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VISIBLE SPECTROPHOTOMETRIC DETERMINATION OF LACIDIPINE IN ITS PHARMACEUTICAL DOSAGE FORMULATIONS

G. VIDYA SAGAR*[1]., B. S. SASTRY [2] and N.V.S.GANGADHARA RAO[3]

[1]Department of Pharmaceutical Analysis and Quality Assurance, Bapatla College of Pharmacy, Bapatla – 522 101. Guntur Dist. (A.P.) INDIA

[2]Division of Pharmaceutical Chemistry, Department of Pharmaceutical Sciences, Andhra University, Vishakapatnam – 530 003. (A.P.) INDIA

[3]Quality Control and Assurance, Triveni Pharma Laboratories, Hanumanpet, Vijayawada – 520 003 (A.P.) INDIA

ABSTRACT

Two simple and sensitive spectrophotometric methods in the visible region are developed for the estimation of lacidipine in its dosage forms. In method A, lacidipine reacts with sodium nitroprusside and hydroxylamine hydrochloride in alkaline medium to produce a yellow colored chromogen having λ_{max} at 440 nm. Beer's law is obeyed in the concentration range of 15–75 µg/mL. In method B, lacidipine reacts with chloranil and acetaldehyde to give a dark bluish violet colored chromogen having λ_{max} at 640 nm. Linearity is 10–60 µg/mL. The reproducibility of the methods is 99.2% – 99.9%. Commercial dosage forms of the drug have been evaluated by the proposed methods and found satisfactory.

Key words: Spectrophotometry, Lacidipine, Sodium nitroprusside, Chloranil, Tablets.

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, which is useful in the treatment of hypertension. Lacidipine is official in Martindale Extra Pharmacopoeia[1]. Literature cites only high performance liquid chromatographic (HPLC) methods[2,3,4,5] 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 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, cyclic secondary amine and presence of double bond have not been fully exploited for the development of new analytical useful methods. Hence this accord resulted in the development of two simple spectrophotometric methods for estimation of LCD in its formulations.

EXPERIMENTAL

Instrument: An Elico SL 171 visible spectrometer.

Reagents

Method A

1. Working standard drug solution 150 µg/mL in methanol: 100 mg of lacidipine is dissolved in 100 mL of methanol in a 100 mL calibrated flask to get 1mg/mL solution. This solution is further diluted step wise with methanol to get a solution of 150 µg/mL.
2. Sodium nitroprusside (E.merck, 0.4%) prepared by dissolving 400 mg of SNP in 100 mL distilled water.
3. Hydroxylamine hydrochloride (Fluka, 0.4%) prepared by dissolving 400 mg of the reagent in 100 mL of distilled water.
4. Sodium carbonate solution (Loba, 10%w/v) prepared by dissolving 10 g of sodium carbonate in 100 mL of distilled water.
5. Sample preparation: 10 tablets of each formulation T_1, T_2 and T_3 containing 4 mg of LCD were accurately weighed and powdered. Weight of tablet powder equivalent to 40 mg of drug was taken in 20 mL of methanol and shaken for 15 min and filtered through Whatmann filtered paper and 20 mL of methanol was added to get a solution of 1mg/mL. This solution was further diluted step wise with methanol as given in the working standard drug solution and amount of drug was estimated under the given assay procedure.

Method B

1. Working standard drug solution 100 µg/mL in methanol: Standard stock solution of 1 mg/mL of LCD in methanol was prepared and it was further diluted with methanol to get a working standard drug solution of 100 µg/mL.
2. A 2% solution of acetaldehyde in 1,4–dioxane.
3. A 1% solution of chloranil in 1,4–dioxane.
4. Sample preparation: 10 tablets of each formulation T_1, T_2 and T_3 containing 4 mg of LCD were accurately weighed and powdered. Weight of tablet powder equivalent to 40 mg of drug was taken in 20 mL of methanol and shaken for 15 min and filtered through Whatmann filtered paper and 20 mL of methanol was added to get a solution of 1 mg/mL. This solution was further diluted step wise with methanol as given in the working standard drug solution and amount of drug was estimated under the given assay procedure.

