INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Research Article

Development And Validation Of RP- HPLC Method For Estimation Of Lercanidipine HCL In Bulk Drug And Dosage Form

Chandrashekhar. B. Palve*, Pratiksha.M. Jadhav, Hitesh More, Smita s. Aher

R. G. Sapkal College Of Pharmacy

ARTICLE INFO

Received: 20 Aug 2024
Accepted: 24 Aug 2024
Published: 26 Aug 2024
Keywords:
Drug discovery, Extracellular matrix, Fibrosis, Inflammation, TGF-β.
DOI:
10.5281/zenodo.13372194

ABSTRACT

A simple, precise, reliable, rapid and reproducible reversed-phase high performance liquid chromatography method was developed and validated for the simultaneous estimation of Atenolol (ATL) and Lercanidipine Hydrochloride (LER) present in tablet dosage forms. Chromatographic separation achieved isocratically on Luna C18 column (5 µm, 150mm x 4.60mm) and ACN/phosphate buffer (60:40, v/v, pH 3.6) as mobile phase, at a flow rate of 0.5ml/min. Detection was carried out at 235 nm. An effective chromatographic separation was achieved using waters symmetry C18 column of dimensions 150x4.6 mm, 3.5 µm, as a stationary phase. 0.1 percent ortho phosphoric acid and acetonitrile in 50:50 v/v was used as a mobile process with a rate of flow 1 ml/min and UV detection was carried out at 230 nm, respectively. Isocratic chromatography at ambient temperature was performed.

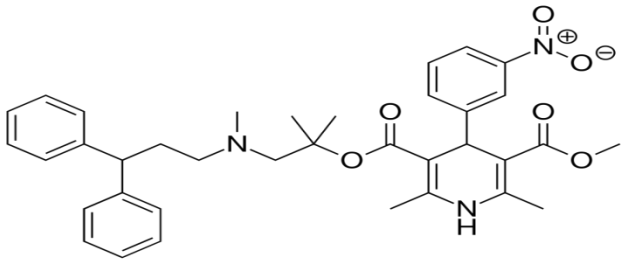
INTRODUCTION

Lercanidipine, 5 O (1 [3,3 diphenylpropyl(methyl)amino] 2 methylpropan 2 yl) 3 O methyl 2,6 dimethyl 4 (3 nitrophenyl) l, 4 dihydropyridine 3,5 dicarboxylate is a dihydropyridine calcium antagonist [Figure 1]. It is used for the management of Stage I and Stage II hypertension and is also perhaps useful in relieving angina pectoris.[1,2] Lercanidipine HCl is soluble in dimethylformamide, dichloromethane, and methanol.[3] It has a pKa value of about 6.83.[4] It is extremely lipophilic, possess octanol: water partition coefficient (Log P) value of about 6.4.[1] Preclinical and clinical findings propose that lercanidipine may have protective effects on the kidneys, cardiovascular system, and target organs. Lercanidipine (10 mg/day) produces a smooth antihypertensive effect without unfavorable hemodynamic or sympathetic effects due to its vascular selectivity. Lercanidipine emerged as a flexible choice for antihypertensive treatment across a wide range of patients due to its favorable efficacy and safety profile. Lercanidipine attains maximum plasma concentration within 2–3 h after oral

***Corresponding Author:** Chandrashekhar. B. Palve
Address: *R. G. Sapkal College Of Pharmacy*
Email : sachinpalve8603@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

administration and exhibits a slow onset of action. However, it is extensively metabolized by cytochrome P450 3A4.[5] Its low water solubility (5 µg/ml), poor permeability, extensive first pass metabolism, and food dependent absorption result in its low bioavailability of 10%.[2]



Chemical structures of lercanidipine HCl

MATERIALS AND METHODS Chemicals

Lercanidipine HCl hemihydrate obtained as gift sample from Lupin Limited, Research Park, Pune. HPLC grade methanol and acetonitrile were obtained from Finar Chemicals, Gujarat (India). All the surfactants and/or polymers were procured from Loba Chemie Ltd. Mumbai and Sigma Aldrich Bengaluru, India

Instrumentation

Instrumentation Liquid chromatographic system from Shimadzu (LC20AT) comprising of manual injector, double reciprocating plunger pump LC-20ATVp for constant flow and constant pressure delivery and Photodiodearray detector SPD-M20A connected to software LC solution for controlling the instrumentation as well as processing the data generated was used.

