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# Assay of Lacidipine in Tablets by Extraction Spectrophotometry

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**Three simple spectrophotometric methods for the analysis of lacidipine in pure form or in tablets have been developed based on the formation of chloroform soluble ion associates under specific experimental conditions. Three acidic dyes, tropaeolin 000 (method A), bromocresol green (method B) and azocarmine G (method C) were utilized. The extracts of ion associates exhibited absorption maxima at 420, 500 and 540 nm for methods A, B and C, respectively. Good agreement with Beer's law was found in the range of 10–60 μg/ml (method A), 10-60 μg/ml (method B) and 10-70 μg/ml (method C). These methods are simple, precise and accurate with excellent recovery of 98–102% and also do not require any separation of soluble excipients in tablets. The results obtained are reproducible with coefficient of variation of less than 1.0%.**

Lacidipine (LCD), 4-[2-(3-(1,1-dimethyl ethoxy)-3-oxo-1-propenyl phenyl)]-1,4-dihydro-2,6-dimethyl-3,5-pyridine dicarboxylic acid diethyl ester is a dihydropyridine derivative useful in the treatment of hypertension. Lacidipine is official in Martindale Extra Pharmacopoeia[1]. Literature cites only High Performance Liquid Chromatographic methods[2-5] and a spectrophotometric method[6] for its estimation in dosage forms. The reported spectrophotometric method is based on oxidative coupling reaction of the drug with 3-methyl-2-benzothiazolinone hydrazone (MBTH). This method suffers from low sensitivity and low lmax. The method involves the use of MBTH, which is an expensive reagent. Moreover, the analytically useful functional groups in LCD like ester group and vinyl imino group has not been fully exploited for the development of new analytical useful methods. Hence the need for a fast, low cost and selective methods are obvious especially for routine quality control analysis of pharmaceutical products containing LCD. As the extraction spectrophotometric procedures are popular for their sensitivity and selectivity in the assay of drugs[7,8], this technique was therefore utilized in the present work for the estimation of LCD. The present paper describes three simple extraction spectrophotometric methods for the determination of LCD, based on its tendency to form chloroform extractable ion-association complexes with acidic dyes belonging to different chemical classes viz., tropaeolin 000 (TP 000, Mono azo), bromocresol green (BCG, triphenyl methane) and azocarmine G (AG, azine) under specified experimental conditions by exploiting the basic nature of the drug molecule.

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An Elico SL 171 spectrophotometer with 1 cm matched quartz cells was used in the present study. All reagents used were of analytical grade and solutions were prepared in distilled water. Aqueous solutions of TP 000 (0.02%), BCG

(0.1%) and AG (0.2%) were prepared. Potassium acid phthalate buffer solution (pH 3.5) for method B and glycine HCl buffer solution (pH 1.5) for method C were prepared.

A standard solution containing 1 mg/ml of LCD was prepared in methanol by dissolving 100 mg of pure LCD in 100 ml of methanol. From this solution, working standard solutions were prepared by dilution with methanol. This solution was further diluted with methanol to give a working standard solution of a concentration of 100 μg/ml. Twenty five tablets were weighed accurately and powdered thoroughly. Weight of the powder equivalent to 100 mg of LCD was transferred to a container, dissolved in methanol and the resulting solution was filtered. More amount of methanol was passed through the filter paper containing the tablet powder and the volume was finally made up to 100 ml with methanol. Ten millilitres of this solution was diluted to 100 ml with methanol and 1 ml of the resulting solution was used for colour development by the method described above. The concentration of drug corresponding to the absorbance values was found from the calibration curve and the content of LCD in tablets was calculated using the dilution factor.

