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VISIBLE SPECTROPHOTOMETRIC METHODS FOR THE DETERMINATION OF LACIDIPINE IN PHARMACEUTICAL FORMULATIONS THROUGH SCHIFF'S BASE FORMATION

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ABSTRACT

Three simple spectrophotometic methods for the analysis of Lacidipine in pure form or in pharmaceutical formulations have been developed based on the reaction of the drug with aromatic aldehydes, p–dimethylamino benzaldehyde (PDAB), p–dimethylamino cinnamaldehyde (PDAC) and vanillin in acidic medium producing coloured Schiff's bases having λ_{max} at 415, 420 and 520 nm, respectively. Good agreement with Beer's law was found in the range of 80– 400 µg/mL (Method A), 50–200 µg/mL (Method B) and 40–160 µg/mL (Method C). The methods are simple, precise and accurate with excellent recovery of 98–102% and also does not require any separation of soluble excipients in pharmaecutical preparations. The results obtained are reproducible with coefficient of variation of less than 1.0%.

Key words : Spectrophotometric method; Lacipidine; Schiff's base, Pharmaceutical formulations

INTRODUCTION

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 offical in Martindale Extra Pharmacopoeia[1]. Literature cites only High Performance Liquid Chromatographic methods[2,3,4,5] and a spectrophotometric method[6] for its estimation in dosage forms. The reported spectrophotometric mehod is based on oxidative coupling reaction of the drug with 3–methyl–2–benothiazolinone hydrazone (MBTH). This method suffers from low sensitivity and low λ_{max}. The method involves the use of MBTH, which is a costly reagent. More over, the analytically useful functional groups in LCD like ester group and vinyl imino group have not been fully exploited for the development of new analytical useful methods. Hence in this paper, the authors report three simple, sensitive and reproducible spectrophotometric methods for the

determination of LCD in pure form as well as in pharmaceutical formulations using aromatic aldehydes namely PDAB, PDAC and vanillin. It is well known that aldehydes form coloured condensation Schiff's bases with primary amines in particular. This famous reaction has been used as a basis for development of three simple methods based on visible spectrophotometry for the estimation of LCD in pharmaceutical formulations.

EXPERIMENTAL

Instrument and Reagents : An Elico SL 171 spectrophotometer with 1 cm matched quartz cells was used in the present study. All reagents used were of analytical grade. PDAB (BDH, 0.4%), PDAC (BDH, 0.4%) and Vanillin (CDH, 0.3%) were prepared by dissolving specified quantities of the reagents in 100 mL of chloroform. Concentrated sulfuric acid and methanol were obtained from Qualigens and were used as such. The reagents were freshly prepared and used. LCD formulations were obtained from local market.

Preparation of Standard Drug Solutions : 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. For Method A– 800 µg/mL, Method B–500 µg/mL and Method C– 00 µg/mL.

Preparation of Sample Drug Solutions : Two brands of commercial tablets of LCD were analyzed by the proposed methods. 10 tablets were accurately weighed and powdered and tablet powder equivalent to 100 mg of LCD was treated with sufficient quantity of methanol and diluted to 100 mL with the same solvent and filtered. The filtrate was suitably diluted and analyzed as given under the assay procedure for bulk samples.

Assay Procedure : Aliquots of standard drug solution (1.0–5.0 mL, 800 µg/mL for method A; 1.0–4.0 ml, 500 µg/mL, method B and 1.0–4.0 mL, 400µg/mL, method C) were transferred into a series of 10 mL volumetric flasks. Then 3 mL of PDAB (Method A), PDAC (Method B) and Vanillin (Method C) were added to respective volumetric flasks. 3 mL concentrated sulfuric acid as added in all the methods and the total volume in each flask was brought to 7 mL with methanol and the flasks were placed in hot water bath for 10 min. The flasks were cooled to room temperature and volume in each flask was made up to 10 mL with methanol and after 15 min, absorbances were measured at 415 nm (Method A), 420 nm (Method B) and 520 nm (Method C) against a reagent blank. The concentrations of LCD present in sample solutions were computed from calibration curves.

RESULTS AND DISCUSSION

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 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 interfere in the analysis of LCD by the proposed methods. As an additional check of accuracy, recovery experiments were performed by standard addition method. When pharmaceutical preparations (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%.

Table 1. Optical characteristics and precision of the proposed methods

Parameter	Method A	Method B	Method C
λ_{max} (nm)	415	420	520
Beer's law Limit (μg/mL)	80–400	50–200	40–160
Molar absorptivity (L mol^{-1} cm^{-1})	1.04×10^4	8.10×10^4	3.92×10^4
Sandell's sensitivity (mg cm^{-2} per 0.001 absorbance unit)	0.0480	0.010	0.027
Regression equation ($y = a + bC$)* Slope (b)	1.52×10^{-2}	1.0×10^{-2}	1.8×10^{-3}
Intercept (a)	3.2×10^{-3}	4.0×10^{-3}	3.1×10^{-2}
Correlation coefficient (r)	0.9992	0.9998	0.9999
Relative standard deviation (%)**	0.402	0.781	0.301
% Range of error (confidence limits)**	0.318	0.312	0.301
0.05 level	0.512	0.418	0.202
0.01 level	0.59	0.42	0.21
% Error in bulk samples***			

*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 method (mg)	% Recovery by proposed method**
Tablet 1	4	3.95	99.92
Tablet 2	4	3.96	99.85

*Drug from different pharmaceutical companies; ** Recovery of 10 mg added to the pre–analyzed pharmaceutical dosage forms (average of 3 determinations).

The aromatic aldehydes have lead to numerous applications as analytical reagents, PDAB (p–dimethylamino benzaldehyde) allows the determination of trace amounts of hydrazine[7]. Aldehydes were applied to the colorimetric determination of primary alkylamines[8] and primary

aromatic amines in acidic medium. The condensation of indole derivatives in acidic medium gives the coloured product[9].

CONCLUSION

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 decreasing order of sensitivity of the methods is $M_3 > M_2 > M_1$ and the increasing order of λ_{max} among the proposed methods is $M_1 > M_2 > M_3$. 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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