Assay Procedure

Method A : Aliquots of standard LCD solution (1–5 mL, 150 µg/mL) were transferred into a series of 10 mL volumetric flasks. Then 1 mL of SNP reagent and 1 mL of hydroxylamine

hydrochloride were added successively and kept aside for 5 min. Then 1 mL of Na_2CO_3 solution was added and shaken for 15 min. The volume was made upto the mark with methanol. The absorbance was measured after 10 min at 440 nm against a similar reagent blank. 1 mL of each sample preparation of T_1, T_2 and T_3 were taken into 10 mL volumetric flasks and the above procedure was subsequently followed.

Method B : Aliquots of standard LCD solution (1–6 mL, 100 µg/mL) were transferred into a series of 10 mL volumetric flasks. Then 1 mL of chloranil and 1 mL of acetaldehyde were added and the flasks were kept aside for 5 min at room temperature and diluted to 10 mL with methanol and the absorbances were measured at 640 nm. 1mL of each sample preparation of T_1, T_2 and T_3 were taken into 10 mL volumetric flasks and the above procedure was subsequently followed.

Chemistry of Colored Species

Method A : Sodium nitroprusside (SNP) is known as disodium pentacyanonitrosylferrate (II) dihydrate[7], sodium nitro ferric cyanide or sodium nitroprussate. Aqueous solution of nitroprusside reacts with a wide variety of inorganic and organic substances to form usually highly coloured reaction products[8,9]. The coloration obtained with SNP under different experimental conditions may be due to the formation of ferric ferricyanide (orange yellow) or $[Fe(CN_5M]^{3-}$, where M was the drug exhibiting liganding properties[10].

Method B : The N–alkyl vinyl amine obtained by condensing the drug with acetaldehyde reacts with chloranil to give a vinyl amino–substituted quinone, which is violet in colour.

RESULTS AND DISCUSSION

The optimum conditions were established by varying one parameter at a time and keeping the other fixed by observing the effect produced on the absorbance of the colored species. The various parameters involved in the color development like, the concentration of the various reagents and time involved for maximum color development were optimised. The optical characteristics and figures of merit are given in Table 1, together with regression equations (obtained by linear least square treatment) for the calibration plots. The precision and accuracy were found by analyzing six replicate samples containing known amount of drug and the results are summarized in Table 1. Some commercially available dosage forms of LCD are analysed by both the methods and the results obtained are given in Table 2. As an additional check on the accuracy of the methods, recovery experiments were performed by adding known amounts of pure drug to preanalysed dosage forms and percent recovery values obtained are listed in Table 2. Recovery experiments indicated the absence of interference from the commonly encountered pharameceutical additives and excipients. The proposed methods can be employed for the routine determination of lacidipine in bulk sample and pharmaceutical formulations.

Table 1. Optical characteristics and precision of the proposed methods.

Parameter	Method A	Method B
λ_{max} (nm)	440	640
Beer's law Limit (µg/ mL)	15–75	10–60
Molar absorptivity ($Lmol^{-1} cm^{-1}$)	3.92×10^4	8.14×10^4
Sandell's sensitivity ($mg\ cm^{-2}$ per 0.001 absorbance unit)	0.010	0.0480
Regression equation (y = a + bC)* Slope (b)	0.035	0.010
Intercept (a)	0.0018	0.0015
Correlation coefficient (r)	0.9999	0.9998
Relative standard deviation (%)**	0.31	0.71
% Range of error (confidence limits – 95%)**	0.139	0.653

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

Table 2. Assay of LCD in pharmaceutical formulations by the proposed methods

Drug*	Label Claim mg/tablet	Amount found by Proposed Methods ** (mg)		Reference Method[6] (mg)	% Recovery by proposed methods ***	
		Method A	Method B		Method A	Method B
Tablet	4	3.90	3.90	3.9	99.08±0.12	99.09±0.10
Tablet	4	3.91	3.92	3.9	99.09±0.18	99.09±0.19
Tablet	4	3.90	3.80	3.9	99.08±0.12	99.09±0.13

* Drugs from different pharmaceutical companies; ** Average ± Standard deviation of 6 determinations; *** Recovery of 10 mg added to the preanalysed pharmaceutical dosage forms (average of 3 determinations).

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