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*NOTE*

# Extractive Spectrophotometric Determination of Cyclopentolate Hydrochloride

M.N. REDDY†, K.V. KANNA RAO,* T.K. MURTHY†, and M.D. REDDY†
*Roland Institute of Pharmaceutical Sciences*
*Ambapura,, Berhampur, (Orissa)-760 010, India*

Two simple and sensitive extractive spectrophotometric methods have been developed for the determination of cyclopentolate hydrochloride in bulk samples and in pharmaceutical preparations which are based on the formation of coloured complexes of the drug with reagents such as bromothymol blue and methyl orange. The ion pair complexes formed were quantitatively extracted into chloroform under the experimental conditions. All the variables have been optimized and the concentration measurements are reproducible within a relative standard derivation of 1.0% and recoveries are 99–101%.

Cyclopentolate hydrochloride (CP) is a tetriary amine antimuscarnic agent with actions similar to those of atropine[1]. It is used as eye drops to produce mydriasis and cycloplegia. Chemically, CP is 2-dimethylamino ethyl-1-hydroxy-α-phenyl cyclopentane acetate hydrochloride[2] and it is official in BP[3], USP[4], and NF[5]. The effects of pH, buffers, and temperature on the hydrolysis kinetics of cyclopentolate hydrochloride in alkaline solutions were studied using HPLC[6]. Literature survey revealed very few analytical methods such as non-aqueous titration[3] and HPCL[4,5].

Because there was no spectrophotometric method (visible region) reported for the determination of CP, the authors have made an attempt to establish two colorimetric methods for its estimation. The proposed extractive spectrophotometric methods are based on the formation of ion-pair complexes with bromothymol blue (BTB) or methyl orange (MO) and these complexes are quantitatively extracted into chloroform exhibiting maximum absorbances at 415 nm and 426 nm respectively.

0.2% Aqueous solutions of BTB (Loba Chemie) and 0.1% MO (BDH) were prepared in distilled water. Analytical grade chloroform was used in the investigation. All spectral measurements were made on Systronics UV-VIS spectrophotometer model 117 with 1-cm matched glass cells.

†Dept. of Pharmaceutical Sciences, Andhra Univeristy, Visakhapatnum-530 003, India.

**Standard and Sample Solutions:** The required quantity of standard CP or formulations (eye drops) was dissolved in distilled water to get a solution of 1 mg/mL and the stock solution was further diluted to get a working standard solution of 100 μg/mL for method A and 40 μg/mL for method B.

**Assay Procedures**

Aliquots of the CP solutions (0.5–3.0 mL, 100 μg/mL) for methods A or (0.5–4.0 mL, 40 μg/mL) for method B were transferred into a series of 150 mL separating funnels, 2 mL of 0.2% BTB (method A) or 2 mL of 0.1% MO (method B) solutions were added to each separating funnel and the total volume of the aqueous phase was made up to 10 mL with distilled water. 10 mL of chloroform was added and the contents were shaken for 2 min. The two phases were allowed to separate and the absorbance of the chloroform layer was measured at 415 nm for method A and 426 nm for method B against a reagent blank. The amount of CP from formulations was computed from its respective calibration curve.

The optical characteristics such as absorption maxima, Beer's law limits, molar absorptivity and Sandell's sensitivity are presentated in Table-1. The per cent relative standard deviation and per cent range of error (0.05 level confidence limit) calculated from the eight measurements containing 3/4 amount of upper Beer's law limit of CP are given in Table-1. The stoichiometric relationship of drug : dye in each case obtained by slope analysis method is given in Table-1. The results showed that the methods have reasonable precision; a comparison of the results obtained with the proposed and reference methods for dosage forms (Table-2) confirms the suitability of these methods for the pharmaceutical dosage forms. The other active ingredients and excipients usually present in pharmaceutical dosage forms did not interfere.

TABLE-1
OPTICAL CHARACTERISTICS AND PRECISION

| Parameters | Method A | Method B |
|---|---|---|
| $\lambda_{max}$ (nm) | 415 | 426 |
| Beer's law limits (μg/mL) | 5–35 | 2–16 |
| Sandell's sensitivity (μg/cm$^2$/0.001 absorbance unit) | 0.0577 | 0.0139 |
| Molar extinction coefficient (L mole$^{-1}$ cm$^{-1}$) | $5.683 \times 10^4$ | $2.35 \times 10^4$ |
| % Relative standard deviation** | 1.4727 | 1.3496 |
| % Range of error, 0.05 confidence limits | ± 0.9067 | ± 0.853 |
| Correlation coefficient | ± 0.9994 | ± 0.9865 |
| Mole ratio (drug : dye) | 1 : 1 | 1 : 1 |

**Calculated from eight replicate samples.

The proposed methods are found to be simple, rapid, sensitive and accurate and can be used for the determination of CP and their pharmaceutical dosage forms in a routine manner.

TABLE-2
ESTIMATION OF CYCLOPENTOLATE HYDROCHLORIDE BY THE PROPOSED METHODS

| Formulations (Eye drops) | Labeled amount (mg/5 mL) | Amount obtained (mg) | | | Percent recovery* | |
|---|---|---|---|---|---|---|
| | | Proposed methods | | Reported method[3] | Method A[a] | Method B[a] |
| | | Method A | Method B | | Mean ± SD | Mean ± SD |
| Brand I | 50 | 50.01 | 50.02 | 49.60 | 100.2 ± 0.8 | 100.1 ± 1.2 |
| Brand II | 50 | 50.05 | 49.90 | 49.81 | 99.8 ± 0.3 | 100.1 ± 0.4 |

*Average of four determinations, a = amount added 10 mg.

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