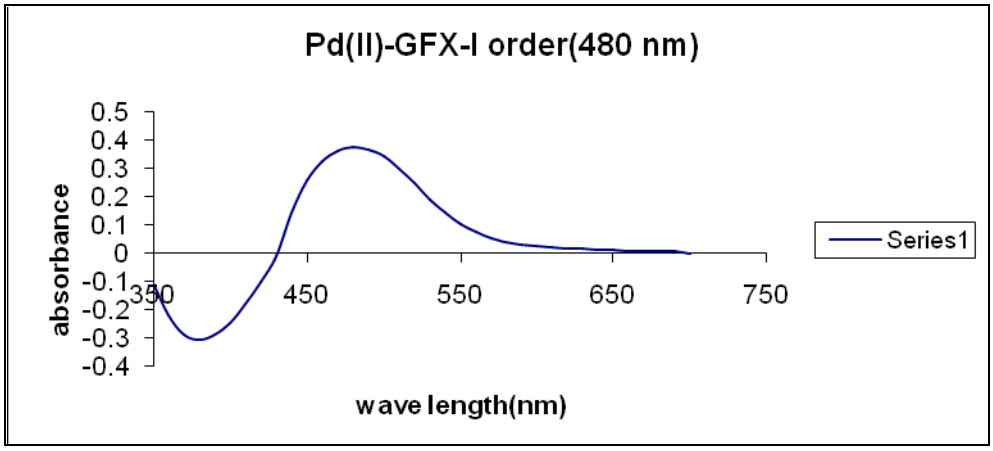

Fig.-2: First order derivative spectra of40µg/ml GFX complex with $1x10^{-2}$M Pd(II)ion solution

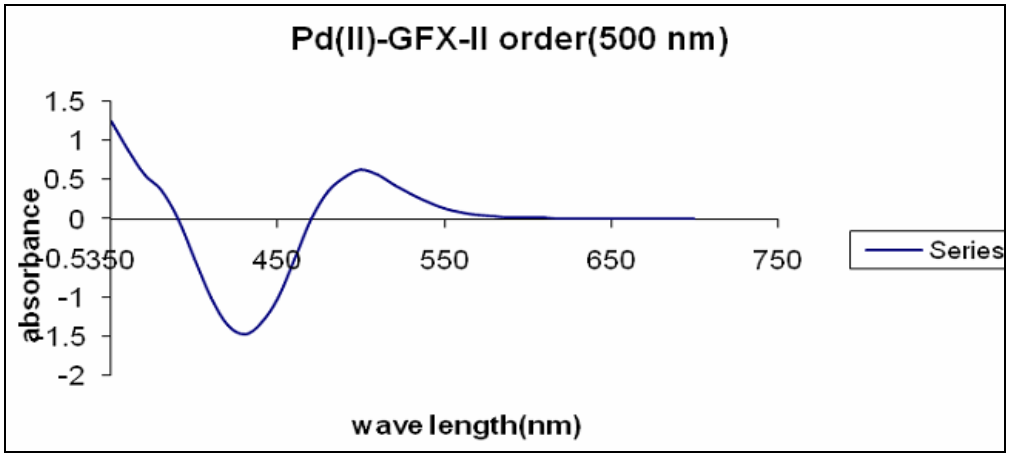

Fig.-3: Second order derivative spectra of of40µg/ml GFX complex with $1x10^{-2}$M Pd(II)ion solution