Method validation

The developed method was validated for the parameters such as accuracy, precision, repeatability, intermediate precision, specificity, LOD, LOQ, linearity, range, system suitability, and robustness as described below.

Linearity

The linearity of an analytical method is its capability to obtain a test result, which has a certain mathematical relationship to the concentration of analytes. A standard solution of lercanidipine HCl (500 µg/mL) was prepared by dissolving

Reagents and chemicals

Analytically pure sample of LER was kindly supplied by Glenmark Pharmaceuticals Ltd. (Nashik, India). Acetonitrile, Potassium dihydrogen phosphate, Disodium hydrogen phosphate was of HPLC grade supplied by Merck Ltd., India. The pharmaceutical dosage form used in this study was a Lotensyl AT (Sun Pharmaceuticals Industries Ltd. Mumbai) tablets containing 50 mg 10 mg lercanidipine hydrochloride were obtained from the local drug market. Triple distilled water was generated in house.

Chromatographic condition

The isocratic mobile phase consisted of ACN/phosphate buffer (pH 3.6) in the ratio of (60:40 v/v), flowing through the column at a constant flow rate of 0.5 ml/ min. A Luna C18 column (5 µm, 150mm x 4.60mm) was used as the stationary phase. Although the LER have different λmax viz 224, 275 and 238, 358 nm respectively, but considering the chromatographic parameter, sensitivity and selectivity of method for two drugs, 235 nm was selected as the detection wavelength for UV-PDA detector.

Diluent

Mobile phase

Preparation of standard solution

Standard stock solution of Lercanidipine HCl was prepared by appropriately estimating about 10 mg drug 100 ml volumetric flask. Then the drug was liquified insolvent and filter through a 0.45µ filter. Standard stock solution concentrations of 100µg/ml and 500µg/ml were obtained.

Preparation of the solution for samples

Ten lercanidipine HCl tablets were accurately weighed and triturated to get a fine powder. A 10 mg Lercanidipine HCl equivalent weight tablet powder was transferred into a 100 ml volumetric flask and dissolved in the diluent. The solution was

RESULTS AND DISCUSSION

Chromatography The mobile phase was chosen after several trials with methanol, isopropyl alcohol, acetonitrile, water and buffer solutions in various proportions and at different pH values. A mobile phase consisting of acetonitrile/phosphate buffer (60:40, v/v, pH 3.6) was selected to achieve maximum separation and sensitivity. Flow rates between 0.5 and 1.5/min were studied. A flow rate of 0.5 ml/min gave an optimal signal to noise ratio with a reasonable separation time. Using a reversed-phase C18 column, the retention times for Lercanidipine Hydrochloride were observed to be 2.27 and 5.97 min respectively. Total time of analysis was less than 6 min. The maximum absorption of Lercanidipine Hydrochloride together as detected at 235 nm and this wavelength was chosen for the analysis (Figure 2).

System suitability

System suitability parameters such as number of theoretical plates, HETP and peak tailing are determined. The results obtained are shown in Table-1. The number of theoretical plates for LER were 7023 respectively.