Into a series of 60 ml separating funnels, aliquots of standard drug solution (0.1–0.8 ml) were pippetted out. To each separating funnel (methods B and C) 1 ml of buffer solution and for all methods 2 ml of dye solution was added. The aqueous phase was made up to 10 ml with distilled water. To each separating funnel, 10 ml of chloroform was added to extract the ion pair complex. The contents were shaken for 2 min and allowed to stand for clear separation of two layers and the absorbance of the chloroform layer was measured against reagent blank at the respective absorption maxima. The absorbances were measured at 420 nm for method A, 500 nm for method B and 540 nm for method C. In each case, absorbance values were plotted against the corresponding concentration of the drug in μg/ml and calibration curves were drawn. The amount of LCD present was calculated from calibration graphs. The stability period for all the three methods is 5 min–5 h.

Optimum operating conditions used in the procedures were established adopting variation of one variable at a time (OVAT) method. The optical characteristics of the methods are presented in Table 1. The precision and accuracy of the methods were tested by measuring six replicate samples of the drug in Beer's law limits. Commercial formulations containing LCD were successfully analyzed by the proposed methods. The results are presented in Table 2. None of the usual excipients employed in the formulation of dosage forms

TABLE 1: OPTICAL CHARACTERISTICS AND PRECISION OF THE PROPOSED METHODS

| Parameter | Method A | Method B | Method C |
|---|---|---|---|
| λmax (nm) | 420 | 500 | 540 |
| Beer's law Limit (μg/ml) | 10 – 60 | 10-60 | 10-70 |
| Molar absorptivity (l/mol.cm) | $1.77x10^4$ | $8.26x\ 0^3$ | $7.10x10^4$ |
| Sandell's sensitivity (mg/cm²per 0.001 absorbance unit) | 0.041 | 0.020 | 0.026 |
| Regression equation (y=a+bC)* | | | |
| Slope (b) | $2.50x10^{-2}$ | $0.7x10^{-2}$ | $4.49x10^{-2}$ |
| Intercept (a) | $4.31x10^{-3}$ | $5.8x10^{-3}$ | $-1.60x10^{-3}$ |
| Correlation coefficient (r) | 0.9999 | 0.9998 | 0.9998 |
| Relative standard deviation (%)** | 0.48 | 0.34 | 0.31 |
| % Range of error (confidence limits)** | | | |
| 0.05 level | 0.31 | 0.31 | 0.20 |
| 0.01 level | 0.50 | 0.37 | 0.21 |
| % Error in bulk samples*** | 0.30 | 0.28 | 0.23 |

*Y=a+bC, where C is concentration of analyte and Y is absorbance unit. **average of six determinations, ***average of three determinations.

TABLE 2: ASSAY OF LCD IN PHARMACEUTICAL FORMULATIONS

| Drug | Label Claim mg/tablet | Amount found by Proposed Methods (mg) | Amount found by the reference method[6] | % Recovery by proposed Methods** |
|---|---|---|---|---|
| Tablet 1 | 4 | 3.95 | 3.94 | 99.92±0.08 |
| Tablet 2 | 4 | 3.96 | 3.95 | 99.85±0.15 |

Tablet 1 is lucivas, 2 mg and tablet 2 is lucivas 4 mg from Sun Pharmaceuticals Ltd, Mumbai. **Recovery of 10 mg added to the pre-analyzed tablets (average of 3 determinations).

interfered in the analysis of LCD by the proposed methods. As an additional check of accuracy, recovery experiments were performed by standard addition method. When tablets containing LCD were analyzed, the results obtained by the proposed methods were in good agreement with the labeled amounts. The recovery with the methods was found to be 99–101%. The proposed methods are simple, convenient, accurate, sensitive and reproducible. The proposed methods are applicable for the assay of LCD and have the advantage of wider range. The order of sensitivity among the proposed methods and reference method (R) in the determination of LCD is C>B>A>R and the λmax order is C>B>R>A. The λmax of the proposed methods were considerably higher than reference method. The higher λmax of the proposed methods is a decisive advantage since the interference form the associated ingredients shall be far less at higher wavelengths. As the formation of coloured species differ from one another in the proposed methods depending on the chromogenic reagents, the appropriate method can be used for the assay of LCD in bulk form and tablets with good precision and accuracy depending on the availability of chemicals, needs of specific situations and nature of concomitants present in the sample under analysis.


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