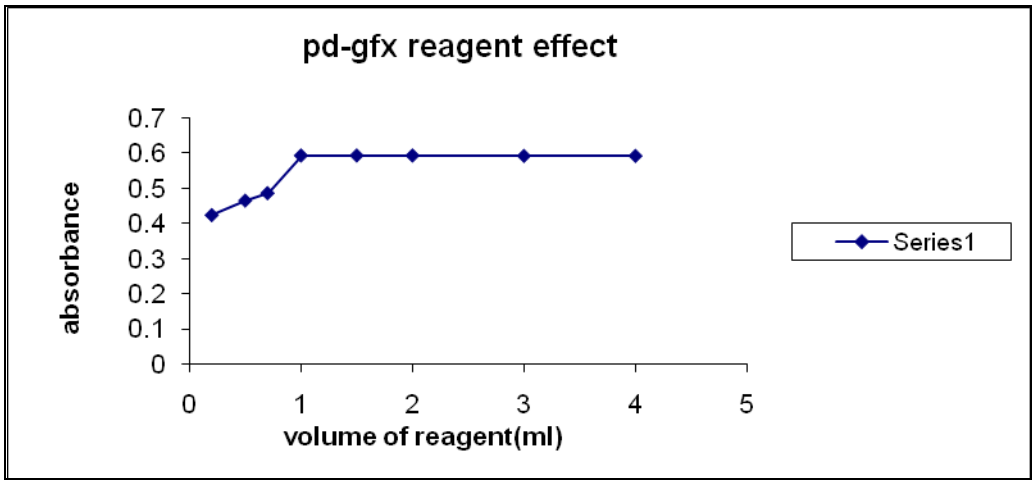

Fig.-4: Effect of Pd(II)ionsolution concentration ($1x10^{-2}$M) on the formation of GFX complex with Pd(II)ion

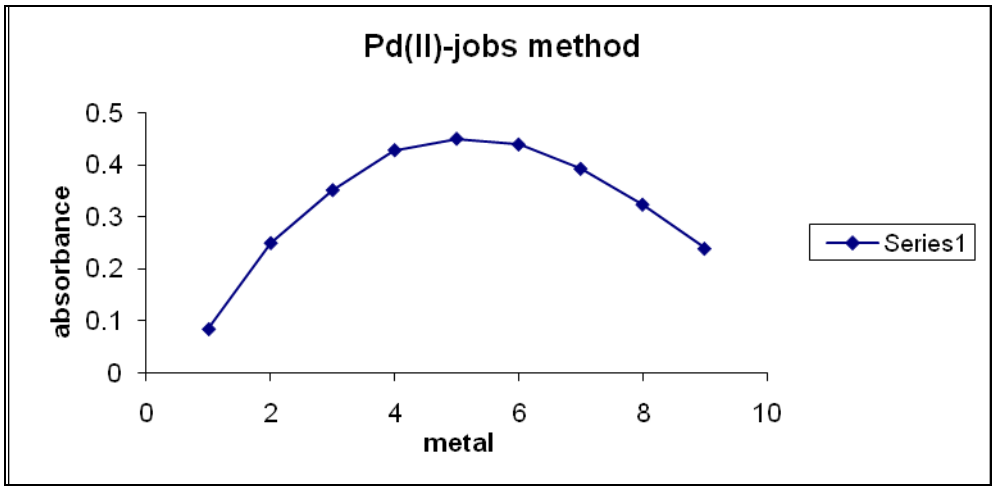

Fig.-5: Job,s method for GFX complex with Pd(II) ion at 430nm using $1x10^{-5}$M concentration.

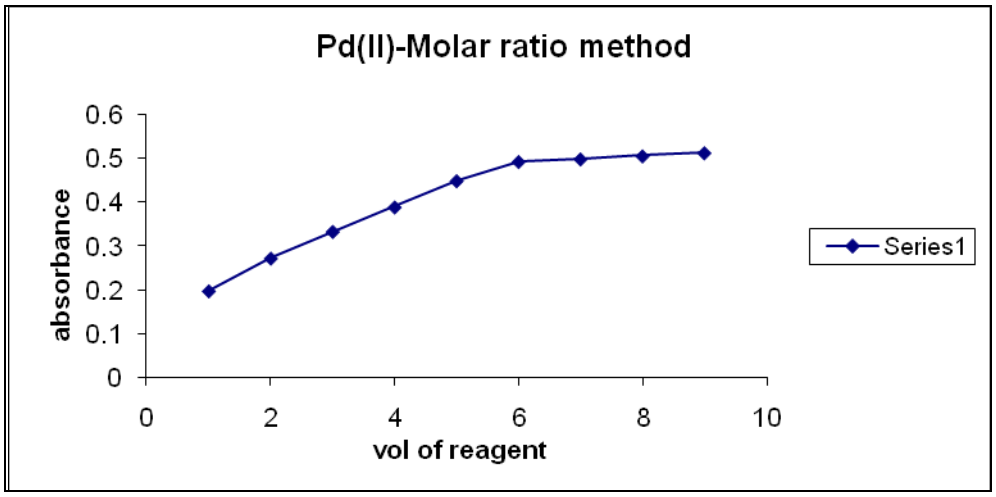

Fig.-6: Mole ratio method for GFX complex with Pd(II) ion at 430nm using $1x10^{-5}$M concentration.

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