Linearity

LER showed a linearity of response between 50-250 and 10-50µg/ml respectively. The linearity was represented by a linear regression equation as follows. Y (LER)= 90997 conc. - 6978 (r2 =0.9999)

Accuracy

Accuracy of the method was calculated by recovery studies at three levels by standard addition method Table-2. The mean percentage recoveries obtained for Lercanidipine Hydrochloride were 99.47±0.32%, respectively

Table-1 System suitability parameters

Parameter	Lercanidipine HCl
Retention time*	5.97±0.04
No. of theoretical plate*	7023.33±54.00
Tailing factor*	1.26±0.01
HETP*	0.04±0.00
Linearity range	10-50-mg/ml

Each value is the Mean ± S.D of six determinations

Table-2 Result of recovery studies with statically evaluation

Serial. No.	Conc. of drug in preanalyzed samples (mg/ml	Std. drug sol. Added (mg/ml)	Recovered amount* (mg/ml)		% Recovered
	LER	LER	LER		LER
	10	10	9.89		99.100
	20	20	19.82		99.683
			Mean %R.S.D	99.857	99.472
				0.160	0.325

Mean of Nine determinations (3 replicates at 3 concentration level)

Repeatability

Five dilutions in three replicates were analyzed in same day for repeatability and results were found within acceptable limits (RSD ‹ 2) as shown in Table3.

Intermediate Precision

Five dilutions in three replicates were analyzed on two different days and by two analysts for day to day and analyst to analyst variation and results were found within acceptable limits (RSD ‹ 2)

. **Robustness**

As per ICH norms, small, but deliberate variations, by altering the pH or concentration of the mobile phasewere made to check the method's capacity to remain unaffected. The change was made in the ratio of mobile phase, instead of acetonitrile:

phosphate buffer (pH 3.6) (60:40v/v), acetonitrile: phosphate buffer (pH 3.6) (55:45 v/v), was used as a mobile phase. Results of analysis were summarized in Table- 4.

Tablet Analysis

Content of LER found in the tablets by the proposed method are shown in Table-5. The low values of R.S.D. indicate that the method is precise and accurate

Table-3 Result of precision

Validation Parameter	Percentage Mean ± S.D*. (n=15)	Percentage RSD*
	LER	LER
Repeatability Intermediate precision	99.66±0.084	0.310
Day to Day	99.90±0.095	0.404
Analyst to Analyst	99.43±0.088	0.381

Mean of six determinations

Table-4 Results of robustness

Serial. No.	Validation Parameter	% Mean*	S.D	% R.S.D.
		LER	LER	LER
1	Robustness	99.41	0.119	0.573

Tablet-5 Result of marketed tablet analysis

Parameter	Lotensyl AT
	LER
Mean % estimated	99.05
Standard deviation(S.D.)	0.56
% Coefficient of variation	0.57
*Standard error (SEσ)	0.13

* Mean of fifteen determinations (3 replicates at 5 concentration level)

CONCLUSION

RP-HPLC method was developed and validated for simultaneous estimation of lercanidipine hydrochloride in tablet dosage form. The developed method is suitable for the identification and quantification of binary combination of lercanidipine hydrochloride. A high percentage of recovery shows that the method can be successfully used on a routine basis. Proposed method is simple, fast, accurate, precise and sensitive and could be applied for quality and stability monitoring of lercanidipine hydrochloride combination.

REFERENCES

1. US Pharmacopoeia, US Pharmacopeial Convention, 2005, 28,193.
2. Indian Pharmacopoeia, Government of India, Ministry of Health and Family Welfare, Delhi, 1996, 1, 72.
3. British Pharmacopoeia, International edn, HMSO, Cambridge, 2004, 1,179.
4. Budavari S, Maryadele J and Smith A, The Merck Index, Merk & Co., Inc. Ruchway: U.S.A.1989, 973.
5. Reynolds F E J, Martindale The extra Pharmacopoeia, The Pharmaceutical Press, London, 1999.
6. CIMS-101, Sri Sudhindra Printing Press, 8th Cross, Malleshwaram: Bangalore-03, India. 2008, 100.
7. Argekar A P and Powar S G, J Pharm Biomed Anal., 2000, 21, 1137–1142.
8. Sivakumar T, Venkatesan R and Valliappan K, Indian. J. Pharm. Sci., 2007, 69, 154-7.

