

NOTE

A Simple Spectrophotometric Method for the Determination of Clarithromycin from Pharmaceutical Preparation

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A spectroscopic method is developed for the estimation of clarithromycin in its dosage forms using 0.02 M solution (w/v) of 2-nitrobenzaldehyde in glacial acetic acid in presence of hydrochloric acid. 2-Nitrobenzaldehyde reagent forms a reddish pink coloured complex with the drug, which has an absorption maximum at 486 nm. The colour, so produced, is stable perfectly for about 30 min. Both drugs obey the Lambert-Beer's law in the concentration range employed for this method. The results of analysis have been validated statistically and by recovery study. The proposed method is simple, selective, rapid and economical for the determination of clarithromycin.

Clarithromycin is official in U.S.P¹-23 and is estimated by HPLC method,^{1,2} using phosphate buffer and methanol as a mobile phase at 40°C at 210 nm. Clarithromycin^{1,3-5} (C₃₈H₆₉NO₁₃) is structurally shown as (2R, 3S, 4S, 5R, 6R, 8R, 10R, 11R, 12S, 13R)-3-(2,6-dideoxy-3-c-3-o-dimethyl- α -L-ribohexo-pyranosyloxy) - 11,12 - dihydroxy-6-methoxy - 2,4,6,8,10,12 - hexamethyl - 9 - oxo- 5-(3,4,6 - trideoxy - 3 - dimethylamino - β - D-xylo-hexopyranosyloxy)pentadecane-13- olide.

Literature survey⁶⁻⁹ indicates that only HPLC is used for assay of these drugs. As the HPLC assay methods described in USP are tedious, time consuming and costly, we have developed simple colorimetric method for the estimation of clarithromycin in dosage form, since spectrophotometry is found to be much reliable, precise and accurate technique for the assay. Therefore, the present work deals with the spectrophotometric estimation of the clarithromycin in its dosage forms using 2-nitrobenzaldehyde (2-NBA) as a reagent. In the proposed method, clarithromycin in glacial acetic acid is hydrolysed by concentrated hydrochloric acid liberating a free amino group, which reacts with 2-nitrobenzaldehyde in glacial acetic acid to give Schiff's base with maximum absorbance at 486 nm.

All reagents and chemicals of AR grade were used. A Shimadzu UV/VIS recording spectrophotometer (model UV 2100) with 1 cm glass cells and wavelength accuracy of ± 0.5 nm were used for measurements of absorbance. Freshly prepared 0.02 M 2-nitrobenzaldehyde (w/v) reagent solution in glacial acetic acid were used for the determination.

Linearity: Standard solutions of Clarithromycin were prepared as 10, 15, 20, ... 45 µg/mL. Aliquots of 1 mL of each standard solution were transferred to a series of 10 mL volumetric flasks. To each of these 2 mL of 2-NBA reagent was added followed by 3 mL of concentrated hydrochloric acid. The mixtures were shaken well and left for 15 min aside for colour development. Immediately after this time period, reddish pink colour was developed. The volumes were then adjusted to 10 mL with glacial acetic acid and absorbances were measured against the reagent blank at the wavelength of maximum absorbance (486 nm) within 30 min after addition of concentrated hydrochloric acid. A plot of absorbance *v/s* drug concentration obeys Lambert's-Berr's Law in the concentration range of 10 to 45 µg/mL.

Working standard solution: Accurately weighed quantities of the clarithromycin were dissolved in little glacial acetic acid and finally diluted up to the mark with glacial acetic acid. The working standard solution of drug was prepared by diluting 10 mL of the stock solution to 50 mL using glacial acetic acid and further analysis was carried out as described under 'Linearity'.

Formulations

Preparation of tablet sample solution: Twenty tablets were crushed well separately and then the analytical sample subjected to fine powder, equivalent to 100 mg of drug, was weighed and dissolved in glacial acetic acid and the resulting solution was filtered and diluted to 100 mL. Working sample solution of drug was prepared by diluting 10 mL of this solution using glacial acetic acid for 50 mL, and further analysis was carried out as described under 'Linearity'.

The content of clarithromycin was then estimated from the standard curve.

Preparation of suspension sample solution: Sample equivalent to 100 mg of clarithromycin was dissolved in glacial acetic acid, degassed in ultrasonic cleaner and filtered through Whatman's filter paper No. 41. The filtrate was adjusted to 100 mL with glacial acetic acid and 10 mL of this solution was diluted to 50 mL with the same solvent to obtain working solution. The analysis was carried out in similar manner as described under 'Linearity'.

The content of clarithromycin was then estimated from the standard curve. The recovery study conducted by addition of different amounts of pure drugs to a pre-analysed tablet and suspension sample solution gave satisfactory recovery data, which is tabulated in Table-2.

Literature survey indicates that only HPLC is used for assay of these drugs. This proposed method was found to be simple, accurate and rapid for routine simultaneous estimation of clarithromycin in tablet formulation. The values of standard deviation were satisfactorily low and recovery was close to 100% indicating the reproducibility and accuracy of the method. Various marketed formulations of clarithromycin were analysed, utilising the proposed method. The excipients and the colouring matter in the formulation did not interfere with the proposed method. The proposed method can be employed for the routine determination of clarithromycin in pharmaceutical formulation. The results are given in Tables 1 and 2.

TABLE-1
RESULTS OF ANALYSIS OF COMMERCIAL TABLETS BY PRESENT METHOD

Product	Amount labelled (mg)	Amount found by the proposed method (mg)	Standard deviation
	CLA	CLA	CLA
<i>Tablets</i>			
T _a	100	100.48	±0.6268
T _b	250	250.03	±0.5178
<i>Suspensions</i>			
S _a	100	101.23	±0.7921
S _a	100	102.09	±0.9496

CLA = Clarithromycin, T = Tablet, S = Suspension.

*Mean of five readings

TABLE-2
RECOVERY STUDY DATA

Product	Amount label (mg)	Amount added (mg)	Amount found (mg)	% of recovery	Standard deviation
	CLA	CLA	CLA	CLA	CLA
<i>Tablets</i>					
T _a	100	20	120.30	100.95	±0.2752
T _b	100	40	141.28	103.21	±0.8929
<i>Suspensions</i>					
S _a	100	20	121.78	102.11	±0.6584
S _b	100	40	139.89	99.78	±0.7043

*Mean of five readings

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