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Spectrophotometric Estimation of Clarithromycin in Pharmaceutical Formulations

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Two simple and sensitive spectrophotometric methods A and B have been developed for the estimation of clarithromycin in pure and pharmaceutical dosage forms. Method A is based on the reaction of the drug with iron(III) and a subsequent reaction with potassium ferricyanide to yield a prussian blue coloured product with a maximum absorption at 740 nm. In method B, the drug forms a blue coloured complex with Folin-Ciocalteu reagent, showing maximum absorption at 775 nm. The methods obey Beer's law in the concentration range of 12.5–75.0 μg/mL (method A) and 250–125.0 μg/mL (method B). The common excipients used as additives in tablets do not interfere with the proposed methods. Analytical data for determination of the pure compound are presented together with the applications of the proposed methods to the analysis of some tablets. The methods have been statistically evaluated and are found to be precise and accurate.

Key words: Spectrophotometric, Estimation, Clarithromycin.

INTRODUCTION

Clarithromycin (CMN) is designated chemically as 6-methoxy erythromycin[1]. It is used in the treatment of streptococcal pharyngitis, community-acquired respiratory tract infections, skin and soft tissue infections and acute sinusitis. It is being currently evaluated for the treatment of some refractory infections in AIDS patients. The drug is official in USP.[2] Literature survey reveals the presence of a few analytical methods which include ion-pair HPLC,[3] capillary electrophoresis[4] and RP-HPLC[5,6] methods in biological fluids like gastric juice, plasma, serum and urine. Two HPLC[7,8] methods and one extractive spectrophotometric method[9] have been reported for the assay of CMN in various dosage forms and in bulk drugs.

The proposed methods are based on the formation of prussian blue coloured product with Fe(III) and potassium ferricyanide (Method A) with a maximum absorption at 740 nm and a blue coloured complex with Folin Ciocalteu reagent (method B) having maximum absorption at 775 nm.

EXPERIMENTAL

All the chemicals used were of analytical grade and all the solutions were prepared with double distilled water. Freshly prepared solutions were always used. Aqueous solutions of Fe(III) (S.D. Fine Chem) 0.9%, $K_3[Fe(CN)_6]$ (Loba) 1.0% , Folin Ciocalteu reagent (FCR) (Loba) 1 M and Na_2CO_3 (S.D. Fine Chem) 10% and 2% were prepared. A Systronics model 117 UV-Visible spectrophotometer with 1 cm matched quartz cells was used for all the absorbance measurements.

Preparation of standard drug solution

100 mg of the CMN was accurately weighed and dissolved in 100 mL of methanol in a standard volumetric flask to obtain a stock solution of 1 mg/mL. This solution was further diluted with distilled water to get a working standard solution of 500 μg/mL.

Assay procedures

Method A: Aliquots of the working standard solution of CMN ranging from 0.25–1.25 mL were transferred into a series of 10 mL graduated test tubes. Then 0.5 mL of Fe(III) and 1.0 mL of $K_3[Fe(CN)_6]$ were added and the volume made up to 10 mL with distilled water and kept aside for 15 min at room temperature. The absorbance of the coloured species formed was measured at 740 nm against a reagent blank. The amount of CMN in the sample was computed from Beer-Lambert plot.

Method B: To a series of 10 mL volumetric flasks, volumes of standard drug solution ranging from 0.5 to 2.5 mL were transferred. To that 0.5 mL of Na_2CO_3 (10%) and 1.0 mL of Folin ciocalteu reagent (FCR) were added; then the volume was made up to 10 mL with 2% Na_2CO_3. The flasks were kept aside for 15 min at room temperature for complete colour development. The absorbance of each solution was measured at 775 nm against a reagent blank. The amount of CMN in the sample was computed from its calibration curve.

Determination of CMN in pharmaceutical formulations

20 Tablets were accurately weighed and an amount of tablet powder equivalent to 100 mg of the CMN was transferred into a 100 mL volumetric flask and the volume was made up with methanol and filtered. Appropriate aliquots of the drug solution were taken and the assay procedures were followed for analysis of drug content. The results of analysis are given in Table-2.

RESULTS AND DISCUSSION

The optical characteristics such as Beer's law limits, Sandell's sensitivity, molar coefficient, per cent relative standard deviation, per cent range of error (0.05 to 0.01 confidence limits) were calculated for all the methods and the results are summarized in Table-1. The values obtained for the determination of CMN in several pharmaceutical formulations (tablets) by the proposed and reported methods are compared in Table-2. Interference studies revealed that the common excipients and other additives usually present in dosage form did not interfere in the proposed methods.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION DATA

Parameters	Method A	Method B
Beer's law limit (μg mL^{-1})	12.5–75.0	25.0–125.0
Molar absorptivity(l mol^{-1} cm^{-1})	1.166×10^4	4.368×10^3
Sandell's sensitivity (μg cm^{-2} absorbance unit/0.001)	0.06410	0.1712
Regression equation (Y)[a]:		
Slope (b)	0.01000	0.00580
Intercept (a)	0.06280	0.00048
Correlation coefficient (r)	0.99540	0.99990
Relative standard deviation (%)[b]	0.67570	0.50080
% Range of error[b]:		
(95% confidence limit)	0.56500	0.41880
(99% confidence limit)	0.83590	0.61960

[a]With respect to Y = a + bC, where C is concentration (μg mL^{-1}) and Y is absorbance.

[b]eight replicate samples.

TABLE-2
DETERMINATION OF CMN IN COMMERCIAL PHARMACEUTICAL FORMULATIONS

Sample (tablets)	Labelled amount (mg)	Amount obtained (mg)			Per cent recovery of the proposed method*	
		Reported method[9]	Proposed method			
			A	B	A	B
1	250	248.61	249.12	248.92	99.64	99.56
2	250	249.02	250.63	247.97	100.25	99.18
3	250	247.84	248.01	250.17	99.20	100.68

* Average of six determinations.

In method A, CMN reduces iron(III) salts in aqueous medium to form iron(II) salts, which subsequently chelate with ferricyanide to form prussian blue coloured product. In method B, the colour formation by FCR with CMN may be explained in the following manner based on the analogy[10]. With the reports of the earlier workers, the mixed acids in the FCR preparation involve the following chemical species.

$3H_2O{\cdot}P_2O_5{\cdot}13WO_3{\cdot}5MoO_3{\cdot}10H_2O$ and $3H_2O{\cdot}P_2O_5{\cdot}14WO_3{\cdot}4MoO_3{\cdot}10H_2O$.

CMN probably effects a reduction of 1, 2 or 3 oxygen atoms from tungstate and/or molybdate in FCR thereby producing one or more of the possible reduced species which have a characteristic intense blue colour. In conclusion the proposed methods are simple, sensitive, cheap, accurate and can be used for the routine quality control analysis CMN pharmaceutical preparations.

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