9. Available from: http://www.pubchem.ncbi.nlm.nih.gov/compound/ Lercanidipine#section=Top. [Last accessed on 2015 Jun 10].
10. Abramowitz W, Kapil R, Riccobene TA, Dedhia M, Rastogi S, Chhettry A. Lercanidipine pH dependant pulsatile release composition US2006/0165788; July 2007.
11. More details were not available in Certificate of analysis obtained with lercandipine drug sample.
12. Testa R, Leonardi A, Tajana A, Riscassi E, Magliocca R, Sartani A, Lercanidipine: A Novel 1, 4 Dihydropyridine Calcium Antagonist for hypertension. Cardiovascular Drug Reviews 1997;15:187-219.
13. Borghi C. Lercanidipine in hypertension. Vasc Health Risk Manag 2005;1:173-82.
14. Alvarez-Lueje A, Pujol S, Squella JA, Núñez-Vergara LJ. A selective HPLC method for determination of lercanidipine in tablets. J Pharm Biomed Anal 2003;31:1-9.
15. Kaila HO, Ambasana MA, Thakkar RS, Saravaia HT, Shah AK. A Stability-indicating HPLC method for assay of lercanidipine hydrochloride in tablets and for determining content uniformity. Indian J Pharm Sci 2010;72:381-4.
16. Validation of analytical procedure; text and methodology Q2(R1), International conference on harmonization of technical requirements for registration of pharmaceuticals for human use. ICH harmonized tripartite guidelines. 2005.
17. Whelton PK, Williams B. The 2018 European Society of Cardiology/European Society of Hypertension and 2017 American College of Cardiology/American Heart Association Blood Pressure Guidelines: More Similar Than Different. JAMA. 2018;320(17):1749-50. doi: 10.1001/jama.2018.16755, PMID 30398611.
18. Parekh N, Page A, Ali K, Davies K, Rajkumar C. A practical approach to the pharmacological management of hypertension in older people. Ther Adv Drug Saf. 2017;8(4):117-32. doi: 19..1177/2042098616682721, PMID 28439398.
19. Tekol Y. The medieval physician Avicenna used an herbal calcium channel blocker, taxus baccata L. Phytother Res. 2007;21(7):701-2. doi: 10.1002/ptr.2173, PMID 17533639.
20. Sica DA. Calcium channel blocker-related peripheral Edema: Can It Be Resolved? J Clin Hypertens. 2003;5(4):291-5. doi: 10.1111/j.1524-6175.2003.02402.x.
21. Barrios V, Escobar C, Navarro A, Barrios L, Navarro-Cid J, Calderon A, Laura Investigators. Lercanidipine is an effective and well-tolerated antihypertensive drug regardless the cardiovascular risk profile: The LAURA study. Int J Clin Pract. 2006;60(11):1364-70. doi: 10.1111/j.1742-1241.2006.01176.x, PMID 17073834.
22. Banks K, Lo M, Khera A. Angina in women without obstructive coronary artery disease. Curr Cardiol Rev. 2010;6(1):71-81. doi: 10.2174/157340310790231608, PMID 21286281.
23. Vaccarino V. Ischemic heart disease in women: many questions, few facts. Circ Cardiovasc Qual Outcomes. 2010;3(2):111-5. doi: 10.1161/CIRCOUTCOMES.109.925313, PMID 20160161.
24. Kotecha D, Holmes J, Krum H, Altman DG, Manzano L, Cleland JG, Lip GY, Coats AJ, Andersson B, Kirchhof P, von Lueder TG, Wedel

HOW TO CITE: Chandrashekhar. B. Palve, Pratiksha.M. Jadhav, Hitesh More, Smita s. Aher, Development And Validation Of RP- HPLC Method For Estimation Of Lercanidipine HCL In Bulk Drug And Dosage Form, and Drug Development, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 8, 3855-3860. https://doi.org/10.5281/zenodo.13372194